IMC Response to PMPRB Draft Guidelines – February 14, 2020

Executive Summary [1]

The Patented Medicine Prices Review Board (PMPRB) draft Guidelines released on November 21, 2019 will have a significant and negative impact on patient access to new medicines in Canada. Many Canadians are rightfully concerned that the Guidelines are being advanced in isolation from broader health and innovation policy objectives. Innovative Medicines Canada (IMC) understands the budgetary pressures confronting Canadian governments and, as previously offered, is more than willing to assist with healthcare sustainability. However, an appropriate balance must be struck to preserve Canadians' timely access to life saving and life improving innovative medicines. IMC submits that this critical balance will be undermined by the complex, wide-ranging and severe pricing controls proposed within the draft Guidelines.

The draft Guidelines set out a new regime that cannot be operationalized unless a fundamentally different approach is developed through technical working groups with patentees. There are, for example, numerous product launch risks and fundamental operational barriers to proposals regarding the new economic factors and the flawed maximum rebated price (MRP) concept, which does not adequately protect confidential and internationally sensitive business information.

While the innovative industry wishes to continue to bring affordable new medicines to Canadians, the unprecedented disruption and uncertainty created by the PMPRB's proposals are already impacting product launches and clinical trial investments in Canada. To date, IMC has been notified of nine specific planned drug launches, including rare disease and oncology medicines, which have been delayed or suspended due to the proposed PMPRB changes. It is reasonable to anticipate that additional drug launches will be delayed or suspended given that the regime has not yet been implemented.

The proposed regime is inconsistent with an excessive price standard as reflected in the *Patent Act*. It is not risk-based since it subjects all medicines to a high level of scrutiny and severe pricing tests, regardless of excessive price risk. It does not permit companies to reliably predict allowable price ceilings and does not provide a fair and appropriate transition for in-market medicines.

The draft Guidelines will have a significantly greater negative financial impact than the estimate provided by Health Canada in the cost-benefit analysis (CBA) associated with the regulatory amendments published in Canada Gazette Part II on August 21st, 2019. An assessment prepared by a third-party expert suggests the proposals will result in up to $41.8 billion net present value (NPV) in negative impacts over ten years.[2] This compares to the $8.8 billion impact estimate in Health Canada's revised CBA. This significant difference is partially explained by the fact that the CBA was not based on the draft Guidelines, but rather, was based on a notional Guideline scenario that is materially less impactful than the PMPRB's subsequent November 2019 implementation proposals.

The draft Guidelines are excessively complex and are not in a sufficiently advanced state of development to be effectively implemented by July 1, 2020, the effective date of the regulatory amendments. IMC notes that although this is the effective date of the regulatory amendments, there is no requirement that the Guidelines be implemented on that date, and appropriate time should be taken to refine the proposals to mitigate the impacts set out above.

IMC is concerned by a potential approach which interprets operational issues and ambiguities as minor concerns that can be addressed on an ad hoc basis as they emerge over time. We would refer readers to the case studies appended to this submission which illustrate specific operational barriers and other impacts in this regard. However, while industry and other stakeholders can assist with flagging potential issues and proposing alternatives, ultimately it is incumbent on the regulator – not the regulated – to establish a system that is practical, functional and comprehensible from the first day that it comes into effect.

IMC's key positions on the Guidelines are substantively consistent with its input provided in past submissions, and we would refer readers to those documents rather than reiterate them here at length.[3] Our industry has consistently advocated coherent alternative policy approaches including risk-based forms of regulation. It is a matter of public record that industry is willing to help realize significant changes to drug pricing in Canada. However, like any regulated party, we require basic standards of regulatory predictability which are not met by the proposed new economic factor implementation and MRP concept. Moreover, if implemented as set out in the draft Guidelines, these new factors will obstruct effective Federal- Provincial-Territorial policy regarding drugs for rare diseases and National Pharmacare.

In addition to the central concerns we continue to raise in relation to the new economic factors and proposed use of pharmacoeonconmics, our key positions can be summarized as follows:

- **Technical working groups should be struck in the coming months**. These groups should be given adequate time to generate an alternative Guidelines package consistent with core regulatory principles of feasibility, fairness, predictability and transparency, and to ensure that Canadians can access new medicines in a timeframe comparable to the present day. Working groups could have a particular emphasis on policy areas that meet the standard of operational feasibility, versus those policy tools such as the new economic factors and MRP that cannot be effectively implemented at this time. Without limitation, working groups should include the following topics: reporting compliance; international price comparisons, processes and other price tests, transition for existing products including 'Gap'[4] products, and new economic factor alternatives. These should be composed of industry technical experts and PMPRB staff, including regulatory compliance staff.
- **Adequate transitional measures for in-market medicines are needed**. Existing products should not be subject to the accumulation of excessive revenues for the 2021 calendar year, regardless of price test applied. Any impacts should be gradually phased in over subsequent years, as further discussed below.
- **Proposals that compromise confidential business information should be discontinued**. This will help to mitigate some product launch risks.
- **Appropriate and reasonable price floors should be applied to all products**.
- **The proposed median therapeutic class comparison test should be discontinued**. Any pricing tools that would see the lowest international price establish the Canadian price should be reconsidered.
- **Continuity is needed for new indications and line extensions.**

