Patented Medicine Prices Review Board

*Since 1987*

# PMPRB NEWSletter

Volume 14, Issue No. 2, April 2010

## Inside...



## Since our last issue...

### Our recent key events

| | |
|---|---|
| February 17: | The HDAP held its quarterly meeting. |
| February 26: | Sylvie Dupont and Catherine Lombardo made a presentation by videoconference to students at the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta. |
| March 4-5: | The hearing continued in the matter of ratiopharm Inc., and the medicine ratio-Salbutamol HFA. |
| March 8: | The Board issued a Notice of Hearing in the matter of Sandoz Canada Inc. More details on this matter can be found on page 5. |
| March 9: | The NPDUIS Steering Committee held a teleconference call in which PMPRB Staff provided a status update on current research projects. |
| March 11: | The Board held its quarterly meeting. |
| March 16: | The Board issued an Order in the matter of sanofi pasteur Limited and the medicines Quadracel and Pentacel. The Order is posted on the PMPRB Web site under Regulatory; Hearings; Quadracel and Pentacel. |
| March 24-25: | The Chairman of the Board made a presentation on the revised Excessive Price Guidelines to the Pharma Pricing & Market Access Outlook Europe 2010 conference in London, UK. |
| March 26: | Gregory Gillespie met with officials from the UK Department of Health in London, UK. |
| April 6: | The Chairman of the Board accepted a VCU submitted by Baxter Corporation regarding the price of the patented drug FSME-IMMUN. Details of the VCU are available on page 4.<br><br>The Chairman of the Board accepted a Voluntary Compliance Undertaking (VCU) submitted by GlaxoSmithKline Inc., regarding the price of the patented drug Paxil CR. Details of the VCU are available on page 4. |
| April 12-16: | The hearing continued in the matter of ratiopharm Inc., and the medicine ratio-Salbutamol HFA. |
| April 18-20: | Derek Jones participated in the 2010 Canadian Agency for Drugs and Technologies in Health Symposium, in Halifax, N.S. ■ |

PMPRB speeches and presentations are available on the Web site under Publications; Speech Series.



If you wish to know more about the PMPRB, please contact us at our toll-free number, 1 877 861-2350, or consult our Web site.

The PMPRB is an independent quasi-judicial body with a dual mandate.
**Regulatory:** to ensure that prices of patented drug products sold in Canada are not excessive; and
**Reporting:** to report annually to Parliament on pharmaceutical trends of all drug products and on R&D spending by patentees.

ISSN 1920-3713

# News from the Chairman

My five-year term as Board Member, Chairman and CEO of the PMPRB ends on May 18, 2010. It has been an honour and a privilege to have served on this Board.

I joined the Board at a time when several new issues and challenges were emerging. I had the pleasure of joining seasoned members, our past Vice-Chairperson, Réal Sureau, and Members Tim Armstrong and Anthony Boardman, who enthusiastically shared their knowledge and expertise. Dr. Robert Elgie, former Chairman of the Board, also provided invaluable advice. In June 2006, I was appointed Chair and CEO of the PMPRB, and was joined by Mary Catherine Lindberg as Vice-Chair, and a year later, by Anne Warner La Forest.

In March 2005, the Board had issued a Discussion Paper on Price Increases for Patented Medicines. Shortly thereafter, in response to stakeholders' feedback, the Board initiated an in-depth review of its Excessive Price Guidelines. Its main objective was to ensure that the Guidelines remained relevant and appropriate to the ever evolving pharmaceutical environment. In order to ensure the broadest input into the process, the Board embarked on an unprecedented level of consultation with all interested stakeholders, including the pharmaceutical industry, federal, provincial and territorial governments, consumer and patient advocacy groups, third party payers and others. The Board held a series of face-to-face consultations with stakeholders across the country, organized bilateral meetings with all stakeholder groups, and established multilateral working groups to examine specific issues. This consultation culminated with the released of new Guidelines in June 2009, which came into effect on January 1, 2010.

