



Patented
Medicine Prices
Review Board

Conseil d'examen
du prix des médicaments
brevetés

Canada

A stylized graphic of the map of Canada, composed of thick, overlapping lines in shades of blue and grey. The lines are arranged to form the outline of the country, with some lines being solid blue and others being semi-transparent grey, creating a layered effect.

BACKGROUND

**ON JUNE 2020
DRAFT GUIDELINES:
Explanation of Changes
from November 2019
Draft Guidelines**

PMPRB, JUNE 19, 2020

The Patented Medicine Prices Review Board

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Table of Contents

The PMPRB Guidelines	2
The PMPRB Guidelines Consultation.....	2
Reaching out to Canadians: Overview of the PMPRB Consultation	3
Explanation of Changes to the Draft Guidelines	4
1. Domestic Therapeutic Class Comparison (dTCC).....	5
2. Maximum List Price (MLP) Test - International Price Comparison.....	6
3. Classifying a patented medicine as Category I.....	7
4. Pharmacoeconomic Value (PV) Threshold & Accounting for Therapeutic Comparators - <i>High Cost Medicines</i>	9
5. Market Size Adjustments	11
6. Confidentiality of Maximum Rebated Price (MRP)	13
7. Regulatory review of patented biosimilars and generics	14
8. Other issues raised by stakeholders that have been addressed by these changes	15

The PMPRB Guidelines

The Patented Medicine Prices Review Board (PMPRB) is a quasi-judicial body with a regulatory mandate to prevent pharmaceutical patentees from charging consumers excessive prices during the statutory monopoly period. Its creation arose out of concern that stronger patent protection for medicines might cause their prices to rise unacceptably to the detriment of consumers.

Pursuant to subsection 96(4) of the *Patent Act*, the PMPRB issues guidelines (“Guidelines”) which are intended to provide transparency and predictability to patentees regarding the process typically engaged in by public servant employees of the PMPRB (“Staff”) in seeking to determine whether a patented medicine appears to be priced excessively in any market in Canada.

Before making or amending its Guidelines, the PMPRB has an obligation to consult under subsection 96(5) of the *Patent Act*. The PMPRB takes its obligations in this regard very seriously and has pursued all necessary steps to ensure a meaningful consultation process predicated on an open and transparent dialogue with Canadians.

The PMPRB Guidelines Consultation

On January 1, 2021, the amended *Patented Medicines Regulations* (“Amended Regulations”)¹ will come into force. Changes to the PMPRB’s pricing Guidelines are necessary for the Amended Regulations to be implemented and to enable the PMPRB’s move to a more risk-based approach to regulating the ceiling prices of patented medicines. On November 21, 2019, the PMPRB published a draft set of new Guidelines (“the November 2019 Draft”) for consultation with stakeholders and the public. Extensive feedback followed and the written submissions we received are available on the PMPRB [website](#).

In response to the feedback received during the consultation period, the PMPRB has made a number of substantive changes to the November 2019 Draft. These changes are reflected in a second draft set of Guidelines published on June 19, 2020 (“the June 2020 Draft”) which the PMPRB is now consulting on for a period of 30-days.² The purpose of the present document is to explain in general terms the nature of the changes and why they were made. It is intended to be read as a companion piece to the June 2020 Draft to support the reader’s understanding of the changes. A similar document accompanied the publication of the November 2019 Draft Guidelines and is available on the [PMPRB website](#). As is the case for the Guidelines, the Background is not binding on the PMPRB or patentees.

The publication of the June 2020 Draft Guidelines and the ensuing 30-day consultation process is the last and final step in a process that dates back to the release of the [PMPRB’s Discussion Paper on Guidelines Modernization](#) in June 2016, and follows the roadmap for reform laid out in its [2015-2018 Strategic Plan](#). From the beginning, the PMPRB’s consultation process has been consistent with government best practices to ensure maximum inclusion, clarity, and productive discussion.

1 SOR/2019-298.

2 This consultation focuses only on the responsive changes, i.e., the substantive differences between the November 2019 Draft and the June 2020 Draft. It is not intended to revisit elements of the Draft Guidelines that did not change from the previous version.

The deadline for providing written submissions to the PMPRB on the June 2020 Draft Guidelines is July 20, 2020. The PMPRB remains committed to hearing from all Canadians who have an interest in and opinion on how it carries out its regulatory mandate and looks forward to receiving constructive and meaningful feedback from this consultation process with a view to issuing final Guidelines in the fall of 2020.

Reaching out to Canadians: Overview of the PMPRB Consultation

The publication of the November 2019 Draft Guidelines was followed by an 85-day consultation period. During that time, the PMPRB sought to engage with as many stakeholders as possible in various ways, including face-to-face meetings across the country, day-long outreach sessions in Ottawa with industry and civil society, webinars and working groups.

The following is a summary of the PMPRB's consultation efforts following the release of the November 2019 Draft Guidelines:

- **Health Partners Working Groups:** two one-day outreach sessions in November 2020 and January 2020 with health partner representatives including public drug plan representatives, the Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et services sociaux (INESSS), pan-Canadian Pharmaceutical Alliance (pCPA), Health Canada, and Cancer Agencies;
- **An Industry Forum:** a one-day outreach session in December 2019 with representatives from Innovative Medicines Canada (IMC), BIOTECanada and some of their member companies;
- **A Civil Society Forum:** a one-day outreach session in December 2019 with patient groups and other non-institutional stakeholders;
- **An Industry Webinar:** in January 2020 with 187 participants from across the pharmaceutical industry;

- **Cross country consultation meetings:** over 60 meetings with more than 260 participants from stakeholder groups across the country. These included ministries of health, public and private payers, patient and patient groups, clinicians, industry and trade associations, pharmacists and distributors, health care organizations, etc.;
- **Bilateral meetings with pharmaceutical companies, trade associations and consultants:** over 40 meetings, mainly in Ottawa.