Since 2016, IMC and its member companies have attempted to engage constructively with Health Canada and the PMPRB. Despite the numerous and legitimate concerns raised by industry, patients, provincial governments, and other stakeholders, their collective feedback has largely been ignored or disregarded. As a result, there is a widespread impression among informed stakeholders that the material aspects of the new PMPRB regime were immutable from the outset, and that subsequent consultations with stakeholders, while numerous, have essentially been pro forma exercises.

Despite our fundamental concerns with the proposed system and the very limited changes made in response to the stakeholder input provided during the previous consultations, our industry remains open to working with the PMPRB to develop more predictable regulatory tools that promote a functional regime that does not destabilize the pricing and reimbursement landscape in Canada.

Guidelines Considerations and Concerns

Impacts and predictability

The proposed regime poses risks to Canadian patients with respect to global product launch decisions because it does not permit the reliable prediction of an allowable price ceiling at launch or throughout the product lifecycle due to the new economic factors and broad criteria for reassessments. These and other features of the proposed regime will negatively impact product launch and investment decision-making. Employment will also be significantly impacted. Moreover, it is not only the innovative industry that will be affected: over time, pharmacies, distributors, generic drug manufacturers, clinical trial investigators, and ultimately patients will also be adversely impacted by the new system.

In addition to the top-line impacts noted above, we have significant concerns with select product categories that would be subject to particularly large price reductions due to the application of the new economic factors. For example, third-party expert analysis suggests that 82.8% price reductions for rare disease medicines and 60.8% price reductions for oncology medicines would be required. [5] Reductions of this kind will challenge or delay drug launches in these product categories.

Fundamental concerns with the regulatory approach

Core elements of the draft Guidelines are either unclear, deficient or lacking in operational feasibility. The draft Guidelines do not simplify the PMPRB's regulatory approach nor do they provide "bright-line" rules. Although positioned as a streamlined approach, they introduce more complex and challenging regulatory mechanisms. We are concerned by the significant operational barriers to implementation. For example, the MRP concept is disconnected from how drug prices are negotiated with payers and reimbursed within the Canadian system. At the time that PMPRB is assessing ceiling price, most manufacturers would not have any product listing agreements in place with payers and therefore would have no rebated price to assess against an MRP. It can take upwards of two years to achieve formulary listings on government-sponsored plans and, in some instances, a listing is never achieved. Consequently, an MRP is not operationally feasible in this context.

Similarly, pharmacoeconomic analyses cannot be validly used to regulate excessive price ceilings and the proposed implementation would extend the role of the PMPRB well beyond its current mandate. Cost-effectiveness evaluations conducted by Health Technology Assessment (HTA) bodies such as CADTH and INESSS are used downstream in reimbursement decision-making and are intended to inform payers

regarding value-based negotiations. It is inappropriate to use such evaluations for any purpose other than the intended objective of supporting reimbursement decision making at the public drug plan level. This issue is discussed in greater detail in our previous commentary on the new economic factors.[6] The proposed formulaic use of pharmacoeconomics as the central price determination factor for Category 1 products also constitutes a significant and unwarranted federal intervention into provincial payer processes. Furthermore, it is unclear how the uncertainty inherent in pharmacoeconomic evaluations can be managed in the quasi-judicial regulatory context of the PMPRB.

The draft Guidelines introduce a de facto revenue control mechanism through the market size factor, which represents a major change to PMPRB's role with respect to the regulation of price ceilings. This revenue-based tiering approach also represents a significant intervention into provincial drug markets. Price is notionally tiered downward and the proposals do not acknowledge the possibility of significant market size reductions (e.g. due to changing market dynamics) or situations where forecasted market size is never achieved.

The complexity of the regime will challenge patentee compliance, which in turn may lead to a litigation-based regime where price ceilings will continuously be under investigation or subject to hearings. This will create an adversarial dynamic, to the detriment of both patentees and the PMPRB.

Consequently, the PMPRB should rethink its proposed approach. We note that the specific methods chosen by the PMPRB to implement the new economic factors are not strictly required by the regulations. An alternative approach is needed that is more consistent with the PMPRB's current regulatory methods and where the new economic factors do not play the central role in price determination. Discussion regarding potential alternatives should be a mandate of future expert technical working groups.