Amid this in-depth review exercise, we pursued our regulatory and reporting activities, implemented an integrated business and human resources planning framework, and addressed resource capacity gaps. We responded to new compliance challenges, issuing a total of 15 Notices of Hearing from January 2006 to March 2010, and accepting 28 Voluntary Compliance Undertakings to reduce the prices of patented drugs, while having nearly $60M in excess revenues collected by the Government of Canada. We developed new policies and amended the reporting requirements under the *Patented Medicines Regulations*. We pursued our partnership with the Canadian Institute on Health Information, Health Canada and the provinces through our collaboration on the National Prescription Drug Utilization Information System, refining our goals and providing in-depth analysis and advice.


*Dr. Brien Benoit explains the new Excessive Price Guidelines at the Pharma Pricing & Market Access Outlook Europe 2010 conference in London in March.*

These achievements would not have been possible without talented and dedicated Board Members and Staff. I want to take this opportunity to thank my Board colleagues and each member of the PMPRB Staff for their invaluable contributions, hard work and dedication to this organization. In particular, I want to thank the Executive Director of the PMPRB, Barbara Ouellet, for her important contribution to this organization over the last five years. Barbara will be retiring from the Public Service in June and we wish her all the best.

I have greatly enjoyed my stay at the PMPRB. As I end this unique and exciting chapter in my career, I wish the PMPRB Members and Staff every success in all their future endeavours. ■

Brien G. Benoit, MD

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# Comings and Goings

A number of new employees have joined us since the last NEWSletter. Marie-Christine Lettre joined the Board Secretariat and Communications Branch as Communications Officer. Francine Sanche is the new Human Resources Generalist in the Corporate Services Branch. Ria Mykoo returned to the Legal Services Branch as legal counsel after working at Health Canada. John Raasch left on parental leave after completing a secondment from Industry Canada with the Legal Services Branch. ■

# Farewell to Dr. Boardman

Board members and staff held a small reception for Dr. Anthony Boardman, whose term ended on March 11, 2010. Dr. Boardman thanked the staff and said how much he appreciated their collaboration over the past 10 years.

Dr. Boardman was first appointed in 1999 and was reappointed in 2005. He is currently Van Dusen Professor of Business Administration at the Sauder School of Business at the University of British Columbia. He has been a consultant to many private and public organizations around the world, and to all levels of government in Canada. He taught executive programs in several countries and has won a number of teaching awards. He has published many articles in leading academic journals and recently completed the fourth edition of *Cost-Benefit Analysis: Concepts and Practice*.

We wish him all the best in his future endeavours. ■

# International Therapeutic Class Comparison Test

The PMPRB's updated *Compendium of Policies, Guidelines and Procedures* (Compendium) came into force on January 1, 2010. However, the Board has identified the need to correct some of the text pertaining to the derivation of the "ratio approach" for the International Therapeutic Class Comparison (ITCC) test.

Stakeholders may recall that the ITCC test is not a primary test and is only conducted in order to provide information in the context of an investigation into apparent excessive prices. The intent of the ITCC ratio approach is to determine whether, in the seven countries identified in the *Patented Medicines Regulations*, a patented drug product appears to have obtained a "premium" price over its comparator drug products identified in the domestic price test.

For example, assume that a patented drug product under review has only one therapeutic comparator, which has a price of $1.00 in Canada. In the ratio approach for the ITCC test, the ratio between the price of the patented drug product and the price of the comparator is determined for each of the seven countries. If the median of the international price ratios is 1.2, this would imply that the patented drug product appears to have obtained a 20% price premium over its comparator internationally. The median ratio of 1.2 would then be applied to the price of the comparator in Canada, making the result of the ITCC ratio approach test $1.20.

However, words were inadvertently omitted from the description that appeared in the Compendium published in June 2009. The median of the ratios of prices internationally is not, in fact, applied to the National Average Transaction Price (NATP) of the patented drug product under review. Rather, it is applied to the price of the *pivotal comparator in the domestic price test*, which is then compared to the NATP.

