Patented Medicine Prices Review Board

Since 1987

PMPRB NEWSletter

Volume 13, Issue No. 4, October 2009

Inside...

Since our last issue...

Our recent key events

September 17:	The Board met and discussed the monitoring and evaluation of the Board's new Excessive Price Guidelines, which are coming into force on January 1, 2010.
September 17:	The HDAP held its quarterly teleconference.
September 23:	The NPDUIS Steering Committee held its quarterly teleconference.
October 5:	The Chairman of the Board approved a Voluntary Compliance Undertaking (VCU) submitted by Baxter Corporation for the patented drug product Brevibloc. Details of the VCU are available on page 4. The VCU is posted on the PMPRB Web site under Regulatory; Voluntary Compliance Undertaking.
October 5-7:	The hearing on the merits in the Nicoderm matter was held. The Hearing Panel instructed parties to file final written arguments before the end of November.
October 13-14:	The Board held its hearing in the ratiopharm Inc. matter and requested reply and rebuttal arguments, all to be filed by November 10.
October 16:	The Chairman of the Board approved a VCU submitted by Schering-Plough Canada Inc. for the patented drug product Andriol 40 mg/capsule. Details of the VCU are available on page 4. The VCU is posted on the PMPRB Web site under Regulatory; Voluntary Compliance Undertaking.
October 21:	The Board accepted a VCU and issued an Order in the matter of Amgen Canada Inc. and the medicine Neulasta, bringing this hearing, initiated with the issuance of a Notice of Hearing in March 2009, to a conclusion. Details of the VCU are available on page 3. The Public Record is available on the PMPRB Web site under Regulatory; Hearings; Neulasta.
October 27-28:	The Federal Court of Canada (FC) heard the Application for Judicial Review on the Board's decision in the matter of Teva Neuroscience and the medicine Copaxone. The FC decision is pending.
October 28:	Barbara Ouellet participated in a roundtable discussion – Denmark and Canada Healthcare Systems – organized by the Danish Embassy.
October 28-29:	Board Staff held outreach sessions with patentees, in Montreal and Toronto, on the upcoming application of the Board's new Excessive Price Guidelines on January 1, 2010. The new revised Guidelines are available on the PMPRB Web site under Legislation, Regulations and Guidelines; Compendium of Policies, Guidelines and Procedures – June 9, 2009. ■

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.

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Comings and Goings

Over the last quarter, Marielle Racicot joined the Corporate Services Branch. Welcome!

Our best wishes of success go to Nelson Millar who left the PMPRB in August to take on new challenges at Health Canada. ■

News from the Chairman

Brien G. Benoit, MD, Chairman

The Board is looking forward to the implementation of its recently revised Excessive Price Guidelines on January 1, 2010. This will mark the conclusion of a long consultation process with all stakeholders.

In initiating its review of the Guidelines in the 2005, the Board's main objective was to ensure that the Guidelines were relevant and appropriate in the context of an ever evolving pharmaceutical environment. The revised Guidelines will provide greater transparency and predictability in the price review process. To ensure that the Guidelines remain relevant, Board Staff will be monitoring and evaluating the application and impact of the changes to the Excessive Price Guidelines on an ongoing basis.

As part of its ongoing work to assist patentees in preparing for the implementation of the revised Guidelines, Board Staff held further outreach sessions, in Montreal on October 28 and in Toronto on October 29. Board Staff remains available to provide patentees, and all stakeholders, with guidance on all aspects of the new Guidelines.

Again, I take this opportunity to thank all who have participated in the Guidelines review. Your insights and feedback have been invaluable in this process. ■

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Director, Corporate Services:
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Director, Board Secretariat and Communications:
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The Compendium of Policies, Guidelines and Procedures is available on the PMPRB Web site under Legislation, Regulations and Guidelines.

The Board's legislative framework

The Board draws its authority from the *Patent Act* (Act) as last amended in 1993. More specifically, the pharmaceutical provisions of the Act are found in sections 79 to 103.

The Act and the *Patented Medicines Regulations* stipulate the Board's mandate and the patentees' filing and reporting obligations along with the pricing factors, which the Board applies in its price review process.

Pursuant to the general powers provision of the Act, section 96, the Board may, with the approval of the Governor in Council, make general rules for, among other things, regulating the hearing practice and procedure of the Board. Subsection 96(2) gives the Board the optional power to make rules for matters such as, for example, how many days notice must be given for a motion, how many copies of documents are to be filed, and so on. Although the Board has not yet had its Rules promulgated, they are nonetheless operative in that each hearing panel may adopt them implicitly as the rules that will govern the proceeding.