Lack of "grandfathering" – a more reasonable transition for existing and 'Gap' products is needed

Our industry has consistently advocated for the complete grandfathering of existing products to reflect investments already made in Canada. Grandfathering entails that existing rules apply to existing products and new rules apply to new products, which is a reasonable expectation given the business decisions made based upon patentee compliance with the current PMPRB regime, and at a time when the scope and impact of the new PMPRB regime could not have reasonably been foreseen. However, under the new system, no products have been truly "grandfathered". Rather, it would be accurate to state that, under the new system, some patented medicines are subject to all of the regulatory amendments, while others are not subject to the application of the new economic factors.

While we remain of the view that the complete grandfathering of existing medicines is necessary to reflect business decisions already made in Canada under the current PMPRB system, we remain open to discussing alternative transition measures. The draft Guidelines do not provide sufficient transition periods for existing products, including 'Gap' products (those products receiving a DIN after August 21, 2019 but before July 1, 2020), which is both unrealistic and unacceptable for innovative companies operating in Canada.[7]

At a minimum, a more gradual transition for existing products, including 'Gap' products, is needed. Existing products should not be subject to the accumulation of excessive revenues for the 2021 calendar year. For 2022 and subsequent years, we suggest that there should be fixed maximum annual price

reduction limits (e.g. no more than 5% negative list pricing impact per twelve-month period under the new regime). This should apply regardless of the policy tool or the specific price test applied in Guidelines.

For example, the PMPRB could benchmark a required total level of price reduction and require patentees demonstrate a 5% price reduction to be verified at the end of 2022, and so on, until the identified total price reduction requirement is met.[8] The industry also proposes no use of the non-excessive average price (NEAP) or maximum average potential price (MAPP) and no re-assessment of existing and 'Gap' products as defined above. We note that alternatives to the NEAP and MAPP could include publicly available list prices. Specifically, price reductions should not be required in cases where any available list price is already lower than the price target identified in July 2020. In other words, any prevailing list price already compliant with the price target should entail no required changes to allowable price. This could reduce the administrative burden for all parties. Appropriate transition measures, including specific transitional pricing sources, can be discussed further through technical working groups consisting of PMPRB staff and industry representatives. Ultimately, specific transition provisions must be clearly articulated in the final published Guidelines.

'Gap' products should be regulated in the same manner as existing products – in other words, they should not be subject to the new economic factors. This is a matter of fairness, since the business decisions required to introduce these products to market will have been made long before the finalization of a new regulatory regime. These products were launched under the existing PMPRB Guidelines and therefore should be grandfathered to the existing framework. Moreover, there is no regulatory requirement to apply the Guidelines to 'Gap' products in the same way as applied to new products . It will not be feasible to have multiple and different price ceilings for grandfathered products and their new indications. As such, grandfathering is also needed on a molecule basis and should, for example, apply to all new indications and line extensions of both existing products and 'Gap' products.

Proposals compromise the protection of confidential information

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. This is due to the introduction of a published specific pharmacoeconomic threshold equation and the availability of published public information (e.g. CADTH review reports, IQVIA data, and price lists) within a rules-based system. In other words, anyone will be able to calculate the MRP for a given product once CADTH documents are made public. This is unique internationally and is causing significant concerns within the international biopharmaceutical industry. It is our understanding that other jurisdictions, including the National Institute for Health and Care Excellence (NICE) in the UK (which has been referenced as engaging in similar practices as PMPRB proposals), does not in fact regulate in this manner. Other jurisdictions use pharmacoeconomic information as an input to price negotiation, rather than to establish a regulated price. Based on input from UK industry experts, it is clear that NICE does not allow third parties to back-calculate confidential discounts.[9]

The MRP methodology will facilitate the circumvention of the PMPRB's responsibility to protect confidential pricing information that must be submitted by patentees under the new system. Given the significant international sensitivity associated with this information, it is reasonably foreseeable that the current proposals will negatively impact future product launch decisions, which in turn will result in reduced or delayed patient access to innovative treatments in Canada.

No price tests should use the median of the therapeutic class

Currently, excessive prices through therapeutic class comparison (TCC) are benchmarked against prices in the same therapeutic class. As long as a new market entrant is not priced higher than the class price (i.e. the top of the TCC) it is not considered excessive. The status quo top of the TCC is the only TCC test consistent with an excessive price standard.

A median (current proposal) or average (previous proposal)[10] of a therapeutic class comparison is inconsistent with an excessive price standard because this would force products to be priced lower than similar priced products, even if comparators are clinically inferior. In other words, a price cannot logically be excessive if it is "not lower" than similar drugs.

The median TCC is an unreasonable test that is disconnected with the value and therapeutic improvement of a product. Furthermore, the inclusion of generic drugs is of concern in the context of a possible median TCC as opposed to the highest of the TCC. Pricing would be subject to market-mix dynamics unrelated to excessive pricing (i.e. how many products are available in a given therapeutic area, rather than price, or how clinically effective they may be). The PMPRB's proposal to remove therapeutic improvement assessments reinforces the need for the top of the TCC to remain the standard.