With the missing words inserted, the description of the ratio approach for the ITCC test in Schedule 7, Sub-Section 3.1 (page 33) of the Compendium should read as follows:

> The Ratio Approach: The prices of the drug product under review in the seven countries listed in the Regulations are identified. The prices of all comparable drug products in the seven comparator countries are also identified. The ratios between the price of the drug product under review and the price of comparable drug products **are** determined for each combination within each comparator country. The median of all the resulting ratios is then applied **to the price of the pivotal comparator (i.e., the comparator used to establish the Maximum Average Potential Price in the domestic price test), which is then compared** to the National Average Transaction Price of the patented drug product under review in Canada.

It is important to note that this corrected text is consistent with the methodology historically used by Board Staff when conducting the ITCC test.

The *Compendium of Policies, Guidelines and Procedures* as posted on the PMPRB Web site (www.pmprb-cepmb.gc.ca/english/View.asp?x=1206&mp=73) will be corrected accordingly. Should you have any questions or comments regarding this correction, please contact the Regulatory Affairs and Outreach Branch. ■

# New Patented Medicines Reported to the PMPRB

Since the publication of the January 2010 NEWSletter, one new DIN for human use (representing one medicine) was added to the list of patented medicines reported to the PMPRB. This drug product was not a new active substance.

New patented drug products come under the PMPRB's jurisdiction once they are both patented and sold in Canada. If a patented drug product was first sold during the patent pending period (after the date when the patent was laid open for public inspection and before patent grant), the PMPRB's policy is to review the price of the product back to the date of first sale. ■

# CPI-Adjustment Factors for 2011

*The Patent Act* specifies the factors to be used by the PMPRB in determining whether the price of a patented drug product sold in Canada is excessive. One of these factors is the Consumer Price Index (CPI). The Board's *Compendium of Policies, Guidelines and Procedures* requires that cumulative increases in a product's price over any three-year period be no more than the increase in the CPI over the same period. The Compendium also sets a cap on year-over-year price increases, equal to one and one-half times the CPI-inflation rate for the year in question.

To allow patentees to set prices in advance, the Board´s CPI-Adjustment Methodology provides for the calculation of the CPI-adjustment factors based on forecast changes in the CPI. The Board informs patentees of these CPI-adjustment factors each year through its *NEWSletter*.

The following table provides CPI-adjustment factors for 2011. These factors were based on annual forecast CPI-inflation rates (provided by Finance Canada) of 1.8% and 2.0% for 2010 and 2011, respectively, as well as the actual 2009 CPI-inflation rate of 0.3%.

**Forecast 2011 Price-Adjustment Factors for Patented Drug Products**

| Benchmark Year | (1) 2008 | (2) 2009 | (3) 2010 |
|---|---|---|---|
| Price-Adjustment Factor | 1.041 | 1.038 | 1.020 |

These figures imply: (1) a maximum allowable cumulative price increase between 2008 and 2011 of 4.1% for patented drug products with Canadian sales in 2008 (that is, products whose "benchmark year" is 2008); (2) a maximum allowable cumulative price increase between 2009 and 2011 of 3.8% for products whose first Canadian sales occurred in 2009; and (3) a maximum allowable cumulative price increase between 2010 and 2011 of 2.0% for products whose first Canadian sales occurred in 2010.

In addition, the forecast inflation rate of 2.0% for 2011 implies a year-over-year price increase cap of 3.0% (= 1.5 x 2.0%) for 2011. ■

# Voluntary Compliance Undertakings

A Voluntary Compliance Undertaking (VCU) is a written undertaking by a patentee to adjust its price to conform to the Board´s Excessive Price Guidelines (Guidelines). Under the Guidelines, patentees are given an opportunity to submit a VCU when Board Staff concludes, following an investigation, that the price set forth by the patentee for a patented drug product sold in Canada appears to have exceeded the Guidelines. A VCU can also be submitted by a patentee after a Notice of Hearing is issued.