Specific information on dates, locations and stakeholder groups the PMPRB met with, as well as electronic versions of the documents that were discussed at those meetings are available on the [PMPRB website](#).

The PMPRB's Board had planned to host a public policy forum in Ottawa on March 18, 2020 but was unable to do so because of the emerging COVID-19 pandemic. To provide stakeholders with an opportunity to convey any new or different information they may have intended to present to the Board at that event, the PMPRB extended the timeline for written submissions from interested parties until March 18, 2020.

The PMPRB received 123 written submissions during the consultation period from a diverse array of stakeholders. One-third (33%) of the submissions received were from patentees and their industry associations, and another third (33%) came from consumer and patient advocacy groups. The PMPRB also received almost 900 letters from individuals or patients, the majority of which were from Cystic Fibrosis patients and their caregivers as part of an advocacy initiative spearheaded by Cystic Fibrosis Canada. The 123 written submissions are available on the [PMPRB website](#).

Category	Submissions (#)	Submissions (%)
Consumer/patient advocacy total	41	33%
Patentee	34	28%
Patentee association	4	3%
Generics/biosimilars	2	2%
Patentee/patentee association total	40	33%
Distributor/consultant/pharmacist	11	9%
Industry associations (e.g. life sciences)	6	5%
Consultant	2	2%
Industry total	19	15%
Union	7	6%
Clinician	4	3%
Academic	3	2%
Think tank	1	1%
International	1	1%
Civil academic/clinician/think tank total	16	13%
Public (e.g. agency, health authority, government)	5	4%
Private insurance	2	2%
Public entity or private insurance total	7	6%
Grand Total	123	100%

The efforts outlined above are part of a process that will continue even after the Guidelines are implemented. The PMPRB will work with stakeholders to ensure that the impact of the Guidelines is well understood and to minimize any operational or compliance issues arising from their early application. Adjustments to the Guidelines will be made if it becomes clear that certain aspects of the new regime are not operating as intended, subject as always to further consultation with stakeholders and the public.

Explanation of Changes to the Draft Guidelines

In issuing Guidelines, the PMPRB must reconcile seemingly conflicting public policy objectives, namely, facilitating access to patented medicines at non-excessive prices while recognizing the legitimate interest of pharmaceutical patentees in maximizing the value of their intellectual property. Not surprisingly, the PMPRB's diverse stakeholder community holds divergent and even diametrically opposing points of view on

the policy rationale for the Guidelines and the Amended Regulations upon which they are based. Accordingly, the PMPRB recognizes that consensus is not achievable when consulting on measures to modernize its regulatory framework. However, the PMPRB has made every effort throughout the consultation process to foster a productive, fair and transparent dialogue with our stakeholders and to listen carefully to their concerns. The changes explained below are the result of that effort and represent our best attempt to be responsive to the competing feedback we have received from stakeholders and to craft a modern-day regime that continues to encourage voluntary compliance.

What follows is a concise description of the key changes between the November 2019 and June 2020 Draft Guidelines, the stakeholder feedback upon which they are based, and an explanation of the Board's reasoning in making them. This information is presented to provide context and is not intended to constitute an exhaustive

treatment of all the relevant feedback the PMPRB received in respect of each issue, or of the analysis that prompted the change.

1. Domestic Therapeutic Class Comparison (dTCC)

PROPOSED APPROACH IN NOVEMBER 2019 DRAFT GUIDELINES

One of the factors for assessing whether a price is excessive as set out in s. 85 of the *Patent Act* is “the prices at which other medicines in the same therapeutic class have been sold in the relevant market” (s. 85(1)(b)).

The November 2019 Draft Guidelines proposed to address this factor in two main ways. First, it provided that the Maximum List Price (MLP) for New patented medicines would be set by the lower of the Median International List Price (MIP) for the PMPRB11 comparator countries and the domestic Therapeutic Class Comparison (“dTCC”), subject to a floor set by the Lowest International Price (LIP) for the PMPRB11 countries. Second, it provided that if a cost-utility analysis prepared by a publicly funded Canadian organization was not available for a Category I patented medicine, then the Maximum Rebated Price (MRP) would be set by the lower of the LIP, the dTCC or the international Therapeutic Class Comparison (“iTCC”), with further adjustments based on the Market Size Adjustment Methodology.

Both the dTCC and the iTCC would be calculated based on the median cost of treatment across the comparator medicines, derived by taking into account the lowest public price and price source.

SUMMARY OF STAKEHOLDER FEEDBACK

Patentees object to the proposed approach, asserting that it would push Canadian list prices towards the LIP and fails to recognize that medicines within a class can have differing levels of therapeutic benefit. Patentees also recommend

that the dTCC and the iTCC be calculated based on the highest rather than the median cost of treatment across the comparator medicines.

Public and private payers and other stakeholders involved in health care delivery did not express any concerns with applying the TCC factor in the manner described above.