Appropriate price floors are needed for all products

There is a need for appropriate price floors for all products. The current PMPRB proposals provide an unreasonably low-price floor (lowest international price) and only for a subset of products. Patentees have significant concerns that the "lower-of" tests proposed will drive their pricing to the lowest of the PMPRB 11 schedule in many cases. We further note that 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, is inconsistent with an excessive price standard, and does not reflect Canada's economic status within the OECD. Consequently, a more reasonable international reference price floor should be applied. We would welcome a discussion on appropriate price floors for all products through technical working groups. At a minimum, a reasonable price floor should apply to all products.

An alternative approach to pricing and access for drugs for rare disease is needed

The new economic factors and MRP concept will prevent or delay the launch of drugs for rare diseases (DRDs) in Canada. The price setting methodology for rare diseases in the draft Guidelines is more restrictive than anticipated.[11] Third-party expert analysis suggests that the Guidelines proposal would require average price reductions of 82.8% for rare disease medicines. Regardless of the proposed minor market size adjustments for these products, the new economic factors and the MRP concept are inappropriate for addressing DRDs. Cost-effectiveness analysis does not reflect the value of these products to patients often due to data availability issues resulting from small patient populations. As a result, their cost-per-QALY estimates are far from the thresholds proposed by the PMPRB. There is a fundamental mismatch of the analytical tool and value that cannot be corrected through minor threshold adjustments. We would refer you to the case study below which illustrates some of the feasibility challenges specific to these products.

Our industry continues to work with the federal and provincial governments and other stakeholders on a common framework and pathway to address DRDs in a more holistic manner. We recommend a pause

and fundamental reconsideration with respect to the application of the new economic factors for all products including rare disease medicines.

Reassessment criteria should promote predictability

For the predictability and a more efficient use of resources, IMC recommends that reassessments should be conducted primarily on the basis of exceptional circumstances (for example, on a complaints-only basis). The current proposals involve broad criteria and will create significant unpredictability (e.g. new indication(s), market size change, prevalence change, line extension, HTA reassessment or any publicly funded cost-utility analysis published). We look forward to engaging further in technical working groups on this topic.

Continuity is needed for new indications and line extensions

The currently used method should continue to apply for the reasonable relationship test and additional formulations. The draft Guidelines would fundamentally alter the incentives for launching treatments for special patient populations. Changes in these areas have been proposed without a supporting rationale. As such, the currently used method for line extensions of existing products is both appropriate and necessary. (Please refer to case study 5 below for further discussion).

Ongoing role for Human Drug Advisory Panel (HDAP) in defining comparators

The Human Drug Advisory Panel has an ongoing role to play in defining clinical comparators. This is particularly the case where there may be disagreement between the patentee and PMPRB staff.[12] The current HDAP assessment process is imperfect. However, the present process for defining the relevant indication is the most pragmatic in the near term and preferable to the proposed alternative which lacks clarity.

International Therapeutic Class Comparison (iTCC)

The proposed approach for International Therapeutic Class (iTCC) comparisons has the potential to significantly impact many products and has not been previously discussed. IMC questions why products not available in Canada are relevant comparators for setting prices in the Canadian market. Given that many of the other draft Guidelines tools will significantly lower pricing in Canada, the rationale for an enhanced role for an iTCC is unclear. There is also a lack of predictability associated with the iTCC and the median of medians concept. Differing criteria, labels, and other factors in foreign countries make it extremely challenging for a patentee to determine and comply with an iTCC. We recommend that the PMPRB maintain the current policy for the use and application of the iTCC only to provide information in the context of an investigation into potentially excessive prices.

Jurisdiction and excessive price standard

As referenced above, the move to the median therapeutic class comparison is inconsistent with an excessive price standard, as is the market size tiering approach. The "lower of" test could drive Canadian prices lower than lowest international price (LIP) price in some cases, which is also inconsistent with an excessive price standard and Canada's international economic status.

We also disagree with the PMPRB's expansive view of its jurisdiction as reflected in the section on legal framework (Part 3).[13] The draft Guidelines set out an unbalanced view of its jurisdiction (e.g., references

to its consumer protection mandate to ensure that prices do not become "unaffordable" to the extent that "consumers are denied access to them".)

Tendered products

Based on current information, it is unclear how this regime can be applied to tendered products, such as vaccines. Further technical discussion on these products is needed. The PMPRB should provide case studies on how prices will be set for these products that consider various scenarios for changing market dynamics.

Process and Timing Concerns

Given the many issues set out above, IMC questions both the feasibility and desirability of finalizing the Guidelines package before July 1, 2020. As indicated in our letter dated September 10, 2019, there is no requirement to finalize the Guidelines by the effective date of the regulatory amendments. During previous substantive Guidelines changes, the PMPRB has taken appropriate time to work through highly technical amendments despite the fact that its powers were already specified in legislation and regulations. In other words, the proper implementation of the Guidelines can and should be completed over a longer time horizon. We note that previous Guidelines consultations prudently provided more time for the completion of comparatively minor revisions.