In the last quarter, the Chairman of the Board accepted VCUs for: FSME-IMMUN and Paxil CR.

## FSME-IMMUN, Baxter Corporation

Under the terms of the VCU, Baxter agreed to reduce the price of FSME-IMMUN to $35.6108 per vial as of October 1, 2009, and to offset cumulative excess revenues received from January 1, 2002 to December 31, 2009 in the amount of $53,578.62 by making a payment to the Government of Canada no later than May 6, 2010.

FSME-IMMUN (tick-borne encephalitis vaccine – inactivated) is indicated for immunization against the TBE virus in individuals 16 years and older who are at risk of contact with ticks that carry TBE virus.

## Paxil CR, GlaxoSmithKline Inc.

GlaxoSmithKline offset excess revenues received in the January 2004 to December 2005 reporting periods in the amount of $53,177.88 by making a payment to the Government of Canada.

Paxil CR (paroxetine hydrochloride) is indicated as a selective serotonin reuptake inhibitor in a new dosage form: controlled release tablets for the symptomatic treatment of depression and panic disorder.

The prices of these drugs will remain under the Board's jurisdiction for the duration of their respective patents. ■

# Questions and Comments

## PMPRB E-bulletin

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# Hearings – Update

The PMPRB's regulatory mandate is to ensure that patentees' prices of patented medicines sold in Canada are not excessive.

In the event that the price of a patented medicine appears to be excessive, the Board can hold a public hearing and, if it finds that the price is excessive, it may issue an order to reduce the price and to offset revenues received as a result of excessive prices. Board decisions are subject to judicial review in the Federal Court of Canada.

## Status of Board Proceedings

| Patented Drug Product | Indication / Use | Patentee | Date of Notice of Hearing | Status |
|---|---|---|---|---|
| Apo-Salvent CFC-Free | Relief of chest tightness and wheezing caused by spasms or narrowing in the small air passages of the lungs | Apotex Inc. | July 8, 2008 | **Ongoing** |
| Copaxone – Redetermination | Use in ambulatory patients with relapsing-remitting multitude sclerosis to reduce the frequency of relapses | Teva Neuroscience G.P.-S.E.N.C. | May 8, 2006 | **Federal Court Decision: Nov. 12, 2009 ordered redetermination** |
| Nicoderm | Smoking cessation | sanofi-aventis Canada Inc. | April 20, 1999 | **Board Decision: April 9, 2010** |
| Penlac | Part of a comprehensive nail management program in immunocompetent patients with mild to moderate onychomycosis of fingernails and toenails without lunula involvement | sanofi-aventis Canada Inc. | March 26, 2007 | **Board Decision: pending** |
| Pentacel | Routine immunization of all children between 2 and 59 months of age against diphtheria, tetanus, whooping cough (pertussis), poliomyelitis and haemophilus influenzae type b disease. | sanofi pasteur Limited | March 27, 2007 | **Board Decision: Dec. 21, 2009** (amended March 1, 2010) **Board Order: March 16, 2010** |
| Quadracel | Primary immunization of infants, at or above the age of 2 months, and as a booster in children up to their 7th birthday against diphtheria, tetanus, whooping cough (pertussis) and poliomyelitis | sanofi pasteur Limited | March 27, 2007 | **Board Decision: Dec: 21, 2009** (amended March 1, 2010) **Board Order: March 16, 2010** |
| ratio-Salbutamol HFA | Relief of chest tightness and wheezing caused by spasms or narrowing in the small air passages of the lungs | ratiopharm Inc. | July 18, 2008 | **Final Written Arguments to the Panel on May 14, 2010** |

| Patentee | Issue | Date of Notice of Hearing | Status |
|---|---|---|---|
| Apotex Inc. | Failure to File (jurisdiction) | March 3, 2008 | **Ongoing** |
| ratiopharm Inc. | Failure to File (jurisdiction) | August 28, 2008 | **Board decision pending** |
| Sandoz Canada Inc. | Failure to File (jurisdiction) | March 8, 2010 | **Ongoing** |

