



Via E-Mail: PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca

February 13, 2020

The Patented Medicine Prices Review Board
Standard Life Centre, Box L40
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Ottawa, ON,
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Dear Sir or Madam:

We at Bayer Inc. ("Bayer") would like to thank you for the opportunity to provide a written submission¹ in response to the Patented Medicine Prices Review Board ("PMPRB")'s draft guidelines, published on November 21, 2019 for consultation ("Draft Guidelines"). While we appreciate this opportunity, we have been disappointed with the quality of stakeholder consultation throughout the PMPRB Framework Modernization initiative (the "New PMPRB Framework"), which prompted amendments to the *Patented Medicines Regulations* (the "*Regulations*") and the associated Draft Guidelines. Despite the depth and breadth of all the proposals and input contributed by various stakeholders in response to the New PMPRB Framework, only superficial changes have been incorporated into the *Regulations* and Draft Guidelines. For instance, even though experts in the Technical Working Group convened by the PMPRB Steering Committee could not reach consensus on the application or appropriateness of new pricing factors to regulate drug pricing, these factors still play a prominent role in the Draft Guidelines.

Meaningful stakeholder consultation is important as the process of participative input provides legitimacy to the policy decisions taken. Indeed, the 2019 Prime Minister mandate letter to the Health Minister states, "It is also your responsibility to substantively engage with Canadians, civil society and stakeholders, including businesses of all sizes, organized labour, the broader public sector and the not-for-profit and charitable sectors. You must be proactive in ensuring that a broad array of voices provides you with advice, in both official languages, from every region of the country."² However, Bayer does not believe that the Health Minister has "substantively engaged" with the pharmaceutical industry to fully understand the impact that the New PMPRB Framework will have on Canadian investment and innovative therapies for Canadian patients. We note that patient groups such as the Canadian Organization for Rare Disorders, Diabetes Canada and Myeloma Canada among others, are also dissatisfied with the consultation process and expressed frustration at the PMPRB's lack of meaningful collaboration.^{3,4}



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¹ [This written submission reflects Bayer Inc.'s position in respect to select elements of the Draft Guidelines and should not be taken as Bayer's acceptance of the PMPRB's mandate and operations, including the New PMPRB Framework. Bayer Inc. is a named plaintiff in *Merck Canada Inc. et al v Canada \(Attorney General\)*, Quebec Superior Court file 500-17-109270-192.](#)

² <https://pm.gc.ca/eng/minister-health-mandate-letter>

³ <https://www.diabetes.ca/DiabetesCanadaWebsite/media/Advocacy-and-Policy/Submissions%20to%20Government/Federal/Diabetes-Canada-s-Letter-to-the-PMPRB-20-Feb-2019.pdf>

⁴ <https://www.raredisorders.ca/open-letter-to-prime-minister-justin-trudeau-regarding-pmprb-regulations/>

We sincerely hope that the input received by the PMPRB in this consultation is duly considered. While we acknowledge the importance of keeping health system costs sustainable, drug pricing regulations should not take away patient choice nor opportunities for improved medicines. We also highlight that it is unlikely that such issues can be resolved through a brief consultation period based primarily on written submissions.

Bayer aligned with Innovative Medicines Canada (“IMC”)

Bayer’s position is aligned with the written submission presented by IMC in respect of the Draft Guidelines. The IMC written submission provides a robust technical discussion of the Draft Guidelines and we ask that Bayer’s written submission be read in conjunction with the IMC written submission.

Bayer’s Written Submissions on Select Elements of the Draft Guidelines

Mr. Clark and Ms. Potashnik of the PMPRB often inform the pharmaceutical industry that the New PMPRB Framework will go forward but will require course corrections along the way.⁵ However, sustainability, predictability and fairness are requisite elements for the continued launch of innovative medicines in this country. These very elements are undermined by the Draft Guidelines and could impose significant damage to healthcare and investment in Canada. This damage could take years to repair. The PMPRB must consider the broader impact of the New PMPRB Framework to not just the drug pricing environment, but to Canadian access to innovative medicines. At the very least, the components of the Draft Guidelines, detailed below, must be amended to ensure continued access.