IMC also notes that an amended *Patentee Guide to Reporting* has not yet been released. As a result, basic information such as international price verification sources are missing, creating further uncertainty. Patentees cannot comprehend basic compliance requirements and proposed transition measures based only on currently published information. There will be insufficient time between the anticipated PMPRB Guidelines finalization in the Spring of 2020 and July 1, 2020 for patentees to change their reporting systems to comply with the new Guidelines. For companies with multiple products, reporting and information systems require many months of technical coordination and retooling, all at considerable time and expense.

In addition, it will be important for the PMPRB to provide detailed case studies on specific product scenarios to demonstrate how the regime could function, end-to-end, in practice. The high-level cases shared by the PMPRB on December 9, 2019, are not fit for purpose in this regard. The PMPRB has also not addressed stakeholder input to date including that of its own Technical Working Group, which called for further study of the new economic factors.

Conclusion

In summary, IMC submits that the draft Guidelines framework requires fundamental changes prior to implementation. This is essential to preserve timely patient access to new medicines for Canadian patients, and to avoid significant economic disruption within the life sciences sector. We would welcome an opportunity to engage with the PMPRB through technical working groups, to generate a final Guidelines package aligned with a set of reasonable core principles, specifically: predictability, fairness, and transparency; operational feasibility and efficiency; access to new medicines for Canadians, and the grandfathering, or appropriate transition, for in-market medicines.

APPENDIX: Case Study Examples

The following case studies are provided for illustrative purposes only and are not exhaustive of the many issues arising from the proposed draft Guidelines. The case studies focus on elements of the draft Guidelines that have not been previously discussed and which require further consideration through technical working groups.

The examples are as follows: 1a) a rare disease medicine unlikely to launch in Canada; 1b) a rare disease medicine subject to the PEP that is penalized following a one-time influx of units following reimbursement; 2) a medicine priced well below current comparators and with the potential to drive significant cost savings penalized due to the MRP concept and market size; 3) a medicine where the median domestic therapeutic class comparison drives its price to the lowest of the PMPRB 11 without regard for therapeutic advantages; 4) where the median PMPRB 11 can result in lower-than-generic pricing; and 5) examples of launch barriers created by the proposed changes to the Reasonable Relationship test.

Case 1a: Rare disease medicine unlikely to launch in Canada

Like many rare disease medicines, pharmacoeconomics is not a useful indicator for this product's potential value. In this case, given promising but limited clinical evidence due to a small patient population, pharamacoeconomics "does not allow for the determination" of an MRP.

1st sale:	Jan-2021
MIP:	$95,000
LIP:	$93,000
dTCC:	$8,000
iTCC	$7,800

The product is screened into Category 1 due to an annual cost of $95,000. As per the Draft Guidelines for situations without a PEP*, the price is set by the lowest among: 1) the lowest international price ($93,000); 2) the domestic therapeutic class comparison (dTCC) ($8,000); and 3) the international therapeutic class comparison (iTCC) ($7,800). Therapeutic comparisons are much lower due to older genericized comparators.

MIP	MRP
$95,000	➔ $7,8000

As such the MRP is $7,800 or just 8% of the PMPRB 11 median list price. This example illustrates a potential no launch scenario.

It should be noted that price reductions of this magnitude are not limited to rare disease medicines without a pharmacoeconomic analysis. As noted above, third party expert analysis suggests that PMPRB Guidelines would produce an average price reduction of 82.8% for rare disease medicines.[1]

*(p. 14) " If a patentee does not file a cost-utility analysis prepared by a publicly funded Canadian organization for a Category I patented medicine, or if the analysis submitted does not allow for the determination of the MRP as described above, the MRP may be set by using alternative methods. Such methods may include, but are not limited to:

The MRP being 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."

[1] *PDCI Market Access, 'Impact of the Draft PMPRB Excessive Price Guidelines' February 12, 2020.*

Case 1b: Rare disease medicine subject to the PEP is penalized following a one-time influx of units following reimbursement

This scenario employs similar assumptions as scenario 1a. The rare disease medicine is screened into Category 1 due to an annual cost of $95,000. However, in this case there is an available cost-effectiveness analysis to calculate a pharmacoeconomic price (PEP), and to apply a 1.5*PEP rare disease adjustment.

