Report of the
Working Group on Price Tests
to
The Patented Medicine Prices Review Board

July 2008

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Introduction

In 2006, the Patented Medicine Prices Review Board (PMPRB) launched a series of consultations to ensure that the Board's Excessive Price Guidelines (Guidelines) continue to be relevant and appropriate in the modern pharmaceutical environment. During the consultation process, stakeholders raised concerns that the categories of therapeutic improvement used by the Board do not effectively recognize incremental innovation and that the current price tests do not adequately reward this incremental innovation.

In May 2007, the Board released a *Stakeholder Communiqué* where it launched three Working Groups, one to make recommendations on new levels of therapeutic improvement and another to develop a methodology for appropriately identifying comparable medicines in comparator countries, to be used in the International Therapeutic Class Comparison (ITCC) test. The third Working Group was established as an advisory panel for a contracted report on the costs of "making" and "marketing" a drug product.

The Working Group on Price Tests (WGPT) was launched in early 2008 in order to dovetail with the recommendations of the previous Working Groups. The Board wanted to seek additional advice on how the PMPRB's price tests, among other aspects of the Guidelines, should be changed in order to align with the recommendations of the Working Groups, if necessary.

Mandate of the Working Group on Price Tests

The mandate of the WGPT was to develop advice and options for possible changes to the PMPRB's price tests, aligned with any decisions taken by the Board on the categorization of medicines, the ITCC, and related matters, including the current reasonable relationship test, the market exchange rate methodology and later, the CPI methodology. Please refer to Appendix 1 for a complete Terms of Reference for the WGPT and to Appendix 2 for a list of members.

Issues Discussed

Introductory Price Tests

The WGPT came to general agreement that the following principles should be applied when the Board makes its decision on any modifications to the introductory price tests:

- A greater degree of innovation deserves a greater degree of pricing freedom;
- Canada's prices for patented drug products should not be the highest in the world;

- The Board should not force a price below the price of a comparator (except when its price would be the highest in the world);
- The review process should identify "equivalent" (i.e., slight or no improvement) comparators and, where none exist, those comparators that are "superior" and "inferior," for inclusion in the Therapeutic Class Comparison (TCC) test;
- At introduction, the Maximum Non-Excessive (MNE) price of a new medicine should not be higher than the price of the highest price of a clinically equivalent comparator and, if there are none, not be higher than the price of a "superior" comparator; additionally, it should not be lower than the price of any "inferior" comparator;
- In the selection of comparable drug products, the HDAP can continue to begin with, however, should not be limited to, comparators selected from the 4th level of the World Health Organization (WHO) Anatomical Therapeutic Classification (ATC) System;
- Evidence to select comparators beyond the 4th level ATC class, especially in cases where the comparators within that 4th level ATC are unrelated (e.g., a first entrant in a new class that has been assigned to the 4th level ATC "other") need not be limited to head-to-head clinical trials; and
- Given the greater flexibility in the selection of comparators, HDAP decision reports should be more fulsome and should provide rationales for the selection of comparators, including levels of evidence used and how their conclusions were drawn.

With these principles in mind, the WGPT came to general agreement on proposed introductory price tests in line with the recommendations of the Working Group on Therapeutic Improvement:

Breakthrough:	The Median International Price (MIP) test
Substantial Therapeutic Improvement:	The higher of the top of the TCC test and the MIP test
Moderate Therapeutic Improvement:	The higher of the mid-point between the top of the TCC & MIP tests (or 50% of range between the top of TCC and MIP tests) and the top of the TCC test
Slight/No Therapeutic Improvement:	The top of the TCC

Reasonable Relationship (RR) Test

The WGPT agrees that, unless the patentee makes a submission claiming therapeutic improvement, the RR test should be maintained for new drug products that represent a different strength/line extension of an existing drug product (i.e., same indication use and equivalent or comparable dosage form).

Combination Products
The WGPT agrees that, unless the patentee makes a submission claiming therapeutic improvement, the MNE price of the new combination product will be the sum of the MNE prices of the component drugs. The MNE prices used in this calculation should be based on the new proposed definition of MNE price discussed later in this report.

Review of Line Extensions and Combination Products by HDAP
The WGPT agrees that drug products that are considered line extensions or combination products will only be reviewed by the Human Drug Advisory Panel (HDAP) if the patentee submits scientific evidence in support of a claim of therapeutic improvement.