ANALYSIS

While few patented medicines³ are launched in therapeutic areas dominated by older, genericized medicines, the Board recognizes that the proposed approach would likely have the effect of pushing the MLP for these medicines to the LIP. As a result, the Board has decided to forego this approach where the patentee has filed prices for the medicine in PMPRB11 countries. It is believed that the international prices of the medicine may already reflect, to some extent, the availability and pricing of comparator medicines in those markets.

The Board did elect to retain the domestic dTCC whenever PMPRB11 prices for a medicine are not available. In such cases, the dTCC test will be calculated using the top of the class instead of the median. The dTCC and iTCC will also be retained in the context of setting the MRP for large market size Category 1 medicines.⁴ The Board views the median as the more appropriate bar in this instance given that the prices used for conducting the TCC are gross (list) prices instead of net prices.

DESCRIPTION OF THE CHANGE IN THE JUNE 2020 DRAFT GUIDELINES

For New patented medicines, the MLP will be set by the MIP for the PMPRB11 comparator countries if the patentee has filed prices for at least one country. If there are no available prices in the PMPRB11 countries, then the MLP⁵ will be set by the dTCC, calculated based on the highest instead of the median cost of treatment across the comparator medicines, derived by taking into account the lowest public price in Canada.

3 Based on 2017 and 2018 data, 17% of new DINs launched into a therapeutic class dominated by genericized medicines.

4 The dTCC may also set the MRP for high cost Category 1 medicines where the pharmacoeconomic analysis is a cost minimization.

5 The use of the dTCC is also contemplated during the interim period. If there are no available international prices, the dTCC test or the iTCC may be used to set the initial MLP – iMLP.

If the patentee has not filed international prices by the end of the interim period (maximum 3 years), and there are no domestic therapeutic class comparators, the MLP may be set at the median of the iTCC.

If during the lifecycle of the medicine, it is launched in other countries, the MLP will be subject to the reassessment criteria, which contemplates an increase or a decrease depending on where the Canadian list price sits vis-à-vis international list prices.

The dTCC will be considered in the establishment of the MRP for Category I medicines with an actual market size exceeding \$50 million, as described in Section 5. In such a case, the dTCC will be based on the median cost of treatment across the comparator medicines, derived by taking into account the lowest public price in Canada and subject to the applicable Therapeutic Criteria Level (TCL) floor.

2. Maximum List Price (MLP) Test - International Price Comparison

PROPOSED APPROACH IN NOVEMBER 2019 DRAFT GUIDELINES

One of the excessive pricing factors set out in s. 85 of the *Patent Act* is “the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada” (S. 85 (1) (c)).

The November 2019 Draft Guidelines proposed that the Maximum List Price (MLP) be set by the lower of the Median International Price (MIP) for the PMPRB11 comparator countries and the domestic Therapeutic Class Comparison (“dTCC”), subject to a floor set by the Lowest International Price (LIP) in the PMPRB11. If the patentee does not file international prices by the end of the three years (“Interim Period”), and there are no domestic therapeutic class comparators, it further proposed that the MLP be set using the international Therapeutic Class Comparison (“iTCC”).

SUMMARY OF STAKEHOLDER FEEDBACK

Patentees, the biosimilar industry, distributors, industry consultants and some patients and patient groups argue that the MIP should

be replaced by the Highest International Price (HIP) for Grandfathered medicines, and make a number of points in support of that position. First, they claim that the MIP approach incorrectly assumes that all prices above the median of the comparator countries are excessive. Second, they view the application of the MIP for Grandfathered medicines as inconsistent with the Cost Benefit Analysis (CBA) conducted by Health Canada as part of the Regulatory Impact Analysis Statement (RIAS) that accompanied the Amended Regulations. Third, they maintain that the application of the MIP to the prices of Grandfathered medicines will have a significant impact on industry revenues and result in drug shortages and a decline in support services currently available to patients.

“Recognizing that the application of the new basket is mandated in the amended Regulations, it would be more appropriate to apply the current pricing rules (highest international price comparison or HIPC) to establish the list price ceiling (MLP) for existing medicines. Even with the HIPC, list price reductions will be achieved for existing products, as a result of the change in the international reference basket (PMPRB11)” - Janssen

Conversely, some public and private payers and other patient groups take the position that Canadians have been paying excessive prices for patented medicines for years and view the MIP of the new PMPRB11 basket of comparator countries as a reasonable way to ensure gross (list) prices in Canada align with international norms. In addition, these stakeholders stress that the MIP of the PMPRB11 is the most appropriate price test to adequately protect cash-paying customers from excessive list prices. This is very important given that a significant portion of sales are borne directly by Canadians through cash payments and as contributions to co-payments and deductibles.

Health researchers and provincial cancer agencies support the proposed approach for calculating the MLP and urged the PMPRB not to use the HIP test. One consumer advocacy group applauded the updated schedule of comparator countries and noted that it will “make price-comparisons much more equitable for the Canadian pharmaceutical consumers”.

“...nous ne pouvons qu’accueillir favorablement tout nouveau processus de fixation et de plafonnement des prix s’appuyant sur les données probantes et les pratiques exemplaires, de même que l’utilisation d’une nouvelle annexe de pays de comparaison (le CEPMB11) visant à établir les nouvelles règles de comparaison des prix...”

- Centrale des syndicats du Québec

ANALYSIS

The *Patent Act* does not require the Board to adopt any specific threshold based on the PMPRB11 prices, only that these be considered.