Timely access to innovative medicines requires predictability

During the initial consultation phase, the PMPRB stated that the three new price factors would provide ‘bright lines’ for patentees to determine compliance with the *Regulations* and associated guidelines: “Accordingly, to the extent possible, the framework envisaged by the PMPRB employs economically-derived, bright line tests to yield meaningful ceiling prices that are foreseeable to patentees”.⁶ To meet the standard for a ‘bright line’, both the test and the threshold for determination need to be understandable and predictable. In our view, the Draft Guidelines do not meet the standards of a “bright line” test.

For Canadian affiliates of global companies, having a predictable ceiling price is important for determining the global order of launch of a new medicine. Unacceptably low prices or undeterminable ceiling prices will risk significant delays in the launching of innovative drugs in Canada. With the adoption of international reference pricing (IRP) by many countries worldwide, drug launches have become sequential, whereby higher priced countries typically launch prior to lower priced ones. Canada can launch new drugs earlier than most other countries in the world due to the use of list prices in IRP. Indeed, the launch sequence of the 30 top-selling New Active Substances (NAS) showed that drugs were launched in Canada on average 9.4 months after the first country to launch worldwide – about half a year earlier than Italy and France, which respectively launched

⁵ Industry meeting with the PMPRB on December 9, 2019

⁶ <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1341&wbdisable=true>

14.8 and 15.4 months after the first country.⁷ Italy and France have the lowest prices for single-source patented medicines within the PMPRB.⁸ In addition, while Canada had launched all 30 of these NAS, Italy and France did not launch 3 and 8 of the NAS, respectively.⁹ The actual prices that Canadians pay through public formularies are substantially less than the list price. Thus, Canadians are currently able to access more innovative medicines relatively earlier compared to other countries, at list prices that are globally competitive and at net prices that are comparatively more affordable. Discounted net prices are negotiated with payers and thus deemed to be acceptable by the payers. The economic and affordability factors have already been incorporated into their negotiations so that PMPRB's use in price regulation are redundant.

Several countries, such as Brazil, Columbia and Mexico benchmark their drug prices to Canadian prices.¹⁰ Most pharmaceutical companies in Canada operate as small affiliates, with Canadian drug prices tightly controlled by the global parent company. The global organizations devote significant energy to mitigate potentially detrimental impacts of drug pricing policies between countries. Under the current PMPRB pricing framework, patentees can predict their compliance with the Guidelines with a relatively high degree of accuracy (See Table 1, which outlines the few factors required to estimate a price ceiling under the current Guidelines versus the many factors required to estimate a ceiling price under the Draft Guidelines).

⁷ http://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/NPDUIS_MedsEntryWatch_2015_e.pdf.

⁸ Form 2 Block 5 data submitted to PMPRB. Jul-December 2015. Innovative Medicines Canada members.

⁹ http://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/NPDUIS_MedsEntryWatch_2015_e.pdf.

¹⁰ Pricentric One database

Table 1. Unknown variables required to estimate ceiling prices of patented drug prices in Canada

Current Guidelines	Draft Guidelines
Comparator Medicines	Comparator Medicines
Dosage Regimen of Comparator Medicines	Dosage Regimen of Comparator Medicines
Highest International Price of new drug	-
Median International Price of new drug	Median International Price of new drug
Level of Therapeutic Improvement of new drug	-
	Median Price of domestic Therapeutic Class
	CADTH ICER & CADTH comparator utilized
	Peak unit sales forecast
	Median price of all international Therapeutic Class
	Prevalence of disease state (for rare drugs)
	Reassessment criteria for Non-Grandfathered drugs & Line Extensions
	Delayed timing & invoicing of Payer Rebates
	Estimating rebates by Payer to accurately determine Average Transaction Price
	PMPRB Non-Excessive Average Price of Comparator Medicines
	Lowest International Price of new drug

Clear and predictable guidelines provide pre-launch comfort to the affiliate and its global parent that the Canadian price will not be deemed excessive and will not negatively affect the prices in other jurisdictions. The Draft Guidelines greatly increase the complexity and unpredictability of ceiling prices, especially when these prices are based on variables that are in flux or out of the manufacturers' control until well after launch (e.g. CADTH's Incremental Cost Effectiveness Ratio (ICER), or selection of comparator drugs in the domestic and international therapeutic class [dTCC & iTCC]). This will effectively make it difficult for Canadian affiliates to obtain the necessary approvals to launch drugs ahead of countries that reference Canada.

