Patented Medicine Prices Review Board

PMPRB NEWSletter

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April 2003

Inside...

Board Members

The Patented Medicine Prices Review Board is a quasi-judicial tribunal with the mandate to ensure that manufacturers' prices of patented medicines sold in Canada are not excessive.

Since our last issue...

Here are some of the key events which occurred since January 2003.

February 11:	Pre-Hearing conference in the matter of Schering Canada Inc. and the medicine Remicade.
February 14:	Ginette Tognet, Director of Compliance and Enforcement gave a speech on litigation in the pharmaceutical industry, entitled *Brevets pharmaceutiques et prix des médicaments brevetés : le rôle du CEPMB*, at a conference in Montréal – *Litiges pharmaceutiques*.
February 19:	Wayne D. Critchley gave a speech – *PMPRB Update*, at the *5th Annual Maximizing Market Access* conference, in Toronto.
March 27:	Wayne gave a speech – *Current Issues in Price Controls for Patented Medicines*, at a conference on Drug Patents, in Toronto. The speech is available on our website under Other Publications; Speech Series; 2003.
April 1:	Issuance of a Board Order accepting a Voluntary Compliance Undertaking by Schering Canada Inc. in the matter of Remicade.

Robert G. Elgie, Chairperson

Message from the Chair

The Board approves a VCU to lower the price of Remicade

On April 1, 2003, the Board announced that it had accepted a Voluntary Compliance Undertaking (VCU) by Schering Canada Inc. (Schering) to lower the price of the medicine Remicade.

Among other things, the VCU, agreed to by Schering and Board Staff, benefits patients with an immediate price reduction of approximately 20%, bringing the price of Remicade within the Board's Price Guidelines.

The terms of the VCU require that the average transaction price not exceed $909.51 per vial for the balance of 2003. Under the Guidelines, future price increases for Remicade will be limited to increases in the Consumer Price Index (CPI). Also, to offset excess revenues from past sales of Remicade, Schering made a payment to the Government of Canada in the amount of $7.8 million.

This matter was initiated on December 16, 2002, with the issuance of a Notice of Hearing to consider whether under sections 83 and 85 of the *Patent Act*, the medicine Remicade had been, and is being, sold by Schering at prices exceeding the Guidelines.
The matter was first reported in the January 2003 NEWSletter.

Remicade is sold pursuant to a Notice of Compliance issued by Health Canada on June 6, 2001 for the treatment of Crohn's disease and to a Notice of Compliance issued on September 27, 2001 for the treatment of rheumatoid arthritis.

The Board's Order and relevant documents are available on the PMPRB website under Other Publications; VCUs, ACRs, Hearings and Decisions of the Board; Hearings; Remicade.

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A pre-hearing conference was held in February and the matter scheduled to be heard by a Hearing Panel of the Board in April. On March 18, Schering and Board Staff filed a joint submission proposing that the Board approve a VCU to resolve issues raised by the Notice of Hearing. The acceptance of the VCU concluded the proceeding commenced by the issuance of the Notice of Hearing. ■

PMPRB'S Research Agenda 2003 – 2006

As part of our annual planning process, we develop a Research Agenda. It outlines current or upcoming projects which we are working on or will be undertaken in the near future. Initiatives that are currently, or may become, subject to public consultations are also indicated in the Research Agenda.

Our 2003 – 2006 Research Agenda is available on our website under Other Publications; Research Agenda. As the Research Agenda is updated, it will be published in the NEWSletter and posted on our website. ■

PMPRB Studies for the Federal/Provincial/ Territorial Working Group on Drug Prices

The PMPRB conducted a series of studies on behalf of the Federal/Provincial/Territorial Working Group on Drug Prices, under a Memorandum of Understanding with the Minister of Health. The study on the prices of non-patented single source drugs was recently approved for release by the F/P/T Deputy Ministers of Health and is now available on our website under Other Publications; Study Series.

The six participating provincial drug plans in the NPSS study are British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia.

Top Selling Non-Patented Single Source Drug Products: International Price Comparison

This study examined the ex-factory prices of the top selling non-patented single source (NPSS) prescription drugs in Canada for 1999. During that year, manufacturers' sales of non-patented drugs were $3.6 billion, representing 39% of all manufacturers' sales in Canada.