Advisory Assistance
The WGPT agreed that the PMPRB should publish information on the process for advisory assistance and guidance on what should be contained in submissions that claim therapeutic improvement. It was also agreed that the submission be provided in advance and reviewed by PMPRB Scientific Staff prior to a meeting between the patentee and Board Staff on the actual submission and its merit. This meeting should take place prior to the submission being sent to the HDAP.

Exchange Rate Methodology
The WGPT considered whether a change to the existing 36 months (or 3 years) exchange rate methodology was needed in order to smooth out the effects of currency fluctuations. One option considered was to change the time frame of the exchange rate methodology to 60 months (or 5 years). The WGPT agreed that moving to a 60-month exchange rate was unnecessary. No other alternative methods for correcting for exchange rate fluctuations were discussed or agreed upon.

The WGPT also agreed that conversion based on "Purchasing Power Parity" methodology would also not be useful.

International Therapeutic Class Comparison Test
The WGPT supported the recommendations of the ITCC Working Group, in that:

- The international therapeutic comparators and dosage regimens in each country listed in the Regulations should be the same as those selected for the domestic TCC; and
- The ITCC test should be considered as the most remote test, and should be used to add information in dispute resolutions only, but not as a pivotal (primary) test.

The WGPT considered two methodologies for undertaking an ITCC used by the Board in the past:

1. "The Ratio Approach" - Taking the ratio of the price between the medicine and its comparator in each country and multiplying the median of the international ratios by the Canadian price of the medicine; and
2. "The Straight Class Approach" - Determining the prices of the therapeutic class comparisons in each international market and looking at a range of prices to determine if a price is excessive, including the mean, median and a range (i.e., interval between maximum and minimum price), as no single measure will be appropriate in all circumstances..

The WGPT agreed that neither methodology was appropriate in all cases, and that both should be used, where appropriate, as the ITCC price tests. In general, however, if the new medicine is not sold in many comparator countries, the median of the ratios, by the nature of its calculation, will be less appropriate.

Revised Definition of the MNE Price

The WGPT proposed that the definition of the MNE price should be changed from what is currently contained within the existing Guidelines, such that the MNE price is determined by the highest non-excessive market-specific MNE price. For example, in the introductory period a drug product has a national MNE price established by the price tests of $9, a pharmacy price of $10, a wholesaler price of $9, and a hospital price of $6. In the subsequent period, if the prices in all markets increase by CPI (assuming 2%), and the pharmacy price increases to $10.20, this price should represent the MNE price for all markets (i.e., the national market). Therefore, the MNE price for all markets (i.e., the national market) is established by the highest non-excessive market-specific MNE price.

MNE/ATP & CPI "De-Linking" Methodology

The WGPT defined the concepts of the "De-Linking" methodology in terms of two specific market conditions, namely "gaps" or "dips."

A "gap" is the difference between the current ATP and the MNE, and exists whenever the ATP is below what is considered the MNE price. A "gap" could occur in two specific circumstances:

1) where the introductory ATP is less than the introductory MNE price, set based on the relevant introductory price tests; or
2) when a drug has been sold at an ATP that PMPRB considers not to be excessive, and then the patentee decreases its price in response to market forces (other than “a benefit”). In this case, the "gap" is the difference between the previous higher ATP and the current ATP.

A "dip" exists whenever the ATP declines as a result of a new or enhanced “benefit” to a class of customer or jurisdiction.

The key distinction between the "gap" and "dip" methodology is the potential for price "increases" in the situation of a "gap", and the potential for price "rebounds" in the case of the "dip".

Price Increase Threshold in a "Gap" Situation

Under the "gap" methodology, the WGPT recommends that the price of a drug product could "increase" up to the higher of the introductory MNE price (established by the introductory price tests) or the highest previous non-excessive ATP, but such increases should be limited by a pre-defined price increase threshold.

The WGPT recognizes that the potential for significant single year price increases could be high using the "gap" methodology. The WGPT considered a number of options to limit the overall impact of substantial single year price increase and recommends that, if the Board adopts the "gap" methodology, single year price increases should be limited to 33% of the gap (3 years to close the gap) in any one year with an annual price increase not to exceed 10% to 15% of the current ATP.