It is acknowledged that, in the main, the Cost Benefit Analysis (CBA) assumes MLP ceilings that are generally closer to the highest and median price in the PMPRB11 countries for Grandfathered and New patented medicines respectively. At the same time, the purpose of the CBA was to assess the impact of the Amended Regulations in isolation. It should not be read as precluding changes to the current Guidelines, as significant such changes are necessary to implement the Amended Regulations in the first place.

The Board’s analysis of the impact of the application of the MIP to Grandfathered medicines indicates that it may be less significant than claimed by certain stakeholders who oppose it. List prices are not reflective of true net prices paid by a large segment of the Canadian market and the true impact on the net revenue will thus be less than the nominal impact on the list prices. That being said, the Board has decided to apply the HIP test to Grandfathered medicines as a concession to patentees whose expectations may have been raised by the CBA and in recognition of the impact of changing the schedule of comparator countries. The Board is of the view that the misalignment of Canadian prices vis-à-vis international prices is best addressed by applying the MIP test for New patented medicines moving forward. As a general rule, the Board feels that Canadian list prices higher than international norms smacks of excessiveness and the MIP is an appropriate litmus test for ensuring that Canadian list prices do not become excessive in the future.

DESCRIPTION OF CHANGE IN THE JUNE 2020 DRAFT GUIDELINES

Grandfathered Patented Medicines and their Line Extensions

The gross (list) price ceiling of Grandfathered patented medicines will be set as the lower of the HIP for the PMPRB11 countries, and the applicable ceiling under the previous Guidelines. The MLP of Line Extensions of Grandfathered medicines (i.e., new strengths and dosage forms) will also be set by the HIP.

Gap and New Patented Medicines

The MIP test will be retained for setting the MLP for Gap medicines, (i.e., medicines for which a DIN was assigned on or after August 21, 2019 and the first sale in Canada took place prior to January 1, 2021) and New patented medicines (i.e., all other patented medicines for which a DIN was assigned on or after August 21, 2019).

3. Classifying a patented medicine as Category I

PROPOSED APPROACH IN NOVEMBER 2019 DRAFT GUIDELINES

The November 2019 Draft Guidelines proposed that a patented medicine be classified as Category I if it meets either of the following criteria:

- (i) 12-month treatment cost greater than 50% of Gross Domestic Product (GDP) per capita, and/or
- (ii) an estimated or actual market size (revenue) exceeds annual Market Size Threshold, initially set at \$25 million.

SUMMARY OF STAKEHOLDER FEEDBACK

Pharmaceutical patentees oppose the criteria and associated thresholds. As regards the latter, they contend that the thresholds are too low and would result in a majority of New patented medicines falling into Category I, contrary to the PMPRB's stated intent in adopting a risk-based regulatory approach. Other stakeholders, notably some patient groups and pharmacy associations, echoed concerns about the proportion of patented medicines likely to be screened in as Category I.

"These guidelines are inherently biased against drugs for small, difficult-to-diagnose and previously untreated patient populations with poorly documented natural history of disease and little clinical evidence of direct links between biomarkers and other outcome measures. This description would apply to almost all rare diseases. It is ridiculous to introduce a cost-effectiveness assessment (CEA) at the time of launch..."

Canadian Organization for Rare Disorders (CORD)

Patient groups concerned with access to rare disease medicines are particularly troubled by the fact that virtually all such medicines would fall into Category I due to their high annual treatment costs and, as such, be subject to the new Pharmacoeconomic Value (PV) factor. These products rarely have favorable pharmacoeconomic profiles because of their extreme high prices, which patentees claim are necessary to recoup research and development costs from a relatively small patient population.

Conversely, some representatives of civil society and healthcare organizations are of the view that a lower threshold for annual treatment cost should apply if the PMPRB is to properly scrutinize all patented medicines that are beyond the means of many consumers.

For their part, union groups express strong support for the inclusion of market size as a criterion for Category I medicines, citing the significant impact some medicines have on health insurance plans despite falling under the PV threshold. They note the large year-over-year increases their members' drug plans have struggled with

recently due to medicines that would be considered low cost under the November 2019 Draft Guidelines.

Finally, patentees assert that there should be a mechanism to move medicines out of Category I and into Category II if their revenues fall below the specified thresholds.

ANALYSIS

Further analysis of the data suggests that a significant percentage of medicines would realize over \$25 million in annual revenue at some point over their patent life. Considering that this data reflects historical trends, it is likely an underestimate of expected future revenues for patented medicines launched more recently.

In addition, with high cost medicines increasingly dominating the market, the observation that the proposed Category I criteria would capture a significant number of new medicines is not without merit. As a result, the Board has concluded that in order for its risk-based approach to be administratively feasible for PMPRB Staff and patentees, higher thresholds are warranted, both in terms of treatment cost and market size. To address concerns related to rare disease medicines in particular, the Board has decided to carve out from Category I high cost medicines that are expected to realize below a certain minimum amount in annual revenue.

