Patented Medicine Prices Review Board

Since 1987

PMPRB NEWSletter

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Since our last issue...

Our recent key events

September 14:	The NPDUIS Steering Committee held a teleconference call in which PMPRB Staff provided a status update on current research projects and discussed plans for a fall meeting in Ottawa.
September 15:	The HDAP held its quarterly meeting.
September 16:	The Board held its quarterly meeting.
September 24:	Michelle Boudreau and Ginette Tognet met with Kate Peters of the Medicines Pharmacy and Industry Branch, Department of Health, UK, to explain the role of the PMPRB and the price review process.
October 4:	The redetermination hearing commenced in the matter of Teva Neuroscience G.P. – S.E.N.C. and the medicine Copaxone.
October 6–8:	Michelle Boudreau spoke at the Market Access World USA 2010 conference in Washington D.C.
October 7:	Sylvie Dupont presented an overview of the regulatory functions of the PMPRB by videoconference to the Sedgwick County Health Care Roundtable Seminar in Wichita, Kansas. ■

PMPRB speeches and presentations are available on the Web site at Publications/Speech Series.

What's New @ PMPRB

Readers are invited to check our Web site for the latest information on our activities!

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 at which patentees sell their patented medicines in Canada are not excessive; and
Reporting: to report on pharmaceutical trends of all medicines and on R&D spending by patentees.

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News from the Vice-Chairperson

Each fall, employees of the PMPRB take the time to demonstrate their commitment to building better communities and making a difference in the lives of others through the Government of Canada Workplace Charitable Campaign.

The campaign is about more than just money; it reflects the shared commitment that federal public servants have to making a real difference in the lives of others. The PMPRB has a history of generosity, regularly exceeding its annual financial targets. The dedication of the staff and their enthusiasm for this campaign are a reflection of the core values of our organization and the culture of social responsibility shared by all civil servants.

This year's events included a kick-off breakfast and a Halloween bake sale.

The Board would like to congratulate staff members for their efforts and to support them in their commitment to the betterment of Canada and all Canadians.

Last year federal employees and retirees raised more than $38 million in support of the United Way, Healthpartners, and more than 80,000 other registered charities across Canada. More than $21.6 million of this amount was raised in the National Capital Region alone. ■

Mary Catherine Lindberg

Mary Catherine Lindberg, Vice-Chairperson

Senior Staff

Executive Director:
Michelle Boudreau

Director, Regulatory Affairs and Outreach:
Ginette Tognet

Director, Policy and Economic Analysis:
Gregory Gillespie

Director, Corporate Services:
Marian Eagen

Director, Board Secretariat and Communications:
Sylvie Dupont

General Counsel:
Martine Richard

Comings and Goings

We are pleased to welcome three new employees to the PMPRB. Shirin Paynter joined the Secretariat and Communications Branch as an English/French Editor; Michelle Poirier joined the Regulatory Affairs and Outreach Branch as a Senior Regulatory Officer; and Tanya Potashnik recently returned to the Policy and Economic Analysis Branch as Manager of Economic and Socio-Economic Analysis and Research.

Our best wishes go out to Cecile Clarke, who recently left the PMPRB to continue her career at the CRA, and to Elena Lungu, who recently left on maternity leave. ■

NPDUIS Update

The NPDUIS Steering Committee will meet in Ottawa on November 2. The meeting will be held conjointly with a meeting of the Canadian Institute for Health Information´s NPDUIS Data Advisory Group. The focus will be on the presentation of completed reports and the identification of future work priorities.

Several NPDUIS reports are scheduled for publication. The first of these reports are expected to be available on the PMPRB Web site in December. ■

New Patented Medicines Reported to the PMPRB

New drug products first sold in 2010 will be reviewed based on the Guidelines implemented on January 1, 2010. As of September 30, 2010, a total of 41 new drug products (DINs) were reported to the PMPRB (representing 31 medicines). Information on these patented drug products can be found on the PMPRB Web site at Regulatory/Patented Medicines/New Medicines Introduced in/2010.

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 drug product back to the date of first sale. ■

Voluntary Compliance Undertaking on the Patented Medicine FASLODEX

On June 18, 2010, the Board issued a Notice and Comment on the price of the patented medicine FASLODEX. The purpose of the Notice and Comment was to provide Ministers of Health in the provinces and territories of Canada and other interested persons with an opportunity to make submissions on the appropriateness of accepting a Voluntary Compliance Undertaking (VCU) with respect to the price proposed by AstraZeneca for the medicine FASLODEX.