On April 22, 2010, Celgene Corporation was granted leave to appeal to the Supreme Court of Canada in the Thalomid matter. After a hearing in August 2007, the Board issued its decision in January 2008 asserting its jurisdiction over the price of Thalomid. That decision was appealed to the Federal Court and then to the Federal Court of Appeal, which upheld the Board decision. No date for the Supreme Court of Canada hearing has been set. ■

# March 11 Board Meeting

The Board met on March 11, 2010 and approved the correction to the text on the International Therapeutic Class Comparison. The Board's next meeting is scheduled for May 13, 2010.

For additional information, please contact the Director, Board Secretariat and Communications, at: 1 877 861-2350, or (613) 954-8299, or at sylvie.dupont@pmprb-cepmb.gc.ca.

Summaries of Board meetings are available on the PMPRB Web site under About PMPRB. ■

# Report on New Patented Drugs – Nevanac

Under its transparency initiative, the PMPRB publishes the results of the reviews of new patented drug products conducted by Board Staff for purposes of applying the Board's Excessive Price Guidelines (Guidelines) for all new active substances introduced in Canada after January 1, 2002.

**Brand Name:** Nevanac

**Generic Name:** (*nepafenac*)

**DIN:** 02308983 (1 mg/ml)

**Patentee:** Alcon Canada Inc.

**Indication – as per product monograph:** Management of pain and inflammation associated with cataract surgery.

**Date of Issuance of First Patent Pertaining to the Medicine:** August 13, 2002

**Notice of Compliance:** April 17, 2008

**Date of First Sale:** August 21, 2008

**ATC Class:** S01BC10
*Sensory organs; Ophthalmologicals; Anti-inflammatory agents; Anti-inflammatory agents, non-steroids.*

## Application of the Guidelines

### Summary

The introductory price of Nevanac was found to be within the Guidelines because the cost of therapy did not exceed the cost of therapy of existing drug products in the therapeutic class comparison and the price in Canada did not exceed the range of prices of the same drug product in the comparator countries listed in the *Patented Medicines Regulations* (Regulations) in which Nevanac was sold.

### Scientific Review

Nevanac is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) recommended under the pre-2010 Guidelines that Nevanac be classified as a category 3 new medicine (provides moderate, little or no therapeutic advantage over comparable existing drug products).

The Therapeutic Class Comparison (TCC) test of the pre-2010 Guidelines provides that the price of a category 3 new drug product cannot exceed the prices of other drugs that treat the same disease or condition. Comparators are generally selected from among existing drug products in the same 4th level of the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system that are clinically equivalent in addressing the approved indication. See the PMPRB's pre-2010 *Compendium of Guidelines, Policies and Procedures* for a more complete description of the Guidelines and the policies on TCCs.

The HDAP recommended diclofenac (Voltaren Ophtha) and ketorolac tromethamine (Acular and Acular LS) as appropriate comparators to Nevanac as they are clinically equivalent to Nevanac. These agents share the same 4th level ATC and the same indication as Nevanac, and are also recommended in clinical guidelines for the management of pain and inflammation associated with cataract surgery. There were no data or comparative trials to support the inclusion of drug products outside the 4th level ATC.

The Guidelines provide that the dosage recommended for comparison purposes will normally not be higher than the maximum of the usual recommended dosage. The recommended comparable dosage regimens for Nevanac and the comparable drug products were based on the respective product monographs and supported by clinical literature.

### Price Review

Under the pre-2010 Guidelines, the introductory price of a category 3 new drug product will be presumed to be excessive if it exceeds the prices of all the comparable drug products based on the TCC test or it exceeds the range of prices of the same drug product sold in the seven countries listed in the Regulations.

The introductory price of Nevanac was within the pre-2010 Guidelines as the cost per treatment did not exceed the cost per treatment of the comparable drug products as shown in the table below.