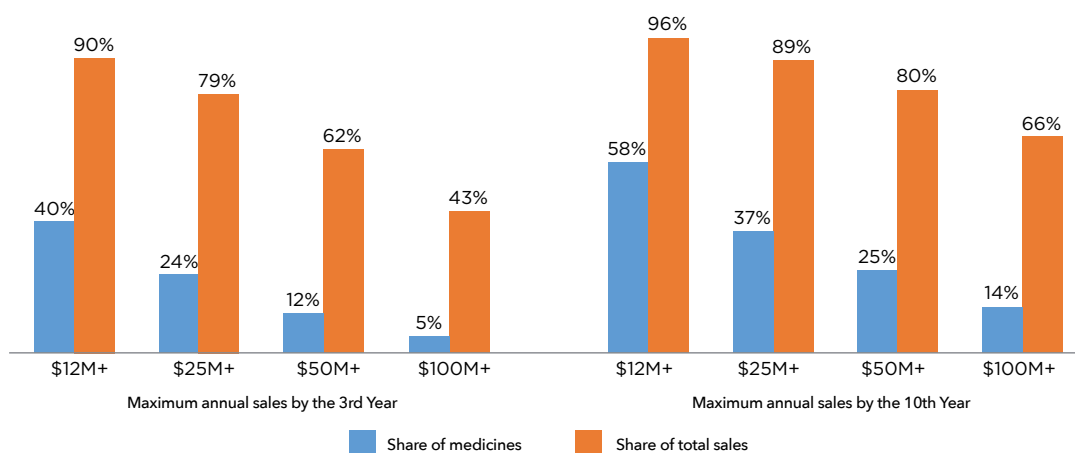
DESCRIPTION OF CHANGES IN JUNE 2020 DRAFT GUIDELINES

The new market size threshold will be \$50M in annual revenues and the new treatment cost threshold will be 150% of GDP *per capita*. It is estimated these revised thresholds will result in approximately 25% of new medicines triggering the Category I criteria, which is more in keeping with the PMPRB's original intent in moving to a risk-based approach. These medicines are expected to account for a majority of patented medicine sales (68%), which will in essence ensure that the PMPRB exercises greater regulatory scrutiny over a minority of medicines that account for the majority of sales.

Medicines that realize less than \$12M in annual revenue will not be subject to an MRP even when they exceed the new annual treatment cost threshold. This will ensure that medicines that treat rare diseases are not discouraged from coming to Canada out of concern that their net price will be substantially reduced by regulation.

Recent data suggests that a sizable portion of patented medicines (42.5%) do not realize \$12M in annual revenues in any of the first 10 years on the market (Figure 1). These medicines only accounted for 3.7% of patented sales, suggesting that even cumulatively these medicines do not give rise to affordability concerns.

Figure 1. Patented medicines in Canada, share of medicines and share of sales, by maximum annual sales



*Included patented drugs launched after 1998 in Canada; Sample Size: N=639 for the 3-year analysis; N=338 for the 10-year analysis
Data source: PMPRB, 2018; CPI applied to bring historical sales into 2018 value

4. Pharmacoeconomic Value (PV) Threshold & Accounting for Therapeutic Comparators – High Cost Medicines

PROPOSED APPROACH IN DRAFT GUIDELINES

Under the November 2019 Draft Guidelines, Category I medicines that are required to report cost-utility analysis would have a maximum rebated price (MRP) ceiling based on the level at which the patented medicine’s Incremental Cost-Effectiveness Ratio (“ICER”) would equate to the Pharmacoeconomic Value (PV) threshold of \$60,000 per Quality-Adjusted-Life-Year (QALY).

For patented medicines for rare diseases with an estimated total prevalence no greater than 1 in 2,000 across all approved indications, the MRP would be set at 50% above the level at which the ICER would equate to the PV threshold of \$60,000 QALY.

“Breast cancer is the poster child for some of the worst practices of pharmaceutical companies, for example, trying to get extremely highly priced drugs on the provincial drug formularies by mobilizing women with breast cancer through “patient advocacy” groups to directly pressure those governments. This tactic has been used for stage 4 breast cancer drugs whose actual benefits do not live up to the claims of the drug companies and whose side effects greatly diminish the quality of life of the women taking them”
~ Breast Cancer Action Quebec

SUMMARY OF STAKEHOLDER FEEDBACK

Patentees are fundamentally opposed to the introduction of PV as a factor for the PMPRB to consider in determining what constitutes an excessive price and, not surprisingly, take issue with the approach proposed for its application in the November 2019 Draft Guidelines. In addition to citing operational and technical challenges arising from its application, patentees and some patient groups objected to the proposed PV threshold of \$60,000/QALY as unreasonably low, especially for medicines for rare diseases, notwithstanding the 50% higher ceiling afforded to this class of products. Whereas some patient groups believe that the PV factor should never apply to medicines for rare diseases, others are extremely concerned with the very high opportunity cost associated with reimbursing these products, especially given that evidence of their clinical benefits at introduction is often ambiguous at best.

Patentees also take issue with the proposed \$60,000/QALY PV threshold as an arbitrary one-size-fits-all approach that runs the risk of exposing what public drug plans are paying under confidential product listing agreements (PLAs). They argue for a more flexible approach that recognizes and rewards therapeutic benefit, as is the case under the current Guidelines, but did not volunteer an alternative which would satisfy them. Specific suggestions on this point did come from some public insurers, who recommend PV thresholds of \$100,000/QALY and \$120,000/QALY for medicines that are therapeutically superior, or even higher for medicines that are potentially curative.

Lastly, in addition or in the alternative to advocating for a more flexible approach predicated on therapeutic benefit, some patentees suggest that the application of the PV threshold be subject to some form of stop-loss mechanism which would blunt its impact and provide much needed certainty to industry about the worst case scenario under the new regime.

ANALYSIS

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.