One set of comments was received from Abbott Laboratories Limited supporting the VCU as proposed.

On October 27, 2010, the Vice-Chairperson approved the VCU as submitted by AstraZeneca. Under this VCU, the patentee undertook, among other things, to reduce the price of FASLODEX so that the price does not exceed the 2010 maximum non-excessive (MNE) price of $558.7899, and will offset cumulative excess revenues by making a payment of $405,030.29 to the Government of Canada. The full text of the VCU is available on the PMPRB Web site under Regulatory/Voluntary Compliance Undertakings.

FASLODEX is indicated for the hormonal treatment of locally advanced or metastatic breast cancer in post menopausal women, regardless of age, who have disease progression following prior endocrine therapy. It is supplied in a pre-filled syringe in a strength of 50 mg/mL and is administered at monthly intervals as a single 5 mL intramuscular injection.

The Notice and Comment is also available on the PMPRB Web site under Consultations/Notice and Comment. ■

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 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, one VCU and one amendment to an existing VCU were accepted for Vancocin and Andriol, respectively.

Andriol, Schering-Plough Canada Inc.

On July 6, 2010, the Vice-Chairperson of the Board accepted an amendment to the September 30, 2009, VCU submitted by Schering-Plough Canada Inc. regarding the price of Andriol.

The patentee, having discontinued the discount price as described in the first VCU, submitted an amendment to offset the remaining excess revenues by making a lump sum payment in the amount of $2,286,632.55.

Andriol (testosterone undecanoate) is indicated for the replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone: for the management of congenital or acquired primary hypogonadism and hypogonadotropic hypogonadism; to develop and maintain secondary sexual characteristics in males with testosterone deficiency; to stimulate puberty in carefully selected males with clearly delayed puberty not secondary to a pathological disorder. It is used as a replacement therapy in impotence or for male climacteric symptoms when the conditions are due to a measured or documented androgen deficiency.

Vancocin, Iroko International LP

On July 21, 2010, the Vice-Chairperson approved a VCU submitted by Iroko International LP for the medicine Vancocin. Under the terms of the VCU, Iroko offset cumulative excess revenues received from January 2008 to July 13, 2010 (patent expiry date) by making payments to the Government of Canada for a total amount of $263,441.79.

Vancocin (vancomycin hydrochloride) is an antibiotic that is indicated for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) and antibiotic-associated pseudomembranous colitis caused by *Clostridium difficile*. ■

September 16 Board Meeting

The Board met on September 16, 2010, and welcomed Michelle Boudreau as the PMPRB's new Executive Director.

The Board dealt with two issues: the application of its Policy on the Use of Patented and Non-Patented Medicines in Price Tests in the context of the April 9, 2010, Board decision in the Nicoderm matter; and, the application of its Policy on the Offset of Excess Revenues. The Board's discussion on these two issues is reflected in the next article.

The Board's next meeting is scheduled for December 9, 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 at About PMPRB. ■

The Guidelines – Update

Direction of the Board on the Application of the 2010 Guidelines with regard to its Policy on the Use of Patented and Non-Patented Drug Products in the Price Tests

The Board's Guidelines currently provide that Board Staff may exclude from the price tests the price of any drug product identified for comparison purposes, both patented and non-patented, if the application of the Board's Guidelines results in the conclusion that the medicine is excessively priced.

In light of the Board's decision in the Nicoderm case, the Board has directed Board Staff to include the price of the relevant non-patented drug product in the price tests unless Board Staff is of the view that the price of the medicine is excessive as a result of the absence of competition or other market conditions.

The Board will consider developing guidelines to assist in the determination of when the absence of competition or other market conditions may be presumed to have resulted in an excessive price. However, the development of such guidelines is not a prerequisite to a decision by Board Staff to exclude the price of a non-patented drug product from the price tests on the basis that it is excessively priced as a result of the absence of competition or other market conditions.

The Board's new Guidelines were released in June 2009 and implemented on January 1, 2010. The Guidelines are available on the PMPRB Web site under Legislation, Regulations and Guidelines (http://www.pmprb-cepmb.gc.ca/cmfiles/Compendium-June09-E.pdf).

