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PMPRB comments / questions
Aug 24, 2006

General Preamble to specific questions on the Issues raised in the Discussion Guideline

PMPRB Mandate:

- to ensure that the prices of medicines in Canada are not excessive.
- further, to ensure that all measures and processes relating to achieving of the mandate are transparent, fair, effective, efficient, respectful and supportive to relevant parties.

There should be fundamental agreement that the PMPRB and Canadian society in general place an increased value on medicines that have a high benefit/risk ratio (the incidence and/or magnitude of the health improvements exceed the incidence and/or magnitude of any unwanted side effects) as compared to the value placed on medicines with a lower benefit/risk ratio, in named patient populations.

This "relative-value" concept should translate into rewarding the development of "better" medicines with higher introductory pricing opportunities as compared to less advantageous medicines.

This recognition should be communicated in a forthright, transparent manner. Undefined and unwritten practices that are not addressed in the guidelines should be avoided wherever possible.

ISSUE 1 Drug Categorization

I-1, Question 1: are the new patented drug categories and their definitions appropriate?

No.

With regard to the preamble, the current categorization could be improved upon, by recognizing an intermediate class of drugs which provide "moderate improvement".

Further, the guidelines should clearly state and recognize that "better drugs" can relate to:

- efficacy improvements (which could relate to any combination of the degree of improvement or the speed of improvement)
- safety improvements (which could relate to seriousness or frequency of side effects) and/or
- improvements in cost efficiency across different silos of the medical health budget.

The proposal below is ordered to reflect an increasing benefit/risk ratio to patients.

Category A	old category 1
Category B	NAS (New Active Substance) providing little or no benefit over comparable medicines used to treat the same indication (part of old category 3)
Category C	NAS providing moderate benefit over comparable medicines use to treat the same indication (part of old category 3)
Category D	NAS providing substantial benefit over comparable medicines used to treat the same indication (part of old category 2)
Category E	Breakthrough with no existing comparators (part of old category 2)

The proposal identifies 5 distinguishable categories of new market entries. As described later in this document, the individual categories would be linked to a pricing gradient that would offer increasing rewards for increasingly "better" products. In particular, as compared to the existing classification system, this system allows for recognition that a product providing "moderate" improvement in health outcomes is more valuable to society than a product offering little or no improvement. Further, it allows for increasing recognition of a "breakthrough" product over one that provides substantial benefit to existing medications, comparative properties that again are "lumped" together in the present classification system.

It should be noted that increasing the number of drug categories brings increased complexity to the process of fitting products into a classification system, and thus increases the potential for differences in judgement as to where a given product might fit into that scheme. Therefore, it will be at least as important as it is presently (likely even more important) to ensure that there is a transparent process of why decisions are made concerning placement of products into drug categories.

Of particular relevance to this matter, given the importance of the HDAP in providing advice on the matter of how to classify new products, the details behind all HDAP decision regarding categorization must be made available to the manufacturer of a product / all Canadians. Regrettably, this is currently not the case (to the detriment of the stated aim and values of the PMPRB). With an increase from 3 to 5 "new-product" categories, the potential for a lack of predictability in categorization decisions would make it even more difficult for manufacturers who have secured a patent for their new drug to plan future operations based on sales revenue. .

I-1, Question 2: Is it important to distinguish moderate improvement from little or no improvement?

Yes.

Given the importance that is placed by physicians and patients on the efficacy and reduced side effects of a medicine, it is important for the Guidelines to distinguish between those medicines that provide a moderate level of improvement and those that do not do so.

Further, it is important to describe the related pricing implications for a new drug that offers moderate improvements as compared to a new drug offering little or no improvement over existing therapy.

I-1, Question 3: On what basis would the new medicine that offers "moderate therapeutic improvement" be distinguished from one that offered "little or no benefit?"

The most forthright manner to do so would be to employ much the scheme in the present version of the Guidelines for distinguishing a "substantial benefit" drug (from the present category 2 drugs) from a Category 3 drug.

This would be done by adding the appropriate adjectives to the same text. Therefore, to mimic the format of the present guidelines, wherein the definition of a substantial improvement is one that:

"…relative to other drug products sold in Canada, provides substantial improvement in therapeutic effects (such as increased efficacy or major reductions in dangerous adverse reactions) or provides significant savings to the Canadian health care system"

the definition for what constituted a moderate improvement would read:

"a moderate improvement is one that, relative to other drug products sold in Canada, provides moderate improvement in therapeutic effects (such as moderate increases in efficacy and/or moderate reductions in dangerous adverse reactions), or provides moderate savings to the Canadian health care system or provides a significant improvement in convenience or acceptability to the patient".

Similar to the language used in the definition of a substantial improvement, this definition provides guidance on principles to be used in making the determination with flexibility to allow recognition that moderate improvements can come from any one or more of a number of areas (efficacy, safety, cost-effectiveness and, in the case of moderate improvements but not significant improvements, increased convenience or patient acceptability).

ISSUE 2: Introductory Price Review Methodology

I-2, Question 1: Are current price tests appropriate?

No.

Pricing tests / criteria should have outcomes that reward the development of more effective medicines with higher introductory prices than those given to less effective medicines.

This is currently not the case with:

- breakthrough drugs
  currently, MNE could be lower than the MNE of a substantial improvement drug
- substantial improvement drugs
  currently, MNE cannot exceed the MNE of a present category 3 drug
- drugs offering moderate improvement (vs. those offering no or little improvement)
  currently MNE cannot exceed that for a drug that offers little or no improvement over existing therapy

I-2, Question 2: How to set pricing criteria for moderate improvement (vs. little or no improvement)

With reference to the categorization naming scheme, listed above, a predictable and transparent mechanism for setting MNEs of drugs in the Category B to Category D range, would be establish a percentage increase in MNE over the MNE definition of Category B drugs.