In this study, Canadian prices of the top selling NPSS drugs were compared to prices in the seven countries used by the PMPRB to regulate patented medicines. Using data for 1999, the study found that Canadian prices for NPSS products were, on an expenditure-weighted basis, 28% higher than the median international prices of the seven countries, with this premium jumping to 75% when the comparison was restricted to the six European countries among the seven countries. This analysis implies that had NPSS medicines been priced at median international levels of the seven countries, spending on such products by six provincial drug plans would have been reduced by approximately 20% in 1999 fiscal year, representing a saving of some $60 million overall.

The top selling NPSS drug products included in this study were identified from the Ontario Drug Benefit Plan (ODB) database. Price and utilization patterns were also constructed from ODB data. The 56 medicines included represented approximately 50% of all NPSS products in the six participating provincial drug plans. ■

Voluntary Compliance Undertaking – Aromasin

On April 26, 2003, the Chairperson of the Board approved a VCU from Pharmacia Canada Inc. (Pharmacia) for the drug product Aromasin (exemestane).

Aromasin is a selective steroidal aromatase inhibitor indicated for the treatment of advanced breast cancer in women with natural or artificially induced postmenopausal status whose disease has progressed following antiestrogen therapy. It is a new active substance introduced to the Canadian market on August 17, 2000.

Following its review, Board Staff concluded that the price of Aromasin appeared to exceed the Guidelines and, as a result, commenced an investigation in 2001. Board Staff advised Pharmacia that, following the procedures outlined in the Guidelines, Aromasin was classified as a category 3 new medicine. A Therapeutic Class Comparison (TCC) test was conducted using Femara (letrozole) and Arimidex (anastrozole) as comparable medicines of the same 4th level class of the Anatomical, Therapeutic, Chemical (ATC) System. Pharmacia had submitted that the TCC should include Megace, but the PMPRB's Human Drug Advisory Panel did not agree as Megace is used as third line therapy.

The results of the TCC indicated that the average selling price of Aromasin, $5.7243 per 25 mg tablet, during the period August 17, 2000 to December 31, 2000 appeared to exceed the maximum non-excessive (MNE) price of $4.9500 per 25 mg tablet by 15.6%. As a result, Pharmacia received revenues in excess of the Guidelines of $26,411.37 during that period.

An international price comparison (IPC) test was also conducted and showed that the Canadian price of Aromasin 25 mg tablet was the lowest among the PMPRB comparator countries and therefore did not exceed the Board's Guideline with respect to the highest international price.

The price review results for the period January 1, 2001 to December 31, 2001 showed that the average selling price of Aromasin declined to $5.3504 per tablet, but continued to exceed the MNE price of $5.0738 per tablet by 5.5%. As a result, Pharmacia received additional excess revenues of $61,073.28 during that period.

During the course of the investigation, Pharmacia lowered the list price of Aromasin to $4.95 per tablet effective April 1, 2002, and provided public notification of this price reduction. The new price is within the Guidelines.

Taking into account the price reduction, the price review results for calendar year 2002 showed that the average selling price of Aromasin, $4.9174 per tablet, was lower than the MNE price of $5.1826 per tablet by 5.2%. As a result, Pharmacia has offset the cumulative amount of revenues in excess of the Guidelines received in previous years.

The terms and conditions of the VCU were agreed to between Board Staff and the patentee. Under the terms of the VCU, Pharmacia has undertaken to ensure that the average selling price of Aromasin 25 mg tablet will continue to be within the Board's Guidelines as long as it is under the jurisdiction of the PMPRB. Having considered the evidence, the Chairperson approved the VCU. ■

Under the Compliance and Enforcement Policy, patentees are given an opportunity to make a Voluntary Compliance Undertaking (VCU) when Board Staff conclude, following an investigation, that a price appears to have exceeded the Board's Excessive Price Guidelines. Approval of a VCU by the Chairperson or Board is an alternative to the commencement of formal proceedings through the issuance of a Notice of Hearing.

The full text of the VCU respecting Aromasin is available on our website under Other Publications; VCUs, ARCs, Hearings and Decisions of the Board.

Report on New Patented Drugs

Pulmozyme

PMPRB

Under its transparency initiative, the Board publishes the results of the reviews of new patented drugs by Board Staff, for purposes of applying the PMPRB's Price Guidelines, for all new active substances introduced after January 1, 2002.