By way of comparison, in the United Kingdom, the National Institute for Health and Care Excellence (NICE) has an explicit cost effectiveness threshold of €30,000/QALY. However, there are certain cases where NICE will allow a higher threshold of £50,000/QALY for end of life treatments and €100,000 to €300,000 for “Highly Specialized Technologies” (HSTs) depending on the absolute QALY gain associated with the medicine. In other countries such as the Netherlands and Norway, the thresholds depend on the severity of the disease, among other factors. In the Netherlands, an informal cost-effectiveness threshold of €20K/QALY (low burden) to €80K/QALY (high burden) is used. Japan has recently implemented a tiered cost-effectiveness assessment scheme that requires a downward price adjustment, the amount of which depends on the drug’s cost-effectiveness. The price reduction is limited to 10-15% of the pre-adjustment National Health Insurance reimbursement price.

“... the MRP concept has no price floor whatsoever and will result in prices below the lowest of the PMPRB 11 schedule. This is contrary to the government’s policy intent...”

Innovative Medicines Canada (IMC)

In addition to the above considerations, the Cost Benefit Analysis (CBA) for the Amended Regulations also assumed a maximum price reduction of 50% for high priority New patented medicines⁶.

6 May 2019 CBA for CGII, Page 34 “Finally, for all elements of the regulatory amendments, a 50% reduction cap was applied so that the price for a medicine cannot be reduced by more than 50%, even if that is required to meet the specific Guidelines’ test.”

DESCRIPTION OF CHANGE IN JUNE 2020 DRAFT GUIDELINES

The following PV thresholds and capped price reduction floors will be applied to set the MRP for high cost Category I medicines based on an evaluation of their therapeutic criteria (for revenues in excess of \$12 million annually):

It should be noted that for Category I high cost medicines, in the absence of a cost-utility analysis being provided by the patentee, a maximum reduction of 50% will automatically be applied.

Table 1. Pharmacoeconomic Value Thresholds Price adjustment based on Therapeutic Criteria Level for MRP calculation

Therapeutic Criteria Level (See Appendix E - The Scientific Review Process)	PVT	Reduction Floor off MLP
Level I	\$200K/ QALY	20%
Level II	\$150K/ QALY	30%
Level III	\$150K/ QALY	40%
Level IV	\$150K/ QALY	50%
Pharmacoeconomic analysis is a cost minimization	Median of dTCC subject to 50% floor	
No pharmacoeconomic assessment	50% of MLP	

5. Market Size Adjustments

PROPOSED APPROACH IN NOVEMBER 2019 DRAFT GUIDELINES

For high cost Category I medicines, the November 2019 Draft Guidelines proposed that the Maximum Rebated Price (MRP) be further adjusted for market size if annual quantities of the medicine are sold such that, after the application of the Pharmacoeconomic Value (PV) Threshold, annual revenues would be in excess of \$25 million. These further adjustments would result in additional 10% reductions in revenue increments of \$25 million to a maximum reduction of 50% for annual revenue in excess of \$125 million. They would apply equally to other Category I medicines that are not high cost but are so categorized because their estimated or actual annual revenues exceed the \$25 million market size threshold.

price regulator. In addition, many patentees argue that the \$25 million increment is arbitrary and that not allowing the MRP to increase if revenue falls below the specified thresholds is inconsistent and unfair.

Stakeholders who are supportive of the Market Size factor recognize that demand and prevalence need to be taken into account in setting ceiling prices that contribute meaningfully to the sustainability of Canada’s health care system. They note that a small number of medicines can account for significant expenditures and pose immediate affordability challenges in the system without necessarily being ‘high cost’.

SUMMARY OF STAKEHOLDER FEEDBACK

The intensity of patentee opposition to the Market Size factor is second only to the sentiment reserved for the PV factor. In general, patentees feel that the effect of this factor is to import into the PMPRB regime considerations that should lie within the exclusive purview of public and private payers, not a federal ceiling

ANALYSIS

Like PV, Market Size is now a s.85(1) factor and the Board has a statutory obligation to consider it. However, a case can be made that the initial \$25 million threshold is too low and the number of incremental adjustments proposed in the November 2019 Draft Guidelines is unduly onerous on patentees. A retrospective analysis indicates that approximately one-quarter of patented medicines realize over \$50 million in annual revenues over the first 10 years of market exclusivity, while only 14% realize over \$100 million.

Many of the other relevant points raised by stakeholders in this context have already been addressed in section 3 of above.

DESCRIPTION OF CHANGE IN JUNE 2020 DRAFT GUIDELINES

The revised thresholds for the Market Size adjustment and the corresponding reductions required at these thresholds are set out in the tables below.

Table 2. Market Size Adjustments

Market size adjustment for Category I patented high cost medicines

Annual revenues	MRP	Incremental MLP adjustment factor	Price ¹ adjustment factor used to calculate MLP adjustment factor
<\$12M	MLP		0%
\$12M-50M	Greater of PEP and Floor	0%	$\frac{\$12M - \$12M * (MRP/MLP)}{\text{Revenues}} + (MRP/MLP)$
\$50M-\$100M		-25%	$\frac{\$21.5M - \$9M * (MRP/MLP)}{\text{Revenues}} + (1 - 25%) * (MRP/MLP)$
>\$100M		-35%	$\frac{\$32M - \$7.8M * (MRP/MLP)}{\text{Revenues}} + (1 - 35%) * (MRP/MLP)$

¹ Lower of the MLP and List Price

Market size adjustment for Category I patented medicines for high market size medicines

