Canadian Agency for Drugs and Technologies in Health
Agence canadienne des médicaments et des technologies de la santé

September 27, 2006

Sylvie Dupont, Secretary of the Board
Patented Medicine Prices Review Board
Box L40
Standard Life Centre
333 Laurier Avenue West
Suite 1400
Ottawa, Ontario
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Dear Sylvie:

As previously discussed by telephone, I would like to take the opportunity to provide you with the attached comments from the Canadian Expert Drug Advisory Committee (CEDAC) on the PMPRB's Excessive Price Guidelines. I apologize for our delay in getting these to you but, as you know, CEDAC only met last week to review this issue.

Please feel free to contact me should you have any questions.

Sincerely,

Mike Tierney
Senior Director
Common Drug Review

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PMPRB Consultation Guide on Excessive Price Guidelines

Comments from the Canadian Expert Drug Advisory Committee (CEDAC)

In addition to providing comment on the three key issues identified by PMPRB, CEDAC would also like to provide some general comments on the role of PMPRB in the Canadian drug approval, pricing and reimbursement framework.

Currently, PMPRB and CDR operate in relative isolation from one another and while there are differences in their mandates, there are clearly some areas of overlap. Although the role of PMPRB (which is to ensure that Canadian prices for patented medicines are not excessive) and CDR/CEDAC (which is to provide formulary listing recommendations on the basis of cost-effectiveness) are clearly distinct, both consider the price of medicines in relation to the therapeutic advantages of comparative therapy. As such, the relative roles of PMPRB and CDR/CEDAC needs to be clearly defined and, where appropriate, coordinated in order to avoid confusion amongst stakeholders (public, patients, health professionals, pharmaceutical industry).

Additionally, although outside the scope of this consultation, it should be recognized that there is also some degree of overlap and confusion with the role of Health Canada in relation to PMPRB and CDR. For example, Health Canada can approve medicines on the basis of promising evidence, such as unvalidated surrogate outcome measures, and yet it is difficult for PMPRB and CDR to come to pricing and reimbursement decisions on the basis of this level of evidence. CEDAC feels that there is a need to consider the drug approval, pricing and reimbursement system in Canada as a whole. (For further thoughts on this, see: Wood AJJ. A proposal for radical changes in the drug-approval process. N Engl J Med 2006;355:618-23.)

CEDAC feels that there is significant potential for increased interaction through information sharing, collaboration and integration of the work of PMPRB and CDR/CEDAC. This could include, but not be limited to:

- presentations to each other on current roles and processes;
- sharing of detailed drug reviews;
- coordination of the timing of reviews, with recognition that the timelines for CDR review should not be delayed while awaiting a PMPRB decision;
- clear definition and, where appropriate, integration of relative roles and processes;
- discuss whether PMPRB may have any role in "setting" a "reasonable" price in addition to a maximum price. While it is clearly important to establish a maximum price, it should be recognized that many other countries have the capacity for national price negotiation which effectively means that the maximum

price is often not the actual cost to the system. In Canada, because there is currently no opportunity for national price negotiation, the maximum allowable price effectively becomes the actual price for most public payers.

Issue 1 - Is the current approach to the categorization of new patented medicines appropriate?

Question 1:
Are the new patented drug categories and their definitions appropriate?

Category 1 is generally appropriate but it is not clear to CEDAC what the role of PMPRB is regarding drugs that are marketed for multiple indications eg. Clonidine (Catapres and Dixirit), Sildenafil (Viagra and Revatio).

The delineation between category 2 and 3 is too simplistic and there is a need to further refine and divide category 2.

Question 2:
Is it important to distinguish a medicine that offers "moderate therapeutic improvement" from a medicine that provides "little or no therapeutic improvement?" If yes, why is it important? If not, why not?

There may be an opportunity to further divide category 2 medicines into substantial and moderate and/or promising improvement. One example of how to do this could be by differentiating on the basis of effect on important clinical outcomes versus validated surrogate outcomes versus unvalidated surrogate outcomes.

It might also be possible to divide category 3 medicines into "moderate" or "no/little improvement" on the basis of surrogates vs clinical outcomes. To be "moderate improvement", there would have to be a statistically significant benefit in a head to head trial based on clinical or validated surrogate endpoints. Everything else would be in the "little/no improvement" category.