Brand Name:	Pulmozyme
Generic Name:	dornase alfa recombinant
DIN:	02046733 2.5 mg/ampul
Patentee:	Hoffmann-La Roche Canada Ltd.
Indication (as per product monograph):	For the management of cystic fibrosis patients to reduce the frequency of respiratory infections requiring parenteral antibiotics and to improve pulmonary function.
Notice of Compliance:	December 1993
Date of First Sale:	August 1994 In most cases, patents are issued before the drugs come to market. In this case, the first patent pertaining to Pulmozyme was issued on February 5, 2002 and it came under the PMPRB's jurisdiction at that time.
ATC Class:	RO5CB13 *Cough and Cold Preparation, expectorants, excluding combinations with cough suppressants, mucolytics*

Application of the Guidelines

PMPRB

The seven countries listed in the *Patented Medicines Regulations, 1994*, for purposes of price comparison are France, Italy, Germany, Sweden, Switzerland, United Kingdom and the United States.

Summary:

The introductory price of Pulmozyme was found to be within the Guidelines because the Canadian price did not exceed the median of the prices for the same drug in the seven countries listed in the *Patented Medicines Regulations, 1994* (Regulations). The price of Pulmozyme continued to be within the Guidelines in 2002 when it came under the PMPRB's jurisdiction.

Scientific Review:

Pulmozyme is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) reviewed it as a category 3 new medicine (provides moderate, little or no therapeutic advantage over comparable medicines.)

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 Anatomical, Therapeutic, Chemical (ATC) System that are clinically equivalent in addressing the approved indication.

The other medications in the same fourth level ATC as Pulmozyme include Mucomyst (N-acetylcystine) and Uromitexan (mesna). However, neither of these agents share the same indication as Pulmozyme nor is there any evidence supporting the use of these agents for the treatment of cystic fibrosis. Consequently, the HDAP recommended no comparators for the conduct of a TCC for Pulmozyme.

The Guidelines provide that when it is inappropriate or impossible to conduct a TCC, the primary weight will be given to the median of the international prices. The price will be presumed excessive if it exceeds the median of the prices of the same drug in the seven countries listed in the Regulations. See the PMPRB's Compendium of Guidelines, Policies and Procedures for a more complete description of the Guidelines and the policies on International Price Comparisons.

Price Review:

The Canadian price of Pulmozyme was within the Guidelines as it did not exceed the median of the prices for the same drug in those countries in which it was being sold. As shown in the following table, the price of Pulmozyme in Canada continued to be below the median international price in 2002.

Country	$ CDN price per 2.5 mg/amp
Canada	$35.00
France	$42.17
Germany	$40.74
Italy	$35.88
Sweden	$44.93
Switzerland	$33.47
UK	$41.26
US	$50.32
Median	$41.26

Sources

Canada: Liste des médicaments, Régie de l'assurance maladie du Québec, 2002
France: Sempex, February 2002
Germany: Rote Liste, January 2002
Italy: L'Informatore Farmaceutico, March 2002
Sweden: Prislista, May 2002
Switzerland: Medwin, September 2002
UK: MIMS, March 2002
US: AWP, Drug Topics Red Book, March 2002; FSS Price, 2002

Evidence/ References:

The references are available on the PMPRB website, under Other Publications; Patented Medicines; Reports on New Patented Drugs; Pulmozyme.

Gleevec

Brand Name: Gleevec

Generic Name: Imatinib mesylate

DIN: 02244725
100 mg capsule

Patentee: Novartis Pharmaceutical Canada Inc.

Indication (as per product monograph): Gleevec (imatinib mesylate) is indicated for the treatment of patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy. Gleevec is also indicated for the treatment of patients with unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST).

Notice of Compliance: NOC with conditions September 20, 2001 for CML and August 7, 2002 for GIST

Date of First Sale: September 25, 2001
The first patent pertaining to Gleevec was issued November 26, 2002 and it came under the PMPRB's jurisdiction at that time.

ATC Class: L01XX28
Antineoplastic and Immunomodulating Agents, Antineoplastic Agents, Other antineoplastic agents

Application of the Guidelines

Summary:

The price of Gleevec was found to be within the Guidelines because the price in Canada did not exceed the median of the prices of the same drug in those countries listed in the *Patented Medicines Regulations, 1994* (Regulations) in which it was sold.

