24 October 2016

Dr. Mitchell Levine
Vice-Chairperson, Patented Medicine Prices Review Board
Rethinking the Guidelines
Box L40, 333 Laurier Avenue West, Suite 1400
Ottawa, ON K1P 1C1

Subject: Patented Medicine Prices Review Board (PMPRB) Guidelines Modernization

Dear Dr. Levine,

The Canadian Association of Provincial Cancer Agencies (CAPCA) provides a forum for the leaders of Canada's cancer care system to focus on issues that affect the delivery of cancer care in Canada. We are concerned about the sustainability of cancer drug funding programs across Canada so are working together to ensure that patients are able to access the most effective cancer drugs in a timely fashion. Ensuring that the price of patented drugs in Canada is an important mechanism for ensuring that sustainability and access are preserved. Our submission addresses six general issues as well as nine of the twelve questions posed in the PMPRB Guidelines Modernization Discussion Paper.

A. OVERARCHING OBSERVATIONS AND RECOMMENDATIONS

1. PMPRB's focus should be the prevention of excessive patented drug pricing in Canada.

While PMPRB was established to stimulate patentee's investment in research and development (R&D) in Canada while simultaneously monitoring and acting on excessive drug pricing, concerns about the future sustainability of provincial cancer drug funding programs requires a singular focus: controlling excessive pricing. To do so requires an ability to compare actual prices rather than the publicly posted price of a drug, net of all rebates and discounts.

RECOMMENDATION

1.1 PMPRB pursue options to gather actual patented drug pricing and encourage those in comparator countries to do the same for the purposes of identifying, managing and ideally preventing excessive drug pricing.

1.2 PMPRB consider whether other ways of stimulating R&D in Canada might be more effective than the current approach.

2. The list of comparator countries (PMPRB7) is narrow.

It is unclear to us why the United States should remain among PMPRB7. Given the extraordinarily high price of pharmaceuticals in the United States, its presence skews the perception of excessive pricing and the introductory price of new cancer drugs. It is also unclear to us why PMPRB is limited to a comparison with only seven countries when several that are not currently among PMPRB are attempting to implement innovative approaches (e.g. indication specific and weighted average pricing).

RECOMMENDATION

2.1 PMPRB consider removing the United States from PMPRB7. If that is not possible, it is desirable that PMPRB lessen the impact that the price of cancer drugs in the United States may have in Canada.

2.2 PMPRB expand the list of comparator countries (hereafter PMPRB7[2])

2.3 PMPRB should confirm and clearly describe how innovative approaches that occur outside the list of comparator countries would be evaluated for relevance in Canada.

3. **PMPRB's approach to value based pricing could be enhanced.**
   By tying the introductory price of new patented drugs to the level of therapeutic improvement (Guideline, Section C11.3-C11.7, pages 26-27), PMPRB has begun to address value based drug pricing. However, the current pricing processes do not reflect changes in the use of a drug over time (See: Example #1). Moreover, PMPRB's current approach does not allow the price of a drug to be re-assessed if the promise of a new cancer drug does not resemble actual patient outcomes in the general population (versus clinical trial setting).

Example #1: *Nivolumab (Opdivo) was first approved as a treatment for metastatic melanoma, a relatively small patient population. However, in spite of the subsequent addition of a second indication for a considerably larger patient population, neither the price of the drug nor the determination of what price would be considered "excessive" were affected.*

RECOMMENDATION

3.1 PMPRB conduct a policy assessment of additional value-based pricing models used in high, medium, and possibly low resource countries to determine possible enhancements to existing PMPRB value-based pricing.

3.2 PMPRB consider amending its pricing processes to allow the re-evaluation when use of the drug may change to enable the re-evaluation of pricing based on an assessment of real world evidence of a drug's effectiveness.

4. **Retrospective assessment of excessive pricing and annual increases leave payers open to significant budget risk**

PMPRB currently investigates whether the price charged by a patentee was excessive after the drug was sold at that price, rather than before the price was imposed. A significant enough price increase may require trade-offs to balance an institution's cancer drug budget, which may include the use of less expensive and/or potentially less effective cancer medicines. Similarly, automatic allowable price increases in accordance with the CPI adjustment methodology allows the price of a patented drug to gradually and continuously creep towards the highest price in PMPRB comparator countries.