Furthermore, the Board ensures that its hearings are conducted according to principles of natural justice.

The general powers of the Act also provide that the Board may issue guidelines with respect to any matter within its jurisdiction, under subsection 96(4). The Board's Guidelines are not subject to approval by the Governor in Council. Moreover, subsection 96(5) requires that the Board, prior to issuing Guidelines, shall consult with the Minister, the provincial ministers of health, consumer groups and representatives of the pharmaceutical industry. As evidenced in the last few years, the Board has extensively consulted with stakeholders on the review of the Excessive Price Guidelines, prior to their implementation on January 1, 2010.

The *Patent Act*, the *Patented Medicines Regulations*, the Board's draft Rules of practice and procedure for hearings, along with the Board's Excessive Price Guidelines (Compendium of Policies, Guidelines and Procedures), are all available on the PMPRB Web site under Legislation, Regulations and Guidelines. ■

Hearings

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 for the reduction of the price and the offsetting of revenues received by the patentee as a result of excessive prices. The Board's decisions are subject to judicial review in the Federal Court (FC).

Amgen Canada Inc. and the medicine Neulasta

On October 21, 2009, the Board issued an Order accepting a Voluntary Compliance Undertaking (VCU) for the medicine Neulasta and concluding the proceeding initiated with the issuance of a Notice of Hearing on March 16, 2009.

The Notice of Hearing pertained to allegations of Board Staff that Neulasta had been, and was being, sold by Amgen Canada Inc. at prices exceeding those indicated by the Board's Excessive Price Guidelines. On October 13, 2009, the Hearing Panel received a Joint Submission by Amgen and Board Staff along with a VCU which proposed to resolve the issues raised in the Neulasta proceedings.

The terms of the VCU require that Amgen reduce the price at which it sells Neulasta to the 2009 maximum price; make a payment to the Government of Canada in the amount of $6,730,120.32 to offset any revenues above the maximum prices from the date of introduction of Neulasta to June 30, 2009; and, offset revenues greater than the 2009 maximum price received by Amgen from July 1, 2009 to December 31, 2009.

Amgen is to ensure that the price of Neulasta remains within the Board's Excessive Price Guidelines for the period it remains under the Board's jurisdiction.

The Board Order is a public document and is available on the PMPRB Web site, along with the parties' Joint Submission and the VCU (under Regulatory; Hearings; Neulasta, and under Voluntary Compliance Undertakings).

Neulasta is a new active substance (pegfilgrastim) indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with cancer receiving myelosuppressive chemotherapy.

ratiopharm Inc. and the medicine ratio-Salbutamol HFA

On July 8, 9 and 10, the Hearing Panel heard the parties on Board Staff's Motions: to add GlaxoSmithKline Inc. (GSK) as a party to the hearing on the merits; and for the issuance of an Inspection and Production Order to ratiopharm.

On August 14, 2009, the Panel issued a subpoena to GSK requiring the production of the information sought by Board Staff and inspection and production orders to ratiopharm.

A pre-hearing conference is scheduled for November 2 and the hearing on the merits is set to start on January 25, 2010.

ratio-Salbutamol HFA is indicated for the relief of chest tightness and wheezing caused by spasms or narrowing in the small air passages of the lungs.

ratiopharm Inc.

The Hearing Panel in the ratiopharm Inc. jurisdiction matter heard the parties on October 13 and 14, 2009. At the conclusion of the hearing session, the Panel requested that Board Staff and the Respondent file written final reply and rebuttal arguments respectively, for the Panel's consideration, all by November 10, 2009.

Hearing Records are available on the PMPRB Web site under Regulatory; Hearings. ■

NPDUIS Update

The National Prescription Drug Utilization Information System (NPDUIS) is a research initiative by the PMPRB in partnership with the Canadian Institute for Health Information (CIHI). NPDUIS seeks to provide policy-makers with information and insights on trends in prices, utilization and costs of interest to participating public drug plans (all federal and provincial drug plans participate in NPDUIS except Québec).

The NPDUIS Steering Committee is holding a meeting in Ottawa on November 3, conjointly with a meeting of the Canadian Institute for Health Information's NPDUIS Data Advisory Group on November 2, and a meeting of the Pharmaceutical Policy Research Collaboration (PPRC) on November 4. The PPRC is a network of academic researchers with funding provided by the Canadian Institutes of Health Research.