The Board's decision in the Nicoderm matter is also available on the PMPRB Web site under Regulatory/ Hearings (http://www.pmprb-cepmb.gc.ca/cmfiles/NICODERM-Merits-Reasons-D10-April9-2010.pdf).

Clarification of the Offset of Excess Revenues (Schedule 13, Subsection 1.3.1)

To monitor the compliance of existing patented drug products with the Board's Guidelines, Board Staff reviews each drug product on an **annual basis**. This review ensures that the average transaction price (ATP) does not exceed either the Consumer Price Index (CPI)-adjusted price or the highest price of the comparator countries. Schedules 6 and 9 of the *Compendium of Policies, Guidelines and Procedures* provide descriptions of the Highest International Price Comparison Test and the CPI-Adjustment Methodology.

Given that the review is undertaken on an annual basis, Board Staff does not commence any new investigations based on the price and sales data for the January to June reporting period; rather, investigations are initiated on the basis of the data submitted for the two reporting periods, covering the full calendar year of January to December.

Board Staff has been made aware of a potential point of confusion relating to the offset of excess revenues. Schedule 13 – Offset of Excess Revenues states: "Excess revenue balances below the amount sufficient to trigger the investigation criteria that are carried for six consecutive six month reporting periods (3 years) will be expected to be offset through a VCU." The reference to "six consecutive six month reporting periods" may give the impression that Board Staff is now undertaking price reviews and calculating any excess revenues/offsets generated during each six month reporting period. This is not the case because, as noted above, the prices of existing patented drug products continue to be reviewed on an annual basis. Existing drug products will not be initially identified as "Does Not Trigger" (i.e., having the possibility to offset excess revenues below $50,000) based on data from the January to June reporting period, nor will Board Staff calculate any offset during this period.

As a result, and in order to be consistent with the annual review cycle, Board Staff has modified the information to be provided to patentees for the January to June reporting period and will henceforth indicate only the calculated national ATP (N-ATP) and the national Non-Excessive Average Price (N-NEAP) for the existing patented drug products reported for that first six month period. ■

Hearings – Update

The PMPRB's regulatory mandate is to ensure that prices charged by patentees for their 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 multiple sclerosis to reduce the frequency of relapses	Teva Neuroscience G.P.-S.E.N.C.	New panel struck February 2010	**Hearing: Oct. 4, 2010 Next hearing session to be announced**
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 and Quadracel	Pentacel is a co-marketing of two licensed vaccines: Act-HIB (the lyophilized Haemophilus b Conjugate Vaccine (Tetanus Protein-Conjugate) to be reconstituted with Quadracel. It is indicated for the 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. Quadracel is a Component Pertussis Vaccine and Diphtheria and Tetanus Toxoids Adsorbed combined with Inactivated Poliomyelitis Vaccine. It is indicated for the 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	Board Decision: December 21, 2009; Board Order: March 16, 2010	**Federal Court of Canada: Date to be announced**
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	**Board decision pending**

Patentee	Issue	Date of Notice of Application	Status
Apotex Inc.	Failure to file (jurisdiction)	March 3, 2008	**Ongoing**
Celgene Corporation	Failure to file (jurisdiction)	Board decision: January 21, 2008	**Supreme Court of Canada: Nov. 10, 2010**
ratiopharm Inc.	Failure to file (jurisdiction)	August 28, 2008	**Board decision pending**
Sandoz Canada Inc.	Failure to file (jurisdiction)	March 8, 2010	**Hearing dates: Dec. 6–8, 2010**

Report on New Patented Drugs – Torisel

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 pre-2010 Guidelines for all new active substances introduced in Canada after January 1, 2002.

Brand Name: Torisel

Generic Name: (temsirolimus)

DIN: 02304104 (25 mg/mL)

Patentee: Wyeth Pharmaceuticals

Indication – as per product monograph: Treatment of metastatic renal cell carcinoma.

Date of Issuance of First Patent Pertaining to the Medicine: October 16, 2007

Notice of Compliance: December 21, 2007

Date of First Sale: February 20, 2008

ATC Class: L01XE09
Antineoplastic and Immunomodulating Agents; Antineoplastic Agents; Other Antineoplastic Agents; Protein kinase inhibitors

Application of the Guidelines

Summary

The introductory price of Torisel was found to be within the pre-2010 Guidelines because the cost of therapy did not exceed the cost of therapy of existing drug products in the Therapeutic Class Comparison and 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 Torisel was sold.