Excessive pricing may be an area of particular concern for drugs accessed through the Special Access Program or during periods of transition (from SAP to Orphan Drug Status or following changes in the distributor in Canada). These situations should be addressed by PMPRB to ensure that all appropriate mechanisms and safeguards have been put in place to prevent the need to control excessive pricing.

Example #2: *On August 24, Baxalta, Inc. issued notification of an immediate price increase of the pegasparaginase (ONCASPAR®) from $4,494 to $13,467.17 per vial, an increase of more than $12 million across Canada. Only after multiple discussions over several months with many clinical and pharmacy experts was the option of launching an investigation for excessive pricing ever raised. Moreover, the actual hearing is scheduled to occur 15 months after the price increase.*

Example #3: *Between 2013 and 2015, access to carmustine for injection (BiCNU®) transitioned from Bristol Myers Squibb, to Special Access Program, to a new distributor (Heritage Pharmaceutical). Over that period, the price of the drug increased from $200 / 100 mg vial to $4,965.14 / 100 mg vial.*

Example #4: *On January 12, 2015 the price of dactinomycin (COSMEGEN®) 0.5 mg injection increased from $9.12 to $300 / vial when a new importer, Recordati Rare Diseases, was announced.*

RECOMMENDATION

4.1. PMPRB consider amending its processes so the introductory price and annual allowable increases are approved proactively for some or all cancer drugs.

4.2. PMPRB establish benchmarks for the maximum allowable duration of an investigation. Where possible these benchmarks should push for completion of the investigation and return of excess revenue charged in the same fiscal year in which excessive pricing occurred.

5. **Excessive revenue repayments are misdirected.**

The Patent Act, Section 83(2)(c) and 83(3)(c), can direct a patentee to repay excess revenue to Her Majesty. While this excess revenue could be returned to the provinces, there is no explicit expectation of repayment.

RECOMMENDATION

5.1. At least 50% of any repayment of excess revenue should be returned to the province(s) that can confirm purchases during the period of excessive pricing.

6. Greater emphasis on driving prices toward the lower end of PMPRB7[2] countries.

Given very substantial concern about the sustainability of cancer drug funding in Canada, an assessment of the areas where changing the language is most likely to result in actual lower introductory prices should be completed. For example, for drugs that offer substantial improvement would a shift in language from "higher of: 1) top of the TCC test comprised of all drug products" to "middle of" or "average of lowest three PMPRB7[2] comparator countries" may have a meaningful impact on drug expenditure.

RECOMMENDATION

6.1 PMPRB conduct an assessment of downgrading language in the Compendium to reflect a desire to be among the lowest (e.g. lowest 1/3) of PMPRB7[2] countries.

B. PMPRB QUESTIONS FOR DISCUSSION

Question #1: What does the word excessive mean to you when you think about drug pricing in Canada today (additional text not included)?

The price of a drug should be considered excessive if it exceeds the agreed upon cost and if the actual clinical outcomes would place the drug in a lower category of clinical outcome (e.g. breakthrough to substantial, etc). Having said that, the following would generally be considered acceptable:

- A situation where a small proportion of cancer drugs cost exponentially more than other cancer drugs because they bring a similar degree of exceptional value over existing drugs (e.g. reduction in administration frequency from lengthy biweekly infusions requiring hospitalization to outpatient administration every three months).
- As cancer care and possibly healthcare moves from blockbuster to high specialized drug treatments, PMPRB and payers will need to be cognizant of the system AND individual impact of exceptionally expensive drugs on provincial drug budgets and affordability. One or two exceptionally high priced drugs may be affordable but the cumulative effect of several of them may not be.
- Where the cost of a drug is similar to the cost of other drugs that treat the same disease and if the drug is also deemed to be affordable based on an assessment of the size of the potential population to treat, duration of treatment, and cumulative drug budget impact.

Question #2: Given that it is standard industry practice worldwide to insist that public prices not reflect discounts and rebates, should the PMPRB generally place less weight on international public list prices when determining the non-excessive price ceiling for a drug?
Yes, less weight should be placed on the public price of a drug. In fact, this is one of the most important aspects of PMPRB's work. Until comparisons of actual pricing can occur, the impact of PMPRB and its ability to identify and control excessive pricing is muted. International cooperation is needed to change the culture of allowing confidential pricing agreements. In the meantime, the actual cost of cancer drugs should be made available confidentially to organizations like PMPRB that are responsible for determining whether pricing is excessive.