### Introductory Period (August to December 2008)

| Brand Name (Generic Name) | Strength | Dosage Regimen* | Unit Price | Cost per Treatment* |
|---|---|---|---|---|
| Nevanac (nepafenac) | 1 mg/ml | 2.88 ml | $3.6960[1] | $10.6445 |
| Voltaren Ophtha (diclofenac, 0.1%) | 1 mg/ml | 7.2 ml | $2.3693[2] | $17.0590 |
| Acular Liquid (ketorolac tromethamine, 0.5%) | 5 mg/ml | 5.4 ml | $3.2000[2] | $17.2800 |
| Acular LS (ketorolac tromethamine, 0.4%) | 4 mg/ml | 7.2 ml | $3.2000[2] | $23.0400 |

* Comparable dosage regimens are 16 days for Nevanac and 30 days for the comparable drug products.

Sources:
1 Publicly available price as per the *Patented Medicines Regulations*
2 *Association québécoise des pharmaciens propriétaires, 2008*

In 2008, Nevanac was sold in two countries listed in the Regulations, namely Sweden and the United States. The price of Nevanac in Canada did not exceed the range of prices of the same drug product in those countries.

The publication of Summary Reports is part of the PMPRB's commitment to make its price review process more transparent.

Where comparators and dosage regimens are referred to in the Summary Reports, they have been selected by the HDAP for the purpose of carrying out the PMPRB's regulatory mandate, which is to review the prices of patented drug products sold in Canada to ensure that such prices are not excessive.

The PMPRB reserves the right to exclude from the therapeutic class comparison test any drug product it has reason to believe is being sold at an excessive price.

In Summary Reports under the pre-2010 Guidelines, the PMPRB refers to the publicly available prices of comparators, provided such prices are not more than 10% above a non-excessive price in which case no price will be made available. As a result, the publication of these prices is for information only and should not be construed as indicating the public prices are considered within the pre-2010 Guidelines.

The information contained in the PMPRB's Summary Reports should not be relied upon for any purpose other than stated and is not to be interpreted as an endorsement, recommendation or approval of any drug product, nor is it intended to be relied upon as a substitute for seeking appropriate advice from a qualified health care practitioner.

This report, including the references, is available on the PMPRB Web site under Patented Medicines; Reports on New Patented Drugs for Human Use; Nevanac. ■

# Upcoming Events

## May

**May 6-7:** Drug Patents in Canada conference, Toronto

**May 10:** HDAP meeting

**May 11-13:** Canadian Association for Health Services and Policy Research (CAHSPR) 2010 conference, Toronto

**May 13:** Board meeting

**May 26-28:** Northwind Professional Institute's 2010 Life Sciences Invitational Forum, Cambridge, Ont.

**May 27:** NPDUIS Steering Committee teleconference

**May 31:** 2009 PMPRB Annual Report submitted to the Minister of Health

**May 30-June 2:** Canadian Council of Administrative Tribunals (CCAT) 26th Annual Conference, Montreal

## June

**June 3-4:** Canadian Pharmaceutical Pricing and Reimbursement Conference, Toronto

**June 14-20:** National Public Service Week

**June 15-16:** Drug Pricing and Reimbursement in Canada conference, Toronto

## July

**July 16:** NPDUIS Steering Committee teleconference

**July 30:** Patentees' Form 2 filings
July NEWSletter

## September

**September 15:** HDAP meeting

**September 16:** Board meeting

## October

**October 4-5:** Market Access Canada Summit, Toronto

**October 5-8:** Market Access World USA conference, Washington, D.C.

**October 29:** October NEWSletter

## November

**November 4-5:** DIA Annual Canadian Meeting, Ottawa

**November 17:** HDAP meeting

## December

**December 9:** Board meeting

**Upcoming Events are available on the PMPRB Web site under Consultations; Events.** ■

## What's New @ PMPRB

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### Comments

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