Scientific Review

Torisel is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) recommended that Torisel 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 drug products 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 *Compendium of Guidelines, Policies and Procedures "up to 2009"* for a more complete description of the pre-2010 Guidelines and the policies on TCCs.

The HDAP recommended Sutent (sunitinib), Nexavar (sorafenib) and Proleuken (aldesleukin) as appropriate comparators to Torisel. Sutent and Nexavar are approved for the same indication as Torisel and share the same 4th level ATC class. Proleukin is used as a first-line treatment option and is listed on BC Cancer Agency (BCCA) and Cancer Care Ontario (CCO) protocols for metastatic renal cell carcinoma (mRCC).

The pre-2010 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 Torisel 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 price of all the comparable drug products based on the TCC test or if it exceeds the range of prices of the same drug product sold in the seven countries listed in the Regulations.

The introductory price of Torisel 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 following table.

Introductory Period (February to June 2008) — Torisel 25 mg/mL

Brand Name (Generic Name)	Strength	Dosage Regimen (per 6 weeks)	Unit Price	Cost per Treatment (per 6 weeks)
Torisel (temsirolimus)	25 mg/mL	6 vials	$1,250.0000[1]	$7,500.0000[1]
Sutent (sunitinib)	50 mg	28 capsules	$248.1425[2]	$6,947.9900[2]
Nexavar (sorafenib)	200 mg	168 capsules	$43.7500[3]	$7,350.0000[3]
Proleuken (aldesleukin)	1.3 mg	56 vials	$488.0600[3]	$27,331.3600[3]

Sources:
1 Publicly available price as per the *Patented Medicines Regulations*
2 Régie de l'assurance maladie du Québec, 2008
3 Association québécoise des pharmaciens propriétaires, 2008

In 2008, Torisel was sold in two countries listed in the Regulations, namely, Germany and the United States. In compliance with the pre-2010 Guidelines, the price of Torisel in Canada did not exceed the prices of the same drug product in these countries. The Canadian price was the lowest of these 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 that such prices are not more than 10% above a non-excessive price, in which case no price will be made available. Publication of these prices is for information only and should not be construed as indicating that the public prices are considered to be 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 at PMPRB/Regulatory/Patented Medicines/Reports on New Patented Drugs for Human Use/Torisel. ■

Subscription Information and Services

The PMPRB NEWSletter is a free quarterly publication available electronically on the Web and in hard copy. For immediate access to timely information, readers are invited to sign up for the PMPRB E-bulletin alert service.

E-bulletin alert: sign up for an email alert and you will be automatically notified as soon as the NEWSletter is published, with a link to the full electronic content. In addition, relevant news items and announcements will be sent to you directly upon their release. To subscribe to this service, please send your email address to pmprb@pmprb-cepmb.gc.ca.

Requests for publications and/or additional information concerning subscriptions can be made to Elaine McGillivray at elaine@pmprb-cepmb.gc.ca.

Readers are reminded to send all updates to their contact information to the above address. ■

Upcoming Events

November

November 2:
NPDUIS Steering Committee meeting in Ottawa

November 4–5:
DIA 8th Annual Canadian Meeting, Ottawa

9th Annual Forum on Pharma Patents, Toronto

November 10:
Supreme Court of Canada Hearing into Celgene/Thalomid matter

November 16–17:
9th Annual Conference on Market Access, Toronto

November 17:
HDAP meeting

November 23–24:
Gestion des risques associés à la conformité réglementaire dans le domaine pharmaceutique, Montréal

December

December 2–3:
Canadian Pharmaceutical Pricing and Reimbursement Conference, Toronto

December 6–8:
Hearing in the Sandoz Inc. matter

December 9–10:
Board meeting

2011 — February

February 7:
HDAP meeting

March

March 23–24:
5th Annual Pharmaceutical Pricing, Reimbursement and Market Access Summit, London, UK

April

April 3–5:
CADTH Symposium, Vancouver

Upcoming Events are available on the PMPRB Web site at Consultations/Events ■

To order our publications, call our toll-free number 1-877-861-2350 or email us at elaine@pmprb-cepmb.gc.ca

Comments

We want to hear from you. If you have any comments, ideas or suggestions on topics you wish to see covered in the NEWSletter, please let us know.

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