The WGPT agreed that a 3 year allowance to close the gap for a price increase is likely more tenable to consumers and payers, and did not act as a disincentive to the provision of benefits. The WGPT was undecided on what percentage 1-year cap/ limit was most appropriate (10% or 15%) and felt this decision should be left to the Board to determine. A dissenting view on the issue was that the 33% rule was limiting enough and any additional price increase barrier would significantly affect its relevance; particularly given that typical window of exclusivity for patented products is around 10 years.

Patentees are not required to provide evidence of benefits to take a price increase under the "gap" methodology.

Price Rebound in a "Dip" Situation

The WGPT recommends that in the situation of a "dip", the available "rebound" in the ATP in one year should be 100% - that is, returning to the non-excessive price at which the medicine was sold to the customer prior to the offering of the benefit. Examples of a “dip” could include, but are not limited to:

- When an existing customer is offered a benefit that is only for a specific period of time, and the price returns to the level of the previous non-excessive ATP at the expiration of the benefit (e.g., the offer and conclusion or loss of a contract, compassionate use program, or other); or
- When a Group Purchasing Organization (GPO) is offered a benefit where the patentee is unaware of the number of potential customers that will eventually take advantage of the benefit (meaning that the amount of

reduction in the ATP will fluctuate below the previous non-excessive ATP depending on the number of participating customers).

To be allowed to rebound 100% of the "dip," patentees would need to provide evidence to the PMPRB supporting the claim that the "dip" is the result of a reduction in or termination of a benefit to a particular customer. The WGPT recommends that clear guidance be provided to patentees regarding the type of evidence that will be considered appropriate and what specifically defines a "benefit".

In the case of both the "gap" and the "dip," the price of the drug product will always be constrained by the highest price in the world through the Highest International Price Comparison (HIPC) Test. The HIPC test could lower the price to which the ATP could increase (gap) or rebound (dip).

Publication of the MNE Price

The WGPT agreed that, in the interests of transparency, MNE price information could be made available to the public, so long as there is an adoption of the de-linking methodology of the ATP from the MNE as noted above. For the gap methodology, the PMPRB already publishes the introductory MNE price in its Summary Reports on new medicine. The WGPT agreed that the MNE price of a medicine set by the highest previous non-excessive ATP could in principle also be published on the PMRPB website until the actual ATP equals or surpasses this previous ATP. One reason to do so is to allow this price to be used in the TCC test for new medicines that are introduced during the dip and for which the medicine whose price has dipped is a comparator.

However, the WGPT acknowledges that ATP information submitted by patentees is confidential under section 87 of the *Patent Act* and can only be made public if the patentee agrees to such a publication. The WGPT is aware that not all patentees will be willing to allow their MNE prices to be published. As such, it recommends that individual patentees be given the option to allow their information to be published, even though this could create a "patchwork" of reported price information.

CPI-Adjustment Methodology

The CPI-Adjustment Methodology would continue to apply in cases where the "de-linking" methodology is not applicable. The WGPT discussed possible modifications to the CPI-adjustment methodology, but could not agree on how the methodology should/ could be modified. Patentees thought that the 3 year "banking" should be retained but the one year "cap" (1.5 x CPI) be removed. Others thought that the methodology should be replaced in favour of allowing simple CPI each year.

Any Market Price Review (Introductory and Existing Drugs)
The WGPT agreed that if any market price reviews are to be conducted, they should be conducted during a drug's introductory period only, so that the average price for any class of customer (i.e., pharmacy, hospital and wholesaler) in Canada would not exceed the MNE price at introduction based on the national MNE price (established by the introductory price tests for the introductory period).

For existing drug products, the PMPRB should only undertake any market price reviews in the case of an investigation where variability in average prices in different markets (class of customer or province/territory) appears to be an issue (as per the criteria of investigation outlined later in this report). Undertaking an any market price review where warranted on a case-by-case basis would allow the PMPRB to effectively meet its mandate of ensuring that prices are not excessive, while reducing the uncertainty and burden for both stakeholders and the PMPRB. This is in line with what the PMPRB already does with respect to price reviews for existing drugs, but would make it more transparent to stakeholders as to when any market price reviews will be undertaken.

Any Market Price Review - Calculation of Excess Revenue
The WGPT has not reached an agreement on the most appropriate means to calculate excess revenue in an "any market price" review.

There are two options:

1. Excess revenue be based on the average price across all markets in Canada (national ATP) and not just on the excess revenue for the market where the price was excessive. The view was that excess revenue calculation take into account foregone revenue in markets priced below the MNE price. Doing otherwise could penalize patentees that offer benefits to other customers.