1st sale:	Jan-2021
MIP:	$95,000
LIP:	$93,000
dTCC:	$8,000
iTCC	$7,800
Time Horizon (yrs):	3
incremental QALYs:	0.30
Treatment Cost:	$93,000
Incremental cost:	$69,000
PEP:	$56,609
1.5*PEP:	$84,913
List Price = MLP:	$93,000

The PEP rare disease adjustment produces a price of $84,913. When public reimbursement is achieved in year 3, there is a one-time influx of units which causes the MRP to drop significantly to $65,448. However, as shown in the table below, this becomes the permanent price because there is no upward adjustment to MRP even when units drop significantly in subsequent years (e.g. in this case following the initial patient influx).

This case illustrates one of many challenges associated with the PEP and the MRP concept given potential real-world scenarios. It should be noted that this is an optimistic scenario for the PEP rare disease adjustment. According to third party expert analysis, the proposed adjustment for rare disease medicines appears to have only a limited mitigating effect (lessening the average impact from an 88.0% to an 82.8% price reduction from current non-excessive levels) and "is therefore unlikely to preserve meaningful product launch incentives" in the context of such significant price reductions.[2]

	2021	2022	2023	2024	2025
Actual Units=	50	150	500	50	50
Units * PEP =	$2,830,435	$8,491,304	$28,304,348	$2,830,435	$2,830,435
adj-MRP =	$84,913	$84,913	$84,913	$65,448	$65,448
MRP%=	91%	91%	91%	70%	70%

One time influx of units at reimbursement

MRP– No readjustments following a decrease in annual units sold or if realized revenues fall into a lower tier

[2] *PDCI Market Access, 'Impact of the Draft PMPRB Excessive Price Guidelines' February 12, 2020.*

Case 2: Medicine priced well below current comparators and with potential to drive significant cost-savings is penalized due to the MRP concept and market size

In this case, a new medicine offers significant cost-saving potential and is to be priced far lower than the existing domestic class price. It is not screened into Category 1 based on annual treatment cost but is Category 1 based on market size. Due to a current lack of clarity regarding PMPRB draft Guidelines, two scenarios must be considered by the patentee:

- Scenario 1: Per the Draft Guidelines (p.31) "if no [Pharmacoeconomic Price or PEP]" the Lowest between the Lowest PMPRB 11 (the LIP), the domestic therapeutic class comparison (dTCC) or the international therapeutic class comparison (iTCC) sets the price.
- Scenario 2: Per PMPRB staff's verbal representations that the MRP would be adjusted from the list price.

NOC:	**Nov 2020**
1st sale:	**Jan 2021**
MIP:	**$1,500**
LIP:	**$1,200**
dTCC at median:	**$2,000**
iTCC:	**$1,750**
MLP:	**$1,500**
List Price:	**$1,500**
Annual Cost:	**$18,000**

In this case, the Median of the PMPRB 11 price ($1500) would already produce significant cost savings in comparison to the current Guidelines. It is 75% of the price of its domestic therapeutic comparators ($2000) for currently available therapies. In either scenario, the maximum rebated price (MRP) that results is far below the price of the therapeutic class, per the median dTCC test (42% and 28% respectively). Both scenarios are inconsistent with an excessive price regulatory standard.

MRP is **42% lower** than **dTCC=$2K**

Scenario 1: As per Draft Guidelines (p. 31) = if no PEP- Lowest between LIP, dTCC or iTCC

	2021	2022	2023	2024	2025
Actual Units=	8,000	19,000	30,000	60,000	80,000
GROSS Market Size (LP) =	$12,000,000	$28,500,000	$45,000,000	$90,000,000	$120,000,000
PEP (LIP)=			**$1,200**	**$1,200**	**$1,200**
adj-MRP =			$1,200	$1,163	$1,122
Max Rebated Sales (adj-MRP) =			$36,000,000	$69,800,000	$89,733,333
MRP%=			20%	22%	25%

MRP is **28% lower** than **dTCC=$2K**

Scenario 2: Potential PMPRB intention= MRP adjustment off the List Price

	2021	2022	2023	2024	2025
Actual Units=	8,000	19,000	30,000	60,000	80,000
GROSS Market Size (LP) =	$12,000,000	$28,500,000	$45,000,000	$90,000,000	$120,000,000
PEP (LP)=			$1,500	$1,500	$1,500
adj-MRP =			$1,482	$1,433	$1,392
Max Rebated Sales (adj-MRP) =			$44,447,368	$86,000,000	$111,333,333
MRP%=			1%	4%	7%

This example demonstrates the lack of clarity within the draft Guidelines. It also remains unclear when the Category 1 MRP calculation is triggered: at launch based on estimated sales, or when actual sales exceed the threshold. It should be noted that no regulatory pricing policy should be triggered based on theoretical estimates of unit sales.

Potential Impact:

- This medicine's price ends up well below international pricing standards, and far below the median PMPRB 11 and the iTCC.
- This medicine experiences between a 28 % and a 42% price reduction relative to current comparators, which are potentially inferior from a therapeutic perspective.
- Pricing does not reflect potential therapeutic benefit versus the domestic therapeutic class comparison. There is no recognition of innovation or payer needs, and no connection with an excessive price regulatory standard.
- If the medicine is delayed or not launched, significant health system cost savings will not be realized.