Additional information on NPDUIS is available on the PMPRB Web site, under Reporting; NPDUIS. ■

Electronic PMPRB NEWSletter

If you wish to receive the NEWSletter electronically, please register by forwarding your e-mail address to: pmprb@pmprb-cepmb.gc.ca.

Readers who have changed e-mail address recently are invited to send us their new coordinates if they wish to keep receiving the NEWSletter.

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 Compliance and Enforcement Policy, patentees are given an opportunity to submit a VCU when Board Staff concludes, following an investigation, that the price at which the patentee sold 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.

Brevibloc, Baxter Corporation

On October 5, 2009, the Chairman of the Board accepted a VCU submitted by Baxter Corporation for the patented drug product Brevibloc.

The terms of the VCU require that, among other things, Baxter offset excess revenues received from January 1, 2007 to June 30, 2009 by making payments totalling $212,440.76 to customers that previously purchased Brevibloc.

Baxter is to ensure that the price of Brevibloc remains within the Guidelines in all future periods in which Brevibloc remains under the PMPRB's jurisdiction.

Brevibloc (esmolol hydrochloride) is indicated for the perioperative management of tachycardia and hypertension in patients in whom there is a concern for compromised myocardial oxygen balance and who, in the judgment of the physician, are clearly at risk of developing hemodynamically-induced myocardial ischemia, and for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in acute situations when the use of a short-acting agent is desirable.

Andriol, Schering-Plough Canada Inc.

On October 16, 2009, the Chairman of the Board accepted a VCU submitted by Schering-Plough Canada Inc. for the patented drug product Andriol 40 mg/capsule.

The terms of the VCU require that Schering-Plough offset excess revenues of $3,392,652,63. Schering-Plough will, among other things, offset excess revenues received from November 1, 2004 to December 31, 2004, by making a payment to the government of Canada totalling $348,605.86. Schering-Plough is also to provide a discount of 21.25% against the 2009 maximum non-excessive (MNE) price to all customers and will file evidence with Board Staff that the discount to all customers is in place in a manner consistent with the terms of the VCU.

Schering-Plough is to ensure that the price of Andriol remains within the Guidelines in all future periods in which it remains under the PMPRB's jurisdiction.

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. Andriol 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. ■

New Drugs introduced since the publication of the July 2009 NEWSletter

Sixteen new DINs for human use (representing 11 medicines) were added to the list of Patented Medicines reported to the PMPRB between July 30 and September 30, 2009. Six of these new medicines are new active substances representing 9 DINs.

The following table presents the new active substances reported to the PMPRB during the period July to September 2009.

Brand Name	Generic Name	Company	Indication
Alrex – 2 mg/mL	loteprednol etabonate	Bauch and Lomb Canada Inc.	Allergic conjunctivitis
Cimzia – 200 mg/mL	certolizumab pegol	UCB Canada Inc.	Rheumatoid arthritis
Lotemax – 5 mg/mL	loteprednol etabonate	Bauch and Lomb Canada Inc.	Inflammation from cataract surgery
Somatuline Autogel – 60 mg/syringe, 90 mg/syringe	lanreotide acetate	Tercica Inc.	Antigrowth
Sprycel – 20 mg/tablet, 50 mg/tablet, 70 mg/tablet	dasatinib	Bristol-Myers Squibb Canada Inc.	Leukemia
Xeomin – 100 unit/vial	Clostridium botulinum neurotoxin Type A	Merz Pharma Canada Ltd.	Muscle relaxant

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. ■

Report on New Patented Drug – Pradax

Under its transparency initiative, the PMPRB publishes the results of the reviews of new patented drug products 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: Pradax

Generic Name: (dabigatran etexilate)

DINs: 02312433 (75 mg capsule)
02312441 (110 mg capsule)

Patentee: Boehringer Ingelheim Canada Ltd.

Indication – as per product monograph: For the prevention of venous thromboembolic events (VTE) in patients who have undergone elective total hip replacement or total knee replacement surgery.

Date of Issuance of First Patent(s) Pertaining to the Medicine: October 3, 2006

Notice of Compliance: June 10, 2008

Date of First Sale: July 3, 2008

ATC Class: B01AE07
Blood and Blood Forming Organs; Antithrombotic Agents; Antithrombotic Agents; Direct thrombin inhibitors

Application of the Guidelines

Summary

The introductory prices of Pradax were 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 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 Pradax was sold.

Scientific Review

Pradax is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) recommended that Pradax 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 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 and are clinically equivalent in addressing the approved indication. See the PMPRB's *Compendium of Guidelines, Policies and Procedures* for a more complete description of the Guidelines and the policies on TCCs.

