

Questions for Discussion

As a first step in giving effect to its duty to consult under section 96(5) of the Act, the PMPRB is asking the following series of questions designed to initiate the discussion on Guidelines modernization. The feedback received in response to these questions will inform the initial phase of the PMPRB's consultations process, as explained previously under the "What are we doing?" section of the paper.

- 1) What does the word "excessive" mean to you when you think about drug pricing in Canada today?
For example:
 - a) Should a drug that costs more annually than a certain agreed upon economic metric be considered potentially excessively priced?

Although it is reasonable for drugs that cost more than an agreed upon metric to be considered 'excessive', defining the economic threshold is challenging and requires in-depth discussion. For example, "excessive" drug pricing should not be defined solely by economic/ financial markers. To determine whether a drug price is "excessive", consideration should be given to the cost effectiveness of the drug, whether there are similar/ comparable drugs that offer similar benefit and the price of those comparable drugs. Other factors that also should be considered include socio-economic factors, affordability with respect to gross national product, customizable product analysis, and market dynamics/distortion in (especially for expensive drugs).

In addition to including comparable health care systems to Canada (e.g. Australia) when conducting price comparisons, the pCPA also suggests that PMPRB use the lowest international price (or average/median among basket of low-priced countries comparable to Canada) to assess the price differential and exclude the comparator country with the highest price from the comparison.

- b) Should a drug that costs exponentially more than other drugs that treat the same disease be considered potentially excessive?

The absence of incremental clinical benefit may be a signal that this drug price is potentially excessive; however this should not be a sole determining factor. One product with a cost equal or less expensive than another product, whose cost is deemed 'excessive', does not necessarily mean it's priced appropriately either. If there are no other drug comparators, the cost of usual care (including supportive therapies, medical/surgical/lifestyle interventions, mobility aids, and comfort care) could be used for comparison purposes.

PMPRB could work with Health Canada and CADTH to use common definitions of therapeutic benefit and should align to ensure that the assessment of therapeutic benefit is consistent. PMPRB needs to ensure that an appropriate breadth of comparators in a therapeutic area is used for comparison. For example, if a new TNF inhibitor is to be introduced for the treatment of rheumatoid arthritis, it would not be sufficient to only compare against other TNF agents for this indication, as there are other classes of drugs that are used to treat same condition. Alternatively, when an innovator drug enters a 'genericized' market, the cost relative to other therapeutic alternatives is quite different.

- c) In considering the above two questions, does it matter to you if a very costly drug only treats a small group of patients such that it accounts for a very small proportion of overall spending on drugs in Canada?

No, regardless of the size of the population (large or small) the price must consider cost effectiveness and whether there a comparable alternative within the standard of care. Previous research by Lynd et al. (presented at conferences, publication pending) has shown that Canadians do not place a value on rarity of a disease, given their opportunity cost.

The proportion of overall drug spending should not be a rationale to support coverage for a single expensive drug, overall affordability and budget impact for a given payer is a more important consideration. It is also important to note that just because a drug treats a small group of patients, it does not necessarily account for a 'very small proportion of overall spending on drugs in Canada'. This highlights the linked but differing aspects of cost, cost-effectiveness and affordability.

- d) Conversely, if a drug's price is below an agreed upon metric and in line with other drugs that treat the same disease, should it be considered potentially excessive if it accounts for a disproportionate amount of overall spending on drugs in Canada?

All drug prices should be reviewed for the potential to be excessive, even if prices for all in the same therapeutic class are aligned. Drugs that have been on the formulary for a long time should be considered for a price reduction, as per mechanisms/schemas in place in the UK or Australia (currently not done by regulators).

For any unforeseen circumstances that emerge later, there should be another PMPRB mechanism in place to allow for subsequent review of drug pricing in the context of other considerations like affordability. The response in 1c above is also relevant here as there is the similar issue of the relationship between 'cost' and 'affordability' as stated above.

- e) What economic considerations should inform a determination of whether a drug is potentially excessively priced?

The context of the health system structure in comparator jurisdictions relative to Canada is an important consideration with respect to policies regarding confidential prices and price differences in different health care settings across the system. Market behaviour can also affect excessive pricing; a product can be replaced in the market by essentially the same drug at very large price increase through a new distributor, special access programs (SAP) or other means. Price increases through SAP are occurring more regularly than ever before which may point to a gap in system oversight.