Question 3:
If the answer to question 2 above is yes, on what basis would a new medicine that offers "moderate therapeutic improvement" be distinguished from a new medicine that provides "little or no therapeutic improvement"?

It should be recognized that there will always be some subjectivity in the distinction between these terms and that it is impossible to create a formula that will work in all situations. Nonetheless, distinction of moderate versus little or no improvement would need to consider the quality of the clinical trial data, the comparators used, the outcome measures evaluated, the length of study duration and follow-up, the effect size noted, the clinical importance of the effect size and comparative harms in relation to other therapies. Perhaps CEDAC could forward their assessment of these criteria to PMPRB after each review, but there would need to be some agreement on predefined criteria.

Issue 2 - Is the current approach used to review the introductory prices of new patented medicines appropriate?

Question 1:
Are the price tests currently used to review the prices of new medicines in the various categories appropriate for that category? Why? Why not? If not, how could these tests be amended to improve their appropriateness?

The price tests are based on the International Price Comparison and the Therapeutic Class Comparison, neither of which assesses the price of the drug in relation to improvements, if any, in health outcomes from the appropriate use of the drug.

The International Price Comparison uses "list prices" in the 7 other countries. It is known that this list price is often not the real price that is paid by many payers in these countries. For example, drug prices of the Veteran's Administration and Federal Supply Service in the US are often substantially lower than Canadian prices.

Question 2:
If you think that medicines that offer "moderate therapeutic improvement" should be distinguished from medicines that provide "little or no therapeutic improvement" what would the appropriate new price test be?

The price test to distinguish between "moderate therapeutic improvement" from "little or no therapeutic improvement", could be based on the incremental cost-effectiveness of the drug. If a drug offered no/little improvement, manufacturers could not charge any more than the comparator. If it was a moderate therapeutic improvement, then cost-effectiveness could be considered in determining an appropriate price. However, it should be recognized that the use of this approach, where new drugs will often be associated with an incremental but acceptable cost-effectiveness ratio, will lead to continued escalation of drug expenditures.

Question 3:
For price review purposes, "comparable medicines" are medicines that are clinically equivalent. Do you have any suggestions as to principles or criteria that should be used in determining how to identify "comparable medicines" for the purpose of inclusion in the above price tests?

CEDAC has no comment on this issue.

Question 4:
Under the current Guidelines, Board Staff compares the Canadian average transaction price of the new medicine to the prices of the same medicine sold in the seven countries listed in the Regulations. However, Section 85(1) of the *Patent Act* states that the Board should take into consideration "the prices of other comparable medicines in other countries". Should the Guidelines address this factor?

If so, how could this factor be incorporated into the price tests for new medicines?

CEDAC has no comment on this issue.

Issue 3 - Should the Board's Guidelines address the direction in the Patent Act to consider "any market"?

Question 1:
Given the price variations by provinces/ territories and classes of customer illustrated in the previous figures, is it appropriate for the Board to only consider an ATP calculated based on the total revenues from the sales for all provinces/territories and all classes of customer? Why? Why not?

If, as indicated through the work of the NPS, we are evolving to a national common formulary it would make sense that there also be a national process to negotiate prices for the publicly funded drug plans. If this is implemented, then PMPRB could consider use the transaction price for these plans in the calculation of the ATP.

Question 2:
If the current ATP calculation is not appropriate, should the Board review the prices to the different classes of customers and/or the different provinces and territories for all DINs? Or should this level of review be done on a case-by-case basis, where there is a significant variation in the prices charged?

CEDAC has no comment on this issue.

Other comments

The PMPRB process needs to be come more dynamic by having the capacity to re-evaluate prior decision when new information becomes available. For instance, manufacturers should have chance to resubmit for a new price if they develop new clinical information. Similarly, if the indication for an existing medicine expands, the PMPRB should be able to review the price in the context of a significant expansion of market (eg. Herceptin).

CDR is seeing the introduction of more fixed dose combinations and many of these products seem to be introduced in a effort to preserve market share upon expiration of patents. A mechanism is needed to prevent manufacturers from using fixed dose combinations to preserve their market share at the expense of the use of lower cost generic products.