This case illustrates one of many concerns with the implementation of the MRP concept and market size factor. As illustrated by the table below, when compared to existing therapeutic options, substantial savings would be achieved through the MLP alone, prior to application of the new economic factors.

Savings under the MLP (versus dTCC)

2021	2022	2023	2024	2025
$4,000,000	$9,500,000	$15,000,000	$30,000,000	$40,000,000

Case 3: Median domestic therapeutic class comparison drives price to the lowest of the PMPRB 11 without regard for therapeutic advantages

This example is of a patented medicine that would have been categorized as a moderate therapeutic improvement under the current PMPRB system given that it provides tangible patient benefits over existing therapies by decreasing side effects.

The case illustrates what would appear to be a frequent issue under the proposed regime – namely, the policy change from the highest of the dTCC to the median of the dTCC will drive many products to the lowest of the PMPRB 11 (LIP) price.

dTCC (highest)	**$1.37**
dTCC (median)	$0.2669
MIP	$1.35
LIP	$0.94
Resulting final MLP	$0.94

The table below is provided to illustrate the complexity of establishing the median dTCC given multiple innovative products and generics. The Guidelines do not precisely specify how the price of generic comparators will be incorporated into the dTCC. It should be noted that under the proposals, the PMPRB would seem to have very broad discretion (see page 25 of the Draft Guidelines) in choosing lower priced comparators in a TCC, and as a result, to drive prices to the LIP.

Under a median dTCC, (as opposed to the current highest of the TCC) the stakes for defining comparators are much higher. For example, the result of the dTCC in this case ($0.2669) is unreasonable for an innovative product and disconnected from its value and therapeutic improvement. Comparator decisions are likely to be routinely subject to challenges, increasing disputes, investigations and potentially hearings. Industry anticipates that this case is not an exceptional example, but rather is broadly illustrative of potential future challenges. The lowest of the PMPBRB 11 should not become Canada's de facto pricing standard for many new products. The proposed median therapeutic class comparison test should be discontinued, and the existing top of the TCC test is more consistent with an excessive price standard.

Product	**Brand Price**	**Generic Price**
A 20mg	$1.397	$1.1827
B 10mg	$1.337	$0.4685
C		$0.2387
D	1.2710	
E 30mg		$0.075
F 0.25mg		$0.2669
G	$0.2412	$0.0699
H 100mg		$0.0989
Median	$0.2669	

Case 4: PMPRB Proposal for Median PMPRB 11 can result in lower-than-generic pricing

In this example, an existing patented medicine launched prior to August 2019 is rapidly becoming the standard of care (most prescribed by specialists) due to meaningful improvements over existing products in the therapeutic class. PMPRB proposes to re-benchmark all existing products to the median PMPRB 11 without any assessment of degrees of therapeutic improvement as practiced under the current Guidelines. As such, the new innovative product must be priced significantly lower than the generic price of an older product. This is a disease area where generic entry is low for various reasons (e.g. lack of incentives due to low margins).

Existing Product A price per unit	**Generic price per unit**	**Existing Innovative Product B price per unit post-PMPRB implementation (Median PMPRB 11)**
$8.0	$6.0	$4.5
		-40% price reduction from current list price though there is no demonstrable patent abuse

In this scenario, the Regulations and Guidelines used to establish the price and make launch and investment decisions have been changed mid-stream, compromising regulatory fairness and predictability. The proposals also present a pricing regime that is inconsistent with PMPRB's mandate as a safeguard against patent abuse and excessive pricing since it forces the patented medicine's price well below comparable generics.

Potential Impact:

- Product B faces ~40% reduction from its current list price which results in below-generic pricing
- No reflection of value as part of the price.
- The scenario further exacerbates a limited attractiveness of therapeutic class for generic entry
- It should be noted that this scenario presents impacts to an existing product but could equally apply to a new product.

Further discussion through technical working groups is required. Grandfathering for existing products would be most appropriate. At a minimum, a grace period plus a stop-loss including percentage limits on total annual price decrease from current list price should be undertaken (see discussion above). For future drugs, there should be ongoing use of therapeutic improvement assessment to establish pricing.

Case 5: New Reasonable Relationship test changes create launch disincentives

This case illustrates the challenges associated with significant changes to the Reasonable Relationship test under the draft Guidelines.* In cases of multiple strengths, launch of some of those strengths would be put at risk due to the adverse incentives created.