International comparisons are one component; however the USA should be removed as they are a significant outlier. If international price comparisons are not reliable or if all international prices are excessive, PMPRB should consider indicators of potential for abuse of statutory monopoly, as well as reviews of other non-drug comparators/standards of care (e.g., supportive therapies, medical/surgical/lifestyle interventions, mobility aids, comfort care) and other drugs that treat related diseases with a similar level of complexity if there are no direct drug comparators

Other considerations include domestic price comparisons, confidential prices (net of discounts and rebates) as revealed by manufacturer in all domestic and international markets, price reviews in all domestic markets (wholesaler, pharmacy, hospital in all jurisdictions), value-for-money, competition, comparison to actual price paid, manufacturing costs, and costs to health care system of drug administration and monitoring.

- 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?

The PMPRB should place less weight on, but not ignore international public list prices. PMPRB could work with other international jurisdictions to establish MOUs/ confidentiality agreements that would allow jurisdictions to share the true price paid by public drug plans. This in turn should inform the PMPRB's assessment of 'excessive' prices. More weight should also be placed on factors mentioned above regarding comparator countries used, incorporating lowest international pricing, etc.

Public plans/payers do not currently have mechanisms to share confidential drug pricing (due to agreements with the manufacturer), if mandated by PMPRB, the onus would shift to the manufacturers to reveal confidential pricing in comparator countries directly to PMPRB. In general, the pCPA feels Canadian pricing should be at the lower end of the pricing comparison among other countries, especially given that those countries are also negotiating and are using confidential prices that are not accessible to PMPRB.

- 3) In your view, given today's pharmaceutical operating environment, is there a particular s. 85 factor that the Guidelines should prioritize or weigh more heavily in examining whether a drug is potentially excessively priced?

The PMPRB should prioritize the prices at which the medicine and other medicines in the same therapeutic class have been sold in the relevant market and in countries other than Canada. However, the PMPRB7 countries were selected based on the research and development investments made within those countries, with the original intent of attracting similar investments in Canada. Given the ineffectiveness of this approach, we recommend that the PMPRB change the comparator countries considered (i.e. the USA should be removed from the PMPRB7 and other countries, such as Australia, South Korea, New Zealand and Brazil should be added as comparator countries).

Given that manufacturing costs account for a small amount of the price of a patented medicine, changes in the consumer price index should be weighed less than the other factors. The economic considerations listed in the response to question 1e above are also important factors.

- 4) Should the PMPRB set its excessive price ceilings at the low, medium or high end of the PMPRB7 countries (i.e., the US, the UK, Sweden, Switzerland, Germany, France and Italy)?

Setting the price ceiling at the low level should set the threshold, assuming other factors are relatively the same, will ensure best value and consistency. As mentioned, the comparator country with the highest price should be excluded from the comparison. Given that public prices do not reflect actual prices paid, the price ceilings should also be weighted to account for this.

- 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?

No. Based on historical trends we have seen, manufacturers have not met the commitment target for research and development investment. We have seen these investments decline but have continued to see high pharmaceutical prices.

In Canada, research and development is also very regionalized (e.g., centred in Ontario and Quebec). As per the discussion paper, there is very little correlation between research and development and drug pricing (i.e., increases in drug pricing have not resulted in increases in research and development in Canada). Revenue should be tied to research and development, not price, as payers all contribute to research and development through providing volume (i.e., increased sales).

- 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 outset and address questions of high relative prices, market dynamics and affordability?

The definition of therapeutic benefit employed should be aligned with Health Canada, CADTH and other reviewers for consistency and accuracy. Ideally the process should be redesigned so that PMPRB does not make a pricing assessment until HTA bodies have provided their assessment of cost effectiveness and therapeutic benefit. PMPRB could complete their drug price review at the same time that HC completes their review for drug approval (NOC) - this would require PMPRB to start earlier when a drug company submits to HC.

One current limitation is that non-drug comparators and drugs without Health Canada Notice of Compliance are not considered; a mechanism is needed to ensure that this is updated for relevant drug files. Other factors to explore include incorporating utilization data when conducting comparisons within a therapeutic class, comparing market value expectations to GNP, and examining cost-effectiveness thresholds compared to affordability.

Drugs without any additional clinical benefit entering a space with numerous existing options should have less priority and should drive costs down for the entire class. Distinguishing this group of products

separately from 'first-in-class' products will be a challenge and specific parameters will need to be discussed. A threshold should be set using the lowest priced comparator or at least an average (with generic comparator prices included).

Another option is to consider the approach that provides the best therapeutic benefit; more detail regarding how PMPRB determines therapeutic benefit would be helpful to determine whether this approach may be appropriate.