Table 2 outlines some of these factors that lower the predictability of pricing for new drugs under the Draft Guidelines. The loss of this predictability will make it extremely difficult for any manufacturer to obtain the necessary approvals to launch an innovative drug ahead of countries that reference Canada.

Table 2. List of Draft Guideline components that add uncertainty to drug pricing

Draft Guideline Component	Description
Reference Country Price Sources	PMPRB indicated that no country price sources would be provided
Median of International Therapeutic Class Comparison (iTCC)	No clear guidance on which drugs would be included in Therapeutic Class; Lack of pricing sources and drug comparators of international markets limits ability of patentee to determine iTCC in advance
Median of Domestic Therapeutic Class Comparison (dTCC)	No clear guidance on which drugs would be included in Therapeutic Class; Reassessment of grandfathered products to lower of Median International price (MIP) & Non-Excessive Average Price (NEAP) on January 1, 2021 will impact MLP of non-grandfathered product launched after this date due to dTCC changing
Pharmacoeconomics	Patentee has no insight as to the CADTH (and INESSS) ICER prior to launch nor the comparator(s) used in the HTA evaluation; CADTH Therapeutic Reviews timing also unknown
Market Size Adjustment	Extraneous factors affecting market size (e.g. out of stock by competitor, competitors choosing not to launch)
Net Sales Reporting	Payer rebate invoicing could be delayed for years requiring patentee to estimate rebates which could significantly affect Average Transaction Price (ATP) reported to the PMPRB; receipt of rebate invoice in the future could require restatement of previous periods' ATP
Maximum Rebated Price (MRP)	MRP compliance cannot be achieved until Product Listing Agreements (PLA's) are signed with payers and could take years after initial sale
Reassessment	Triggers for reassessment unclear, especially with line extensions

The inability of the patentee to accurately estimate the Maximum List Price (MLP) and the Maximum Rebated Price (MRP) prior to launch poses a significant challenge for both the affiliate and the parent company. The most likely outcome is that with time, new drug launches in Canada will be delayed minimizing the IRP risk to countries that reference Canadian drug pricing. Even countries that do not currently reference Canadian drug prices will be motivated to do so as Canadian list prices decrease. This will exacerbate launch delays. It is important to stress that Canada only represents 2% of global pharmaceutical sales¹¹ and that Canadian market exclusivity is typically much shorter (seven to nine years in total length) than the US or Europe because of extensive regulatory

¹¹ https://www.ic.gc.ca/eic/site/lsg-pdsv.nsf/eng/h_hn01703.html

and payer coverage hurdles in Canada, and lack of sufficient patent term restoration.¹² Thus, it is easy for global organizations to hold back Canada's relatively small contribution to global pharmaceutical sales in order to mitigate the negative impact that Canadian drug pricing can have on other larger markets.

“Grandfathered” patented medications not really “grandfathered”

Patented medicines that received a Drug Identification Number (DIN) prior to August 21, 2019 are inaptly labelled as grandfathered as they still may be affected by the Draft Guidelines. These drugs have already been subjected to assessment and negotiation by multiple Canadian bodies and funding decisions based on value for money and affordability has already been made. Embroiling existing medications in the new pricing regime is unfair to patentees and patients because significant investments have already been made based on an existing price control framework.