Scientific Review:

The PMPRB's Human Drug Advisory Panel (HDAP) recommended that Gleevec be reviewed as a category 2 new drug (breakthrough or substantial improvement) based on the following information:

- Gleevec is recognized as the only agent indicated for use in all three stages of CML, i.e., blast crisis, accelerated phase and chronic phase after failure of interferon-alpha therapy and also for use in GIST.
- Under the Guidelines, new DINs with multiple approved indications are categorized based on the approved indication for which the medicine offers the greatest therapeutic advantage in relation to alternative therapies for the same indication in a significant population. This approved indication is considered the primary indication for purposes of selecting comparable medicines.
- Based on the scientific evidence, Gleevec provides the greatest therapeutic advantage in relation to its use in the chronic phase of CML after failure of interferon therapy. This stage of CML is therefore considered to be the primary indication.
- Comparators are generally selected from among existing drug products in the same 4th level of the Anatomical, Therapeutic, Chemical (ATC) System that are clinically equivalent in addressing the approved indication. The Guidelines provide that it may, however, be appropriate to include products from other ATC classes if they are clinically equivalent for the appropriate indication to the drug product under review. See the PMPRB's Compendium of Guidelines, Policies and Procedures for a more complete description of the Guidelines and the policies on TCCs.
- There are a number of drug products in the same 4th level ATC as Gleevec, however none of them are clinically equivalent in addressing the same indication (i.e. in the chronic phase of CML after failure of interferon therapy).
- Although two drug products from other ATC classes, Hydrea (hydroxyurea) and Busulflex (busulfan) may be used in the chronic phase of CML, their uses are recognized as being palliative in nature and therefore are not considered to be clinically equivalent to Gleevec. As a result, the HDAP recommended no comparators for the conduct of a therapeutic class comparison for Gleevec.

PMPRB

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 Anatomical, Therapeutic, Chemical (ATC) System that are clinically equivalent in addressing the approved indication.

Price Review:

Under the Guidelines, the price of a new drug in category 2 should not exceed the higher of the prices of other drugs that treat the same disease (TCC test) and the median of the prices of the same drug in the seven countries listed in the Regulations (IPC test). It was not possible to conduct a TCC test for Gleevec as the HDAP did not identify any comparable medicines. The price of Gleevec was within the Guidelines both at the time it was first introduced in September 2001 and when it became patented in November 2002, as the Canadian price was below the median international price in those countries in which it was sold.

The Regulations require that patentees file publicly available prices in the seven countries listed therein (see ss. 4(1)(g)). Schedule 3 of the Compendium of Guidelines, Policies and Procedures sets out the methodology to conduct an IPC test.

According to information derived from public sources, the ex-factory prices for Gleevec ranged from about $20.06 to $29.61 per capsule in other countries in late 2002. For price review purposes, the PMPRB relies on price information filed by the patentee as required by the Regulations. In the case of Gleevec, the patentee has provided price information for all seven countries for the relevant time periods and the price in Canada did not exceed the median of the foreign prices.

Where comparators and dosage regimens are referred to in the Summary Reports, they have been selected by the PMPRB Staff and the HDAP for the purpose of carrying out the PMPRB's regulatory mandate, which is to review the prices of patented medicines sold in Canada to ensure that such prices are not excessive. The publication of these reports is also part of the PMPRB's commitment to make its price review process more transparent.

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

Country	$CDN price per 100 mg capsule
Canada	$24.3500
Germany	—
France	—
Italy	$20.0620
Sweden	$29.6054
Switzerland	$22.6828
UK	$26.1962
US	$27.1313
Median	$26.1962

Sources

Italy: L'Informatore Farmaceutico, November 2002*
Sweden: Prislista, November 2002*
Switzerland: Medwin, November 2002
UK: MIMS, November 2002*
US: Average prices of US Red Book, November 2002 and prices available on the US Department of Veterans Affairs website.

* Derived from publicly available formulary price using regulated wholesale mark-ups set out in the PMPRB Study S-0215, *Verification of Foreign Patented Drug Prices 2000*.

The *Patented Medicines Regulations, 1994* and the Compendium of Guidelines, Policies and Procedures, are both available on our website under Legislation, Regulations, Guidelines.