7) Should the PMPRB consider different levels of regulatory oversight for patented drugs based on indicators of risk of potential for excessive pricing?

In theory, yes, however this would be challenging to define. This would likely include ongoing re-assessment of drug pricing, and permit a ceiling that is the lowest price of the comparators in any market in Canada. Risk-based approaches to regulating is a best-practice amongst regulators, data analytics can support the operationalization of this approach. Decreases in price could also be mandated.

The pCPA agrees that all products may not require/justify the same investment of resources; products for which market pressures are more significant warrant additional investigation. A more in-depth discussion with PMPRB on this issue is needed to provide more insight

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, the price ceiling for patented drugs should be considered for revision every time a drug has a new indication, a new dose, and when a new drug in the same therapeutic class is approved.

It seems like some countries have experienced price decreases over time and Canada tends to see price increases over time. Ideally, if there was a link to return on investment (especially for expensive drugs), cost should come down substantially over time.

The current approach to price increases should be re-evaluated. Currently PMPRB allows price increases over time (e.g., CPI increases) which increases the price gap between Canada and other (particularly European) countries. Over time manufacturers should have recouped initial investment and efficiencies in production should be possible to support a decrease in prices over time. Canadian jurisdictions may also need to consider the impact of decreasing brand pricing on current strategies for generic pricing.

If a value-for-money approach were to be taken, changes in willingness to pay on the part of Canadians could justify changes to the price ceiling. Timing can also depend on market dynamics domestically and internationally can also trigger the need for review.

Regarding indication expansion, if drug pricing is only assessed at market introduction, this facilitates manufacturers launching a product for a small indication where a certain price could be initially justified. However, the manufacturer may proceed to expand approvals for larger indications, potentially

with less incremental therapeutic benefit, without revisiting price. Additionally, as subsequent indications would build upon some of the same fundamental research, the amount of profit required to recoup investments is different than for initial indications.

9) Should price discrimination between provinces/territories and payer types be considered a form of excessive pricing and, if so, in what circumstances?

Yes, when available, the PMPRB should consider the prices paid by public plans (both within Canada and in comparator countries) and the prices paid by the public and/or private plans (both within Canada and in comparator countries). The differential should be comparable to that experienced in other countries, with the goal of reducing the differential to support access to medicines by all Canadians.

Additionally the discrepancy of pricing between hospital and public drug plans is significant. All expenditures in these settings are paid through public funds but are often leveraged strategically (i.e. lower priced in hospitals so patients are initiated on therapy but are then charged a significantly higher price in the community setting). Differences in prices among Canadian jurisdictions and payer types should reflect differences in costs to supply the market rather than structural disadvantages in bargaining (e.g. small population or loosely organized).

10) Are there other aspects of the Guidelines not mentioned in this paper that warrant reform in light of changes in the PMPRB's operating environment?

- PMPRB's mandate should evolve to ensure Canadian drug prices are reasonable, rather than ensuring Canadian drug prices are not excessive. Regulating excessive drug pricing does not do enough to help control escalating drug costs.
- As we continue to negotiate drug prices for all Provinces and Territories, there is increasing need for non-discriminatory or discriminatory mechanisms and/or schemas to control/reduce the price of brand drugs.
- In other jurisdictions such as the UK or Australia, there are forms of price control and reductions based on profit/growth and how long a drug has been on the formulary.
- More transparency/intel re: international pricing (confidential pricing) to assist with negotiations through pCPA would also help.
- Need to recognize that there is a gap created when patents end and products not necessarily genericized and the 'single source generic' create significant risk re.:
 - Timing of pricing evaluation (ie prior to launch, potential need for different evaluation when product launched prior to marketing in other jurisdictions and evaluation once it is in a more mature market);
 - Investigation and follow up action;
 - The VCU and other follow up process invoked when pricing found to be excessive need to be considered in light of any changes.
- PMPRB doesn't capture all products but still are affected by market behaviour, without a mechanism to address that it's challenging to address.
- Potentially explore generic pricing.

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?

Application to all drugs can be done but is quite challenging. Suggest starting by focusing on areas that are in most need for price control/relief or to address cost-effectiveness for therapeutic categories.

12) Should one or more of the issues identified in this paper also or alternatively be addressed through change at the level of regulation or legislation?

- This requires further analysis to determine effectiveness.
- Price decreases could be mandated in regulation/legislation.
- Enforcement of price increases could also be addressed in regulations.
- Response to Q10 is also relevant here.
- Potentially, based on market behaviour and other factors.
- PMPRB assessment should be done prior to pCPA negotiations to support.