The HDAP recommended products outside the 4th level ATC as they were no comparators in the same 4th level ATC. The HDAP recommended fondaparinux and the low molecular weight heparins (LMWH) (dalteparin, enoxaparin, nadroparin and tinzaparin) as appropriate comparators to Pradax. These agents have the same indication as Pradax. Acenocoumarol, warfarin, acetylsalicylic acid, warfarin and unfractionated heparin were excluded as comparable products because, based on published guidelines and randomized controlled trials, these agents are not as effective and are associated with increased side effects including more stringent laboratory and clinical monitoring.

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 Pradax and the comparable drug products were based on the respective product monographs and supported by clinical literature.

Price Review

Under the Guidelines, the introductory price of a category 3 new drug product will be presumed to be excessive if it exceeds the prices of all of 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 Pradax 110 mg tablet was within the 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 (January to June 2007)

Brand Name (Generic Name)	Strength	Dosage Regimen (30 days)	Unit Price	Cost per Treatment (30 days)
Pradax (dabigatran etexilate)	110 mg/cap	60 capsules	$3.9250[1]	$235.5000
Arixtra (fondaparinux)	2.5 mg/0.5mL	15 mL	$30.1522[2]	$452.2830
Fragmin (dalteparin)	10,000 antiXa IU/mL	15 mL	$15.6000[2]	$234.0000
Fragmin (dalteparin)	25,000 antiXa IU/mL	6 mL	$39.0000[2]	$234.0000
Fragmin (dalteparin)	5,000 antiXa IU/mL	6 mL	$49.1400[2]	$294.8400
Fraxiparine (nadroparin)	5,700 antiXa IU/0.6mL	18 mL	$15.1000[3]	$271.8000
Innohep (tinzaparin)	20,000 antiXa IU/mL	5.25 mL	$32.0000[2]	$168.0000
Lovenox (enoxaparin)	100 mg/mL	36 mL	$20.5000[2]	$738.0000
Lovenox (enoxaparin)	30 mg/0.3 mL	36 mL	$20.6333[2]	$742.7988

Sources:
1 Publicly available price as per the *Patented Medicines Regulations*
2 Ontario Drug Benefit Formulary, June 2008
3 *Association québécoise des pharmaciens propriétaires*, 2008

Due to the titration dosing, a Reasonable Relationship test was conducted for Pradax 75 mg. The introductory price of Pradax 75 mg capsule ($3.9250) was within the Guidelines.

In 2008, Pradax was being sold in two countries listed in the Regulations, namely, Sweden and the United Kingdom. In compliance with the Guidelines, the prices of Pradax 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 list any drug product if it has reason to believe it is being sold at an excessive price.

In its Summary Reports, the PMPRB will also refer 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 purposes only and should not be relied upon as indicating the public prices are considered within the Guidelines.

The information contained in the PMPRB's Summary Reports should not be relied upon for any purpose other than that 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; Pradax. ■

Summary of Board Meeting – September 17, 2009

The Board met on September 17, 2009, to discuss the monitoring and evaluation of the Board's new Excessive Price Guidelines which are coming into effect on January 1, 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. ■

Upcoming Events

November

November 2:
Pre-hearing conference in the ratiopharm Inc. and the medicine ratio-Salbutamol HFA matter, Ottawa

November 2-4:
DIA's 7th Canadian Annual Meeting: "Time to Act", Ottawa

November 3:
PMPRB NPDUIS Steering Committee meeting, Ottawa

November 3-4:
Meeting of the Pharmaceutical Policy Research Collaboration (PPRC), Ottawa

November 4-5:
8th Annual Market Access Summit, Toronto

November 10-11:
Market Access Canada for Pharma, Toronto

November 12:
PMPRB meeting with Rx&D's Sub-Committee on the PMPRB, on the Board's new Excessive Price Guidelines

November 19:
HDAP meeting

November 24:
Presentation on the PMPRB price review process and the Board's new Excessive Price Guidelines, to Bristol-Myers Squibb, Montreal

November 24-25:
Brogan Advanced Seminars, Montreal, Toronto

December

December 1:
Federal Court of Appeal hearing on the Celgene Corporation matter, Ottawa

December 4:
Board meeting

2010 – January

January 25-28:
Hearing in the ratiopharm Inc. and the ratio-Salbutamol HFA matter, Ottawa

March

March 23-26:
Pharma Pricing & Market Access Outlook 2010, London, UK

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

What's New @ PMPRB

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

Questions and Comments

PMPRB E-bulletin

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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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