Using the NEAP creates unfairness for “grandfathered” medicines

The MLP for grandfathered products is also contingent upon how patentees report their sales. While some manufacturers include all benefits, others may not which could result in a disparity of how NEAP is reported between patentees. This would penalize those patentees who choose to report all compassionate units in their semi-annual reporting to the PMPRB as the NEAP may be lower than their MIP. PMPRB's previous position was not to penalize patentees or create disincentives for patentees offering these benefits. We would recommend that the NEAP be eliminated from determining the MLP for grandfathered products to ensure fairness between patentees. NEAP is a measure of the Average Transaction Price (ATP), not a list price, and it should not be used to determine the MLP. The NEAP is also a figure that is derived from the Form 2 Block 4 submissions by patentees whose confidentiality is protected by the Patent Act. As such, the NEAP should not be used to determine the MLP as this would undermine the confidentiality of sales reporting by the patentee.

No incentive for higher therapeutic value medicines

The Draft Guidelines do not confer higher price ceilings commensurate with the level of innovation of the patented drug. Consequently, a 'me too' drug and a drug that offers significant therapeutic benefits over existing therapies are essentially treated the same in the Draft Guidelines. While one could argue that pharmacoeconomics implicitly factors innovation into determining ceiling prices, this would only apply to the segment of the drugs that are classified as Category I and only to a limited degree.

An innovative medicine entering a crowded therapeutic class with ample number of competitors and generic molecules would be penalized due to the likelihood that the median price of the dTCC would determine its list price ceiling. This would be the case whether the new molecule offers no improvement or substantial improvement over existing medicines. This provides little incentive for a patentee to launch an innovative medicine in this environment. Launching a new antibiotic that is effective against drug-resistant bacteria, for example, would face this hurdle and potentially be regulated to a list price equivalent to a generic or the Lowest International Price. The therapeutic class used in a dTCC should be vastly different if the molecule is innovative versus a 'me-too' drug.

¹² <https://www.theglobeandmail.com/report-on-business/canada-needs-tougher-drug-patent-protection-report/article562405/>

Patentee confidential information not sufficiently protected

As mentioned previously, Canadians often have access to innovative medicines relatively early in the global distribution chain as IRP is based on list prices. While Canadians receive relatively early access, the prices paid to the payers are typically significantly lower than the list price due to confidential rebates provided by the patentee. This allows drugs to be launched early in Canada at a price that is affordable.

The issue with the concept of MRP is that with publicly available information (CADTH report, IQVIA data, PMPRB thresholds, and Price Lists), it is feasible to reverse engineer the MRP. The ability to calculate MRP would have dramatic consequences as foreign countries as well as competitors would know a manufacturer's maximum net price including PLA rebates. This will provide significant unfair advantage for non-grandfathered products when they compete in tender markets, and when negotiating with the pan-Canadian Pharmaceutical Alliance (pCPA). Foreign countries would also likely leverage the MRP to confer lower prices in their domestic country based on publicly available information.

PMPRB's transparency of net pricing ceilings could inadvertently cause an unfair competitive environment on one hand (i.e. if an entrant would have otherwise priced below the Pharmacoeconomic Price (PEP)) or cause decreased competition on the other hand (i.e. if the PEP is so low it dissuades an entrant from launching into Canada) — neither are good outcomes for Canada.

Operationalization of Draft Guidelines not feasible

It is currently not feasible to be compliant with the Draft Guidelines. Although the MRP is derived from a public payer perspective from CADTH, actual public coverage may not come to fruition for months, years or ever for a patented medicine. While the construct of the MRP assumes public coverage on the first day of sale, this is never the case. Consequently, it will be impossible for a patentee to be compliant with the MRP given that no listing agreements would have been negotiated with any payer at launch. The alternative is for the patentee to compensate with significant amount of free goods to reduce its average selling price to be below the MRP from the first day of the molecule's introduction. However, this also has a punitive effect in that the units that are given away for free to help Canadians, are being used against the patentee to count towards its market size adjustment¹³.

