PDCI | MARKET ACCESS

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Dr. Mitch Levine
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Re: Response to PMPRB Draft Guidelines Consultation

Dear Dr. Levine,

On behalf of PDCI Market Access Inc. ("PDCI"), I would like to thank you for the opportunity to provide written comments as part of the Patented Medicine Prices Review Board (PMPRB) Draft Guidelines Consultation process.

PDCI is a Canadian pharmaceutical pricing and reimbursement consultancy with core expertise in pharmaceutical pricing, health technology assessment (HTA), clinical and pharmacoeconomic evaluations and modelling. Since 1996, PDCI has provided its advice and expertise to Canadian and global pharmaceutical manufacturers to help navigate the complexities of Canadian pricing and market access landscape with the goal of achieving timely access to the market.

Since discussions about potential PMPRB price reforms began in 2015, PDCI has conducted significant analysis to understand and assess the impact of the proposed changes. In short, the proposed changes as outlined in the Draft Guidelines will make many patented medicines commercially unviable in the Canadian market.

PDCI has witnessed first-hand the unintended consequences the proposed reforms have already had, and will continue to have, on industry's decisions to bring innovative medicines to the Canadian market. It may well be that the PMPRB does not intend to force list prices of most new patented medicines to the lowest international price and rebated prices even lower, however, that is the unescapable conclusion when the Draft Guidelines are applied in their current form. We are hopeful that the PMPRB's consultations will be meaningful and address these concerns.

It would be helpful if the PMPRB could express a clear policy objective in terms of where Canadian prices of patented medicines on average should be relative to international prices. The PMPRB's current policy objective is that Canadian prices, on average, should be at the median of the seven reference countries and that no product should be priced beyond the highest international price (of the seven reference countries).

The initial focus of the PMPRB pricing reforms was on the Organisation for Economic Co-operation and Development (OECD) median as a more appropriate target or policy objective for prices of patented

medicines in Canada. And given that the PMPRB's new reference countries (PMPRB11) are a clear proxy for the OECD, it is a reasonable expectation that the PMPRB reforms would establish a policy objective that prices of patented medicines on average should be at the median (of the PMPRB11) with no price higher than the highest price in the PMPRB11. Indeed, this was an inherent assumption of the Health Canada Regulatory Impact Analysis Statement (RIAS) and Cost-Benefit Analysis (CBA).

Yet, under the Draft Guidelines, the median international price has replaced the highest international price as the price ceiling. As a result, prices of patented medicines will on average be lower than the median international price (of the PMPRB11) and, as our impact analyses have demonstrated, list prices for many new patented medicines will be forced to the lowest international price and rebated prices even lower.

To contribute to the PMPRB's consultations, we offer what we hope will be received as constructive feedback and suggestions regarding how the Draft Guidelines may be amended and to acknowledge the underlying goal of the PMPRB reforms (i.e., lower drug prices) but at the same time ensuring that the Guideline changes are reasonable and that the reforms do not deter manufacturers from bringing innovative products to Canada.

Summary Recommendations:

- **Bilateral Working Groups.** PMPRB should establish bilateral technical working groups with pharmaceutical patentees to revise and refine the Draft Guidelines. Patentees have identified dozens of significant issues, and unanswered questions which PMPRB must consider and address before finalizing the Guidelines. Bilateral working groups are the most effective way of ensuring the Guidelines are practical and workable.
- **Patentees' Guide to Reporting.** PMPRB should publish an updated Patentees' Guide to Reporting to provide patentees with clear guidance on how to report international prices and the new factors outlined in the amended Regulations that were published in August of 2019.
- **Sources of International Prices.** The PMPRB should provide specific publicly available sources which it intends to use for purposes of price verification as well as any backing-out calculations.
- **Prevalence.** The references to "prevalence" in the Draft Guidelines should be replaced with "estimated patient population".
- **Human Drug Advisory Panel (HDAP).** The PMPRB should clarify the role of the HDAP under the PMPRB's scientific and price review procedures. PDCI recommends that the HDAP have a role like that under the existing Guidelines, including establishing primary indication, determining level of therapeutic improvement, and determining relevant comparators and comparable dosing regimens.

- **Recognizing Therapeutic Improvement.** Under the Draft Guidelines there is no consideration of therapeutic improvement as there is under the current Guidelines. The Guidelines should consider clinical evidence and therapeutic improvement when establishing maximum non-excessive prices.
- **Pharmacoeconomics.** Estimates of pharmacoeconomic value (e.g., $/QALY) are fraught with uncertainty and should not be used formulaically to set price ceilings, but rather to inform as a secondary factor (for investigations, hearings), as a screening tool or to trigger a specific price test under the Guidelines.
- **Market Size.** The market size factor should not be applied as a direct price regulation tool, but rather as a secondary factor (for investigations, hearings), as a screening tool or to trigger a specific price test under the Guidelines.
- **Therapeutic Class Comparison (TCC).** The Guidelines should maintain the current TCC test at the level of the highest priced comparator and not the median TCC as proposed under the Draft Guidelines.
- **Rebated Price.** The calculation of maximum revenue based on units and the pharmacoeconomic price (PEP) is inappropriate and illogical. By including free goods in the calculation of market size, the PMPRB is creating a disincentive for patentees to provide free goods to patients. Analyses based on maximum revenue should rely on manufacturer reported net revenues, not on an artificial derivation of revenue.