Further, in setting the MNE criteria for this range of medication, the criterion should be such that category B – D drug MNEs could not exceed those of a breakthrough drug. For this reason, instead of the highest IP setting the upper limit for the IP comparison in categories B - D, it is proposed that the mean of the median price plus the highest IP price be used, while for the breakthrough drugs, some potentially higher formula be set (e.g., the highest IP).

However,
Any pricing scheme employed by the PMPRB must not act to "punish" manufacturers for bringing a drug to Canada early in its patent period. The PMPRB has defined a set of comparator countries against which the pricing of drugs in Canada is compared. What presently not adequately dealt with, is the circumstance wherein at the time of Canadian drug launch, there are only a few countries marketing the product. Presumably, such an "early" launch would be to the benefit of Canadian patients, and no PMPRB policy should give manufacturers reason to avoid committing to early launches in Canada. In the event that the drug was only being marketed in a few of the 7 comparator markets, and further that the price of the drug in those markets was particularly low, then the manufacturer might indeed delay a Canadian launch if the comparator countries were limited and the price of the product in those countries was low.

It is therefore suggested that the determination of whether or not a drug was reasonably priced at introduction not take place until the first time of:

- all reference countries have the product on the market or
- in lieu of there being pricing in all of the reference markets, the company determines that there are relevant comparable medicines whose prices can be used as surrogates to the price of the new product in countries wherein the new product is not yet available. (see I-2, Question 4, below)

This scheme for category definitions should clearly state and recognize that "better drugs" can relate to:

- efficacy improvements (which could encompass any combination of the degree of improvement or the speed of improvement),
- safety improvements (which could encompass ADR seriousness or frequency) and/or
- cost efficiency across different silos in the medical health budget.

<u>Pricing criteria:</u>

- Category B MNE ceiling to be <u>the lower of</u>:
  - TCC [plus CPI adjustments from introductory price?] or
  - $\frac{\text{(median IP plus highest IP)}}{2}$
- Category C* category B plus [X**]% premium
- Category D category B plus [2X]% premium
  - * this is the moderate improvement category
  - ** e.g., 15%

<u>I-2, Questions 3:</u> <u>definition of "comparable medicines"</u>

Many different experts recently confirmed that comparable medicines are those that are used to treat a similar group of patients with the same indication, or the same "phase" of an otherwise chronic

indication. The 4th level of the ATC classification is good reference point. There should be no general exceptions to this point.

The PMPRB reference document itself refers to other "clinically equivalent drug products used to treat the same disease". For clarity and transparency, the term "clinically equivalent" needs to be defined, particularly stressing the lack of the relevance of:

- Mode of action
- Nature of relevant active substance
- Context of the term clinically equivalent: i.e., should not be relevant whether one is considering a medical context, a pricing context or any other context – the definition should be the same

I-2, Question 4 prices of other comparable medicines in other countries

The present guidelines are inadequate, in that they presently do not address this concept, whereas the Patent Act, which the guidelines are meant to help enforce, clearly states that this concept is relevant. In their failure to address this matter, the guidelines do not provide transparent processes/measures for a manufacture to follow when planning their business models.

The PMPRB reference document should provide transparent guidance on the process/measures for analyzing comparable medicines in other countries by stipulating that the prices of such medicines are only relevant in conducting an IPC in the situation of:

- the "same medicine" is not available in a reference country,
  but
- other products relevant to a TCC comparison, and also available in Canada, are present in the other country

In such cases bulleted above, the price of the other medicines would be considered as part of the international pricing comparison, acting as a substitute for the price of the subject medicine in light of the absence of pricing information for the subject medicine itself.

ISSUE 3: Pricing Perspective: any market, vs. a national average over a given time period

I-3, Question 1 should the board continue to consider only an ATP calculated from national figures?

Yes. PMPRB should have a transparent policy of comparing apples to apples.

In making comparisons of pricing in Canada to pricing in other countries (i.e., the IPC), if the PMPRB is to continue using the average drug price in the international comparator countries, then PMPRB must also use the average Canadian drug price (ATP). This is important to avoid the situation wherein one compares the highest price of the drug in Canada to the average price of the drug in other countries.

This principle would also be true in the context of making price comparisons in the situation of the "comparable medicines" clause in the Act, referenced in I-2, Question 4, above. It would not be relevant to compare the highest price of the drug in Canada to an average price of individual comparable medicines in other countries, when the price of the comparable medicines in those other countries can vary from market to market.

The Board must clearly and comprehensively state how it defines a number of terms relating to the calculation of the ATP. Regarding the distribution of free goods, compassionate drug use programs and rebates etc.:

1. manufacturers must be confident that they can be included in the determination of an ATP and
2. patients must be confident that such programs are not discouraged, which would occur following PMPRB adopting a policy of moving away from the ATP being the unit of interest in Canada.

Similar to the intent of inter-provincial "equalization payments", the context of drug pricing review should be on an average, national basis to allow flexibility to deal with special regional / customer class / other relevant Canadian needs.

Conclusion

For all purchasable items, Canadians place increased value on items of an increased level of benefit. It follows that new drug products that offer differing degrees of benefit to patients should be priced at appropriate levels that recognize there relative value. Canadians do and will place a higher value on Pharma products that offer increased health benefits as compared to products that offer less health benefits.

These principles need to be clearly incorporated into any pricing guidelines prepared by and followed by the PMPRB. Ensuring that guidelines possess these properties provides predictability and transparency for all Canadians, whether they be a user, a payer or a manufacturer of the product in question. In particular, guidelines for pricing should avoid unwritten principles or rules, and should avoid any practices that could delay Canadian patients access to new medicines for pricing reasons.

Respectfully submitted
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