Context	Case study	Current Guidelines	Proposed Guidelines	Impact
Multiple strengths	New oncology molecule for indication A – 50mg – 75mg – 100mg • 100mg is main dose; 50mg and 75mg used for pediatric/older patient population or titration purposes • PMPRB11 launching all strengths at $1.00 (flat price)	Flat pricing is permitted. 100mg = $1.00 75mg = $1.00 50mg = $1.00	Mandatory linear pricing. 100mg = $1.00 75mg = **$0.75** 50mg = **$0.50**	• Launch of lower strengths is compromised in Canada. • $0.50 vs $1.00 brings price lower than PMPRB 11 pricing for those strengths
New Relevant indication	New Relevant indication received with new strengths • Original indication A = 20mg set at $20 by dTCC • New Relevant indication B = 20mg and 40mg (new) where dTCC = $20	Maximum usual recommended dosage + Flat pricing is permitted. 20mg = $20 40mg = $20	Maximum usual recommended dosage + Mandatory linear pricing. 20mg = **$10** 40mg = $20	• The 50% price decrease for 20mg will create a significant misalignment with treatment prices for dTCC of indication A and international pricing (lower than PMPRB11). • It may compromise commercial viability of the 20mg and compromises the launch of the 40mg in Canada • It may also compromise the launch of other competitive molecules in indication A given the new lower price thresholds.

Significant implications will result from imposing prices equivalent to the price per standard unit of the existing strength and no longer maintaining the three different Reasonable Relationship tests under the current Guidelines:

1. The draft Guidelines no longer allow multiple DINs to be launched at price parity which would place Canadian prices lower than many OECD countries. This could create significant and unnecessary disincentives to launch lower (or higher) dosages needed for addressing titration, stronger dosages or special patient populations.
2. Where a new strength is being introduced at the same time as a new relevant indication, this could force the prices of lower strengths used as main strengths for other indications to be decreased to a fraction of their original price. As other therapeutic comparators may not all launch the same indications, this would create significant misalignment of therapeutic prices which could make it difficult for the patentee to launch a new indication. It would also indirectly

compromise the launch of other competitive molecules in the original indication given the new lower price thresholds. The lower price would also be lower than the PMPRB 11 countries, creating a further disincentive to launch in Canada.

*(Appendices XIII-B, P. 27) " When a new strength of a medicine that is currently sold in Canada is introduced and meets the above requirements of the RR test, the MLP or MRP of the new strength will be set to be equivalent to the price per standard unit of the existing strength(s). This approach will also be applied when multiple strengths of a new medicine are first sold simultaneously and some strengths are identified specifically as loading, titration, or reduction doses.

*(*Appendixes A, P. 26) *Comparable dosage regimens:* The comparable dosage regimen used for comparison purposes will normally be the maximum of the usual recommended dosage in the Product Monograph (or similar information) taking into account relevant clinical variables.

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

[2] PDCI Market Access, 'Impact of the Draft PMPRB Excessive Price Guidelines' February 12, 2020.

[3] See: 1) our submission to the PMPRB October 2016 (link); 2) our February 2018 response to Canada Gazette Part II (link); 3) our on the record comments as part of the PMPRB's steering committee (link) and technical working group (link); and other verbal representations.

[4] Products receiving a DIN between August 21, 2019 and July 1, 2020.

[5] PDCI Market Access, 'Impact of the Draft PMPRB Excessive Price Guidelines' February 12, 2020.

[6] See: February 2018 response to Canada Gazette Part II (link) and our on the record comments as part of the PMPRB's technical working group (link).

[7] Those products launched between August 21, 2019 and July 1, 2020

[8] After a transitional price verification in July 2021, PMPRB could move to annual price verification process at the end of each calendar year.

[9] NICE has two types of patient access schemes (PAS), which involve either simple or complex discounts from the published list price to satisfy cost-effectiveness. The United Kingdom does not regulate list prices as proposed by the PMPRB. When NICE agrees to use a simple PAS from the published list price, the discount is confidential and the resulting ICER after accounting for the discount is not published if it would mean that

the discount could be calculated. When NICE agrees to use a complex PAS from the published list price (e.g., a manufacturer might supply free product up front or upon progression), the general details of these schemes and the resulting ICERs are published, but it is not possible to back-calculate discounts. This is because there is no linear relationship between the price and the resulting ICER.

[10] We would refer you to our previous commentary on why average (or median) TCC is inappropriate.

[11] In some cases, PMPRB proposed price tests may require list price ceilings lower than the lowest international price of the PMPRB11.

[12] The proposed move from the highest in the TCC to the median dTCC poses significant challenges as this will increase the stakes and potential disagreements between PMPRB and the patentee as to whether specific comparators belong in the therapeutic class. This also decreases predictability.

[13] Despite quoting from the Galderma FCA decision elsewhere in the Draft Guidelines, PMPRB fails to acknowledge how the Court in that case described the Board's regulatory mandate as follows: "The Board's mandate is to ensure that the statutory monopoly granted to patentees of medicines is not abused by excessive pricing of those medicines." (See Canada v. Galderma, 2019 FCA 196, para 10).