Annual revenues	MRP	Incremental MLP adjustment factor	Price ¹ adjustment factor used to calculate MLP adjustment factor
<50M	MLP	0%	0%
\$50M-\$100M	Lowest of the MLP and the median of the dTCC	-25%	$\frac{\$50M - \$37.5M * (MRP/MLP)}{\text{Revenues}} + (1 - 25%) * (MRP/MLP)$
>\$100M		-35%	$\frac{\$56.7M - \$32.5M * (MRP/MLP)}{\text{Revenues}} + (1 - 35%) * (MRP/MLP)$

¹ Lower of the MLP and List Price

For Category I medicines that do not meet the annual treatment cost threshold of 150% of GDP per capita but with an actual market size exceeding \$50 million, the MRP will be based on the lower of the Maximum List Price (MLP) and the domestic Therapeutic Class Comparison (dTCC) adjusted by the applicable factor. The dTCC will be derived based on the median cost of treatment across the comparator medicines, using the lowest public price. The impact of the dTCC will be subject to a price reduction floor that varies based on the therapeutic criteria level.

Therapeutic Criteria Level (See Appendix E - The Scientific Review Process)	dTCC Reduction Floor
Level I	20% off MLP (dTCC not applicable)
Level II	30%
Level III	40%
Level IV	50%

6. Confidentiality of Maximum Rebated Price (MRP)

PROPOSED APPROACH IN DRAFT GUIDELINES

Upon the coming-into-force of the Amended Regulations, all patentees are to report price and revenue information that is net of all adjustments including discounts, rebates and free goods and services, to any party that pays for, or reimburses, the patented medicine. This will ensure that the PMPRB has a complete and accurate picture of what patentees are truly charging for their medicines in Canada. Any information filed by patentees with the PMPRB in this respect enjoys the full protection of the confidentiality provisions of the *Patent Act*.

As already explained, the November 2019 Draft Guidelines proposed that for high cost Category I patented medicines the MRP would be calculated by applying a \$60,000 per Quality-Adjusted-Life-Year (QALY) Pharmacoeconomic Value (PV) threshold to the Incremental Cost-Effectiveness Ratio (“ICER”). For patented medicines for rare diseases, the MRP would be set at 50% above the level at which the ICER would equate to the PV threshold of \$60,000/QALY. Finally, the MRP for all Category I patented medicines would be subject to 10% reductions in revenue increments of \$25 million to a maximum reduction of 50% for annual revenue in excess of \$125 million.

SUMMARY OF STAKEHOLDER FEEDBACK

Patentees are very concerned with the impact of the new regime on their ability to continue to negotiate confidential discounts and rebates with payers in Canada. They do not appear to dispute that their filings with the PMPRB will remain confidential, but are worried that the approach taken in the November 2019 Draft Guidelines would enable third parties (including payers in other countries) to back calculate a

rough estimate of the MRP and extrapolate the levels of price reductions from the list price that would be required in order for the patentee to comply with it. Patentees believe that this would be possible for three reasons. First, the cost-utility reports they will be required to file with the PMPRB are made publicly available by the organizations that issue them (e.g. Canadian Agency for Drugs and Technologies in Health (CADTH) and Institut national d'excellence en santé et services sociaux (INESSS)). Second, the MRP tests are transparently set out in the PMPRB's Guidelines. Third, list price and estimated revenue data are also publicly available from various public sources other than the PMPRB. Patentees believe if other countries and competitors are able to estimate the magnitude of the difference between gross (list) and net price in Canada, this would put their global business model at risk and imperil the introduction of New patented medicines in Canada.

“The new maximum rebated price (MRP) calculation methodology, when combined with publicly available data, may allow third parties to reverse engineer or estimate net prices.”

Innovative Medicines Canada (IMC)

Stakeholders who express the opposite view believe just as strongly that confidential pricing is a key contributing factor to skyrocketing pharmaceutical prices, both domestically and internationally in recent years and that it is imperative that this phenomenon be brought into the light, not only in Canada but around the world.

“The fact that the information underlying the calculation of the ... MRP is confidential will introduce additional obscurity into pharmaceutical prices which is unfortunate.” - Expensive Drugs for Rare Diseases Advisory Committee

ANALYSIS

The Board recognizes the difficulty inherent in crafting ‘brightline’ price tests that are predictable to patentees but do not enable competitors to back calculate rough estimates of their confidential discounts to third parties. At the same time, it notes that a number of the issues raised by patentees, such as the public availability of pharmacoeconomic reports issued by CADTH and INESSS and the public availability of list prices and revenue estimates, are well established features of the status quo in Canada and cannot be unwound by the Guidelines. Formal and informal cost-utility thresholds are standard in a number of countries and yet patentees continue to sell their products in those markets. That being said, the Board is not unsympathetic to the concerns raised by patentees and believes that the revised approach to calculating the MRP in the June 2020 Draft Guidelines has the dual benefit of being responsive to both these concerns and the desire expressed by both patentees and many patient groups to retain an assessment of therapeutic criteria as a key input in setting ceiling prices.

DESCRIPTION OF CHANGE IN JUNE 2020 DRAFT GUIDELINES

As explained in section 4, the MRP calculation will be a function of the Therapeutic Criteria Level (TCL) assigned to the patented medicine and the applicable PV threshold and price floor that corresponds to it. The TCL of a patented medicine will be known only to the PMPRB and the patentee.