As indicated above, PDCI has identified several important issues with respect to the **practicality and feasibility** of the Draft Guidelines. These issues include:

Application of the pharmacoeconomic (PE) price is impractical (sometimes impossible) and often its results are illogical.

- It's unclear whether the relevant comparators and assumptions for the HTA PE analysis and PMPRB analysis would be aligned. Relevant comparators to a drug from an HTA perspective include all treatments that are currently used in the same population in Canadian practice, whereas relevant comparators to a drug from a PMPRB perspective typically include those in the same 4th level ATC class and those with the same approved indication. In addition, assumptions in the HTA PE analysis are typically informed by clinical trial data, whereas the PMPRB will rely on Health Canada product monographs and clinical practice guidelines to inform dosing assumptions. Also, comparator products launched during the Canadian Agency for Drug and Technologies in Health (CADTH) review would not be considered in the CADTH analysis. This would make CADTH's review of the pharmacoeconomic evidence incomplete for PMPRB's purposes.
- Often the reimbursement request for HTA purposes can be narrower than the Health Canada approved indication. Populations considered in cost-effectiveness analyses by Payers may therefore differ from the broader product monograph indication. These narrower groups would

be relevant for CADTH and *Institut national d'excellence en santé et en services sociaux* (INESSS) analyses, but PMPRB's relevant indication for purposes of price regulation could be quite different, making reliance on the CADTH review of the pharmacoeconomic evidence impractical.

- Sequential incremental cost-effectiveness ratios (ICERs) rank products based on increasing total costs, then produce cost-effectiveness results to the next most costly alternative, excluding all comparators that are either dominated or extendedly dominated. It is unclear how to apply PMPRB's PEP formula in the case of sequential ICERs.

There are several concerns surrounding what information will be made available from CADTH to inform PMPRB's analyses of PEP.

- Information required for PMPRB's formula is not currently available in CADTH's reports. One can accomplish the same goal by alternative means for Common Drug Review (CDR) reviews, but not for pan Canadian Oncology Drug Review (pCODR) reviews. PMPRB's new use of CADTH information will therefore require changes to how both CDR and pCODR publish the "total treatment cost" over the time horizon of a model discounted to net present value.
- Questions remain about the timelines surrounding when PMPRB will be performing its tests. Will PMPRB have the information it needs from CADTH by then? Due to the increased importance CADTH reviews will have in supporting price regulation decisions, manufacturers will be placing more burden on CDR/pCODR processes to ensure appropriate outcomes.
- It is unclear where numbers for subpopulations originate. When CADTH reports on subpopulations, one must have robust epidemiology data to perform weighted average calculations of the ICER among the subpopulations. However, this information is not available in CADTH reports and it is often difficult to obtain. This is concerning, as the PMPRB intends to use these values in calculations that may have a large impact on the rebated price.

These comments are just a few examples that highlight why PE models developed to inform HTA decision-making are not fit-for-purpose by PMPRB in ensuring Canadian medicine prices are not excessive.

"Prevalence" should be replaced with "estimated patient population"

- The Draft Guidelines refer to "prevalence" which has a very specific epidemiologic meaning and is not relevant to all therapeutic areas (in some cases "incidence" is more relevant). Moreover, to the extent there is published evidence on prevalence it is often expressed as a range, with ranges varying across jurisdictions. Accordingly, references to "prevalence" in the Draft Guidelines should be changed to "estimated patient population" specific to the approved indications of the patented medicine.

- Prevalence is also referenced in the Draft Guidelines as a tool for assessing whether a drug treats a rare disease. Evidence supporting the assessed prevalence of rare diseases must be rigorous as it could have significant effects on the regulated price.

PDCI's experience working with both the current and proposed new Draft Guidelines have also revealed several technical issues with the proposal as written.

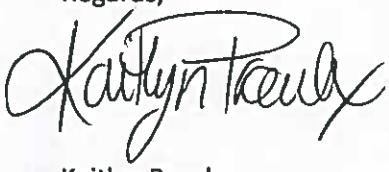
- Many clients have enlisted our services to assess price potential for new products under the Draft Guidelines. Often, we have been unable to provide complete advice, as required information is not available or calculations of maximum prices are well below what is commercially viable, and well below what PMPRB Staff have claimed to be the intended result.
    - For example, PDCI has analyzed the expected impact of the PEP on dozens of medicines. For products currently in market, and compliant with the current PMPRB Guidelines, the PEP assessment suggests price reductions of 50%-90% would have been required under the proposed Draft Guidelines.
    - Patentees have presented this evidence to the PMPRB Staff who have noted on several occasions that it's not their intent to see prices reduced by 90%, however this is what occurs when applying the Draft Guidelines as written. It is imperative that the use and calculation of a PEP be reassessed and if amended, subject to additional consultations.

PDCI is encouraged by a few welcome changes to the Guidelines, such as the cessation of incidental investigations caused by changes to the class of customer, and that PMPRB intends not to regulate rebated prices for Category II medicines.

PDCI is hopeful that the PMPRB will consider these concerns and recommendations seriously as it revises its Draft guidelines and makes the changes necessary to prioritize access to innovative medicines in Canada.

Please do not hesitate to contact me should you have additional questions concerning the information enclosed.

Regards,



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