2. Excess revenue be calculated only considering the market where a price is excessive. The view was that excess revenue be based on the market that paid an excessive price.

Re-Setting the MNE Price
The WGPT agreed that if/when an MNE price is re-set, it should not be forced below the median international price, which would be determined at the time of the re-setting. In the event that a price is re-set downward, a patentee should have a full year or to the end of the following calendar year to reduce its price to the new MNE price, during which time no investigation would be commenced and no excess revenue calculated. This is the same practice currently employed by Board Staff in relation to the Highest International Price Comparison test, where the patentee is given to the end of the calendar year (from the time a notice is issued) to reduce its price to the new MNE price and there is no requirement to offset excess revenue. The current guidelines state that a patentee will be given

a full year, however, based on the conditions of reporting, the Board Staff have traditionally given patentees "only to the end of the calendar year". This imposes significant challenges for many patentees to be able to execute, particularly if much of the calendar year has passed prior to the communiqué/ notice being issued.

Re-Setting Based on Science

The WGPT agreed that if the price of a drug product is to be re-set based on science, evidence should be provided, which identifies that the level of therapeutic improvement has changed or that the comparators used in the applicable price tests were not appropriate.

The WGPT agreed that, during the scientific review of a medicine HDAP identify any gaps in the scientific evidence, which could act as a trigger for re-setting later if there is a submission on such new science. However, submissions for re-setting the MNE price based on science would not necessarily be limited to evidence gaps or weaknesses identified by HDAP.

The WGPT agreed that requests for re-setting should be considered from a variety of sources (patentees, consumers, provinces/territories), but in all cases the onus should be on the requestor to identify and submit the relevant scientific evidence.

Re-Setting Based on Number of Countries where the MIP is the pivotal introductory price test

The WGPT agreed that the status quo should be maintained for re-setting an "interim" MNE price i.e., after 3 years or when the medicine is sold in 5 countries, whichever comes first.

Investigations

The WGPT agreed that the criteria for commencing an investigation should be the same for new and existing drugs, and suggested that 5% above the MNE price or $50,000 or more in excess revenue should be the investigation criteria for all drugs.

The WGPT also recognized the current lack of transparency in cases where the price of a medicine exceeds the MNE price but not by an amount sufficient to trigger the investigation criteria. In these cases, the patentee is advised to reduce the price and offset excess revenues, but publically, the medicine is reported as "within Guidelines."

The WGPT agreed that there should be two categories of compliance:

1. Prices Within Guidelines
2. Prices Under Investigation

PMPRB WGPT, Industry Minority Position on the Final Report:

1. **HIPC:** On page 6 of the final report, there is a note that the HIPC test could, throughout the life of the patent, lower the price of a product. There are numerous examples of when the HIPC test is artificially "violated" when the "highest" priced country discontinues selling (especially poignant when considering combination medicines, as not all countries in the basket sell the "comparable" medicine). In the case of biologics most notably, it is highly likely that fewer than the 7 comparator countries are in the basket to begin with, and as such, there's a higher probability that the Canadian price would be pushed to the "most expensive priced product" in the basket and the affiliate would be required to reduce price. This is further complicated in situations where a manufacturer has and sells the "comparable" medicine for a new chemical entity;
3b. when a manufacturer owns the "comparable" product, the current "standard" practice is to compare to the ATP of the manufacturer owned not the MNE. This has not been addressed within the final report and warrants further attention.

2. **Publishing the De-linked MNE:** this issue could potentially warrant further discussion;

3. **Grandfathering/Transitioning of Products into the new Guidelines:** the method to manage grandfathering/transitioning of products into a system that is governed by revised guidelines needs to be addressed. The WG was instructed that it was outside of the scope of the mandate, but it was discussed by many of the members on how it would be optimally managed;

4. **Lowering of Price because of HIPC or Re-setting:** the guidelines currently describe an allowance of 1-calendar year, however, the language within the report indicates that the patentee would be given to the end of the calendar year which is too difficult/ onerous for patentees to enact, particularly in the case of smaller (few number of molecule) companies. There are notable challenges in the timing around reporting, however, it was suggested that the reporting allowance be 12-months or to the end of the following calendar year, to allow for manufacturers to enact the change, rather then a condensed time frame if a patentee is notified mid year for example.
Further on this issue, it has been noted that for smaller biotechnology companies, the longer time allowance is critical as the overall (negative) impact to the business has a greater impact and is more difficult to enact.