7. Regulatory review of patented biosimilars and generics

PROPOSED APPROACH IN NOVEMBER 2019 DRAFT GUIDELINES

The Amended Regulations removed the requirement for patentees of certain types of patented medicines to file identity, price and sale information with the PMPRB, unless so requested in response to a complaint. These include patented veterinary medicines, an expanded subset of medicines that do not require a prescription (i.e., over-the-counter – “OTC” medicines) and

generic medicines that meet the regulatory definition. Where a complaint is received in respect of one of these types of patented medicines, they would be automatically considered Category II for investigation purposes.

The November 2019 Draft Guidelines made no special provision for ‘biosimilar’ medicines (i.e., subsequent entry biologics approved on the basis of a comparison to an innovator’s reference biologic) which do not fall within the definition of “generic” medicines in the Amended Regulations. Consequently, patentees of these medicines would be required to file price information with the PMPRB and could fall into either Category I or Category II.

SUMMARY OF STAKEHOLDER FEEDBACK

Makers of biosimilar medicines, the generic pharmaceutical industry and some patentees argue that there are other types of patented medicines that should be considered at low risk of excessive pricing from an administrative standpoint and thus exempt from the reporting obligations under the Amended Regulations. In their view, this exemption should apply to biosimilars, the brand version of medicines that face generic competition and patented generic medicines that are authorized for sale by regulatory pathways under the *Food and Drug Regulations* other than just an Abbreviated New Drug Submission (ANDS).

Biosimilar makers in particular stress that their market in Canada is still in its infancy and should be shielded to the greatest extent possible from needless regulatory burden. They contend that having biosimilars subject to the same degree of regulatory scrutiny from the PMPRB as the reference biologic product flies in the face of efforts elsewhere in the health system to reap the potential savings associated with this fledgling market. Regulating biosimilars on a complaints-basis is also said to be more aligned with Canadian Agency for Drugs and Technologies in Health’s (CADTH’s) recent decision to no longer conduct Health Technology Assessment (HTA) reviews of biosimilars in order to simplify and streamline market access for these products. Alternatively, if biosimilars are not exempt from PMPRB oversight, biosimilar makers argue that the domestic price of the reference biologic

should be the only comparator because international price comparisons to other patented biosimilars would be inappropriate.

ANALYSIS

Although the Board cannot exempt patentees of medicines from the prescribed filing requirements under the Amended Regulations, from a day to day administrative standpoint, it does have some flexibility in the degree to which certain non-exempt medicines are proactively scrutinized. The Board is of the view that a strong case can be made that expanding the scope of exempt patented medicines beyond the strict regulatory definition for administrative purposes is consistent with a risk-based approach to regulating ceiling prices.

DESCRIPTION OF CHANGE IN THE JUNE 2020 DRAFT REGULATIONS

Patented biosimilars, generic medicines, medicines for veterinary use and OTC patented medicines will only be subject to investigation if a complaint is received by the PMPRB. In such an event, medicines of this kind will be deemed to be Category II and treated as such notwithstanding the existence of properties that might otherwise meet the criteria for Category I screening. Unlike patented medicines which have reduced reporting requirements under the Amended Regulations, patented biosimilars and generics approved through non-ANDS pathways have a legal requirement to report to the PMPRB.

8. Other issues raised by stakeholders that have been addressed by the above described changes

Medicines for rare diseases

As already explained, the November 2019 Draft Guidelines proposed a 50% higher Maximum Rebated Price (MRP) for medicines with an estimated total prevalence no greater than 1 in 2,000 across all approved indications. The revisions to the MRP approach in the June 2020 Draft Guidelines no longer distinguish between medicines for rare and non-rare conditions. Instead, a full exemption from the MRP has been made for all medicines which would otherwise qualify as Category I because of their annual treatment costs if their annual revenues is below \$12M. This measure, coupled with the higher

Pharmacoeconomic Value (PV) thresholds and capped price reductions for medicines based on their Therapeutic Criteria Level (TCL), go a long way to address concerns raised by certain stakeholders about unfair treatment of medicines for rare diseases under the new regime.

Reasonable Relationship (RR) Test

The November 2019 Draft Guidelines proposed that the Reasonable Relationship (RR) test may be conducted to determine the Maximum List Price (MLP) or Maximum Rebated Price (MRP) of a new or additional strength of a patented medicine with other existing strengths, where the new or additional strength has the same medicinal ingredient, indication, dosage regimen, and same or comparable dosage form as the existing strength(s). The MLP or MRP of the new strength would have been set to be equivalent to the price per standard unit of the existing strength(s). The approach was also intended to be applied when multiple strengths of new medicine are first sold simultaneously, and some strengths are identified specifically as loading, titration, or reduction doses.

Patentees have concerns that this approach would discourage the launch of new strengths that are potentially more convenient for patients. This would particularly be the case for medicines that would otherwise be priced at level with other existing strengths.

In view of these concerns, the Board has decided to revert to a simplified version of the RR test used under the current Guidelines. The test will benchmark one strength as the reference strength and set the ceiling for the other strengths (new or existing) based on their proportional relationship to it, subject to a Highest International Price (HIP) cap. In order to accommodate the practice of level pricing, patentees will be allowed to price lower strengths up to the MLP of the reference strength subject to the HIP. This approach addresses the issue of level pricing within the confines of international price limits.

The RR test will be applied to New patented medicines (i.e., medicines for which a DIN was assigned on or after August 21, 2019 and the first sale took place on or after January 1, 2021).



Patented
Medicine Prices
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