Most pharmaceutical companies sell their product to a wholesaler, who then distribute the product to pharmacies and clinics across the country. The patient that picks up the prescription may be covered by a public plan, a private plan, pay cash, or a combination of the three with varying amounts of rebates dependent on their insurance coverage. At the time of sale, the patentee does not have access to data that will accurately determine the type of patient and corresponding rebate that needs to be paid. Regardless, at the time of sale, the patentee needs to make an estimate and account for any rebates that are associated with the sale. Failure to do so would overstate revenues. Only when we receive an invoice from a payer can the accrued rebate amount be reconciled with the actual rebate owing. Depending upon the drug, the variance that arises could amount to millions

¹³ Based on Dec 2019 newsletter indicating that \$0 goods are to be counted as sales. Such units would go towards the market size threshold of \$25Million as PMPRB will consider the units x MRP set by the PEP in determining the market size. <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1485>

of dollars and is exacerbated when the payer does not provide an invoice on a timely basis.

To complicate matters further, many wholesalers have large distribution warehouses in certain provinces and not others, such that a drug sale to a wholesaler in the province of Ontario, for example, may end up being dispensed to a patient in Quebec where the prices may be lower. As provinces may also have different PLA's, these inter-provincial drug movements could cause wide variations in the actual rebates owed by the manufacturer versus the accrued rebates. As patentees correct the variation between actual and accrued rebates, PMPRB would receive widely swinging sales reports over time.

Other novel rebate agreements will complicate matters even further. Utilization capitation, pay for performance and other novel rebate agreements will cause the average transaction prices to vary widely once actual sales are reconciled with the estimate. The result will be that the manufacturer will be forced to restate prior sales reports. This would cause further uncertainty under the New PMPRB Framework.

Insufficient guidance for “GAP”¹⁴ product launches

The period spanning the publication of the PMPRB Regulations in CG2 (August 21, 2019) and the day preceding the implementation of the *Regulations* (July 1, 2020) is fraught with great uncertainty. During this period, new patented drugs may have launched without a clear understanding of their actual ceiling price. Bayer had requested to meet with its PMPRB compliance officers to receive guidance on the interpretation of the Draft Guidelines but were informed that product specific guidance would not be provided at this time. This has forced patentees to launch based on individual, and potentially flawed, interpretations of an ambiguous set of rules, including the lack of the Patentee Guide to Reporting. Hence, current PMPRB Guidelines should be applied to products that have launched during this blackout period.

Conclusion

Canada represents only 2% of the world's pharmaceutical market and its regulatory environment offers a shorter exclusivity period than other developed nations. The loss of predictability of Canadian patented drug prices is a major concern to our global organization as the uncertainty affects not just Canada, but those countries that reference Canada. Due to this uncertainty, global headquarters will invariably delay Canadian launches until either this uncertainty is rectified or that countries that reference Canada have had the opportunity to launch.

The PMPRB would be better served if its Guidelines provided the 'bright lines' that were originally promised. While bright lines could still result in certain products not being made available in Canada or having a delayed launch due to low prices, the current proposal risks delaying all launches until pricing certainty is obtained. We know of no other regulated industry where the regulated price is not known for months or years after the product or service has been made available to the public. Confidentiality of privileged information, predictability and fairness are critical for any business to function. The lack of these basic elements will cause pharmaceutical companies to bypass Canada or to relegate Canadian launches behind those countries that reference it. Changes to the Guidelines are required and this requires proper and fulsome consultation.

¹⁴ Non-grandfathered patented medicines receiving DIN between August 21, 2019 and June 30, 2020

The drug ecosystem is complex and will require the best minds from industry, government, payers, patients and other stakeholders to develop a sustainable, functional system that can be implemented by industry stakeholders without penalizing patient choice and innovation. Implementing the Draft Guidelines in their current form will inflict damage that will take years for the Canadian healthcare system to recover. This risk can be mitigated in part through effective consultation. The creation of sound public policy requires support, participation and acceptance from engaged stakeholders. Hence, we urge the PMPRB to amend the Draft Guidelines based on stakeholder proposals instead of sidelining concerns that have been repeatedly voiced by patients and industry.

Yours sincerely,

A handwritten signature in black ink that reads "Dale Toki". The signature is written in a cursive, flowing style.

Dale Toki
Director, Strategic Pricing & Contracts
Bayer Inc.