5. **Re-Setting of the MNE:** expansion of re-setting of the MNE beyond the current Guidelines or to expand the any market review is a change that is not supported by industry.

Appendix 1

Terms of Reference for the Working Group on Price Tests

Mandate

The mandate of the Working Group (WG) is to develop advice and options for possible changes to the Patented Medicine Prices Review Board's (PMPRB) price tests, aligned with any decisions taken by the Board on the categorization of medicines, the international therapeutic class comparison, and related matters, including the current reasonable relationship test and the market exchange rate methodology.

Deliverables

- The WG will provide advice and options, in the form of a written report and a presentation to the Board (if requested), evaluating the current price tests and their relevancy following recommendations accepted by the Board from the reports by the Working Groups on International Therapeutic Class Comparison and Therapeutic Improvement, as well as provide options for any changes to the current price tests.
- The price test options for each category of medicine should include thresholds that result in a clear hierarchy of price premium.
- The WG will consider other related price test issues intrinsic to the implementation of the price tests (e.g., reasonable relationship test, exchange rate issues, etc.).
- The advice put forward by the WG will be accompanied by a clear rationale for the options and recommendations, as well as consideration of the impact (e.g., advantages/disadvantages) from a variety of stakeholder perspectives.

Reports and Timeframe

- Executive Summary of Report and Recommendations: Late April, 2008
- Final Report and Recommendations to the Board: May 6, 2008

Membership

The Working Group shall be composed of 6-8 members including:

Chair: Senior Board Staff member

Members: Up to two representatives of the innovative pharmaceutical industry
Up to two representatives of the biotechnology industry
Up to two consumer representatives
Up to two representatives of provincial/territorial governments
One representative of private payers
One economist
One clinician

Secretariat: Board Staff member

Where possible, members may be selected from among those who participated in the previous Working Groups on International Therapeutic Class Comparisons and Therapeutic Improvement.

The names of the Working Group members will be published on the PMPRB Web site.

Organization and Structure

Chair:
The PMPRB will chair this working group. The Chairperson's responsibilities include keeping the Working Group focused on the exercise, maintaining open and effective communication, and ensuring that issues raised and analyses provided are considered and recorded, all while meeting the necessary timelines.

Members:
All members of the WG will have equal status.

Secretariat:
PMPRB Staff will provide secretariat services, including a note-taker for meetings.

Confidentiality of Working Group Deliberations

The deliberations of the WG are confidential and members are expected to respect the confidentiality of any materials provided by the PMPRB Staff and/or collected by the WG during the course of its work.

Meetings

- An initial face-to-face meeting of the Working Group in late March 2008.
- Teleconference/videoconference meetings as needed.
- If requested, a presentation of the final report to the Board in May 2008.

Location of Meetings

Working Group meetings will take place at the PMPRB offices in Ottawa, unless availability of space or other considerations necessitate off-site meetings.

Appendix 2

Membership of the Working Group on Price Tests

Member	Title and Organisation
Mr. Nicolas Gagnon	Director, Government and Stakeholder Relations Pfizer Canada Inc.
Mr. Edward Gudaitis	General Manager Gilead Sciences, Inc.
Ms. Irene Klatt	Vice-President Canadian Life and Health Insurance Association Inc.
Ms. Lynn Macdonald	Consumer and Member of the Operations Committee Best Medicines Coalition
Mr. Steve Morgan	Professor Department of Health Care and Epidemiology University of British Columbia
Mr. Bob Nakagawa	Assistant Deputy Minister Pharmaceutical Services Ministry of Health, British Columbia
Ms. Claudia Neuber	Senior Manager Business Planning and Risk Management AstraZeneca Canada Inc. Rx&D Representative
Ms. Laurene Redding	Director, External Affairs Novo Nordisk Canada Inc. BIOTECanada Representative
Ms. Barbara Ouellet	Executive Director Patented Medicine Prices Review Board **Chairperson**
Mr. Matt Bondy	Senior Analyst Policy and Economic Analysis Patented Medicine Prices Review Board **Secretariat**
Ms. Catherine Lombardo	Scientific Advisor Compliance and Enforcement Patented Medicine Prices Review Board **Resource Person**