Question #3: In your view, given today's pharmaceutical operating environment, is there a particular s. 85 factor that the Guidelines should prioritize or weight more heavily in examining whether a drug is potentially excessively priced?
The factors that the PMPRB should consider most important and weigh more heavily in examining whether a drug is potentially excessively priced are cost of existing drugs used to treat the same disease and comparison of price in other jurisdictions (within Canada and between countries). More broadly, PMPRB should conduct an assessment of the impact of voluntary compliance with its pricing policies, particularly in areas other than healthcare.

Question #4: Should the PMPRB set its excessive price ceilings at the low, medium or high end of the PMPRB7 countries?
If PMPRB accepts that its policy objective should not only be to prevent excessive pricing but to ensure sustainable drug pricing in Canada, the excessive price ceilings should be at the lower end of the group of comparator countries. PMPRB should consider removing the United States from the existing list of PMPRB7 comparator countries or at least lessening the statistical impact of often substantially higher US prices relative to all other PMPRB7 countries, and should also consider expanding the list of comparator countries as previously addressed in this submission.

Question #5: Does the amount of research and development that the pharmaceutical industry conducts in Canada relative to these other countries impact your answer to the above question and if so, why?
Research is vital to the future of cancer control, and measures to support a vibrant research community in Canada will ensure that Canadians will have access to innovative treatment approaches. If one forgoes the possibility that PMPRB is operating under two competing ineffective policy objectives (ensure prices aren't excessive and stimulate R&D investment in Canada), yes excessive price ceilings should have some correlation with the level of R&D.

Question #6: What alternatives to the current approach to categorizing new patented medicines (based on degree of therapeutic benefit) could be used to apply the statutory factors from the outside and address questions of high relative prices, market dynamics and affordability?
PMPRB should consider integrating affordability thresholds, real world evidence, budget impact, and volume based possibly indication based or weighted average pricing. Moreover, PMPRB should consider introducing flexible pricing processes to allow the re-evaluation all relevant price tests when volume increases (multiple indications leading to substantially increases in volume or when the drug is added to other treatment regimens for doublet or triplet combination therapy) or when research suggests significantly longer duration of therapy than was apparent when the drug was introduced to the Canadian market.

Question #8: Should the price ceiling of a patented drug be revised with the passage of time and, if so, how often, in what circumstances and how much?
Yes, PMPRB should consider a flexible, responsive pricing system that allows the price tests (including ceiling price) to be regularly re-evaluated. This would allow evidence of the real world effectiveness of a drug to be considered, which may suggest a reduction in price if outcomes are below what clinical trials initially promised or higher pricing if outcomes prove to be substantially better. Similarly, when there is an increase in the number of sales (for original indication or multiple indications), all relevant price tests, but particularly the price ceiling, should be re-evaluated.

Question #9: Should price discrimination between provinces/territories and payer types be considered a form of excessive pricing add, of so, in what circumstances?
Price discrimination between provinces/territories demonstrates that excess margins exist somewhere in the system. However, to adequately determine the degree to which price discrimination and excess margins exist, prices used in comparisons must be net of all subsidies, rebates, discounts, etcetera.

Question #11: Should the changes that are made to the Guidelines as a result of this consultation process apply to all patented drugs or just ones that are introduced subsequent to the changes?
The changes should apply to price increases and the introductory price of new drugs, but if the resources required to comprehensively address all existing drugs are available, PMPRB should consider application of the changes to drugs for which affordability may be an issue (exceptionally high cost drug with medium to large patient population, for example) and moderate to low clinical benefit.

Finally, though the consultation did not invite comment on the following issues, PMPRB may wish to consider:

1. Enhancing the Human Drug Advisory Panel (HDAP) to include cancer experts, particularly given the trend toward increasingly specialized cancer treatment. Failing that, PMPRB may wish to explore a collaboration with the Canadian Agency for Drugs and Technologies in Health's pan-Canadian Oncology Drug Review given the extensive work their clinical guidance panel does to determine the clinical impact of new cancer drugs.
2. How affordability, in addition to cost effectiveness, could be included into PMPRB drug pricing processes.
3. Whether compulsory listing could be used in exceptional circumstances to address imbalances caused by the patent system.

If we can provide any additional background or you would like to discuss these issues in person with either of us or with the Chair of CAPCA's Board of Directors, Dr. Michael Sherar, please do not hesitate to let us know.

Respectfully,

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