Evidence/ References:

The references are available on the PMPRB website, under Other Publications; Patented Medicines; Reports on New Patented Drugs; Gleevec.

New Patented Medicines Reported to the PMPRB

The list of New Patented Medicines Reported to the PMPRB is posted on our website under Other Publications; Patented Medicines; 2002.

Since the publication of the January 2003 NEWSletter, 18 new DINs for human use were added to the list of New Patented Medicines Reported to the PMPRB for the period ending December 31, 2002.

The new medicines included six new active substances, one of which, Gleevec, is discussed on page 5, representing seven DINs, as set out in the following table:

Brand Name	Generic Name	Company
Alphagan (2mg/mL)	brimonidine tartrate	Allergan Inc.
Lovenox (100mg/mL)	enoxaparin sodium	Aventis Pharma Inc.
Spiriva (18 mcg/cap)	tiotropium bromide	Boehringer Ingelheim (Canada) Ltd.
Pariet (10 mg/tab; 20 mg/tab)	rabeprazole sodium	Janssen-Ortho Inc.
Gleevec (100 mg/cap)	imatinib mesylate	Novartis Pharmaceuticals Canada Inc.
Infergen (0.03 mg/mL)	interferon alfacon-1	Intermune Inc.

CPI-Adjustment Factors for 2004

See the Compendium of Guidelines, Policies and Procedures, Chapter 1, EPG: 6 and Schedule 4. The Compendium is posted on our website under Legislation, Regulations, Guidelines. For additional information, patentees can also contact the compliance officer assigned to their company.

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 Price Guidelines limit price increases to changes in the CPI over a three-year period.

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 PMPRB informs patentees on an annual basis of the CPI-adjustment factors for future pricing periods.

The CPI-adjustment factors for 2004 are as follows:

2004 CPI-Adjustment Factors for All Patented Drug Products (CPI 1992=100)

	Benchmark Year		
	(1) 2001	(2) 2002	(3) 2003
Base CPI	116.41	119.03	n/a
2004 Forecast CPI	124.57	124.57	124.57
2004 CPI-Adjustment Factor	1.070	1.047	1.022

The Base CPI is the average of the monthly CPI figures, as published by Statistics Canada, for the benchmark year.

The 2004 Forecast CPI is 124.57 (1992=100) and is based on the actual CPI figures for 2002 (119.03), as published by Statistics Canada, and the latest available inflation projections (2.4% for 2003 and 2.2% for 2004) from the federal Department of Finance. ■

Filing Electronically

We strongly encourage electronic reporting of the information required under the *Patented Medicines Regulations, 1994* (i.e. information submitted in Form-1, Form-2 and Form-3). Currently more than 90% of the pharmaceutical companies file price and sales data electronically.

The most common method that patentees could use would be Microsoft Excel. Any version of Excel can be submitted. In addition to Microsoft Excel, Lotus 123, Microsoft Access and text files (for example, *.txt with fixed column or tab delimited) are all acceptable for electronic filing.

To be received by the PMPRB, the information should, at minimum, use the same headings as in Form-2. Patentees are responsible for ensuring that the electronic filings include all the information required under the Regulations.

Patentees who wish to use electronic filing should store the information on a diskette and send it to the PMPRB along with a copy of the print out by mail or by e-mail.

In order to facilitate patentees' filings, we are in the process of developing interactive forms starting with Form-1 and the Notification of Intent to Sell. ■

Patentees' filings of price information for the period January 1 to July 1, 2003 are to be submitted to the PMPRB no later than August 1, 2003.

Patentees requiring additional information on this matter should contact the compliance officer assigned to their company or the Secretary of the Board at (613) 952-7360 or at pmprb@pmprb-cepmb.gc.ca

Questions and Comments

Contact Us!

You can reach us on-line through our electronic feedback form at **www.pmprb-cepmb.gc.ca**, under Contact.

The feedback form is another way that you can communicate with us. If you have any questions, comments or ideas we would love to hear from you. Your feedback is important to us and there are a variety of ways you can reach us: e-mail, telephone, fax or mail and through our on-line feedback.

We look forward to hearing from you! ■

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Patented Medicine Prices Review Board – February 10, 2003 Meeting

At its meeting, the Board:

- Considered the scope of its project on assessing the value of new drugs.
- Received staff briefings on:
  - ongoing initiatives under the National Prescription Drug Utilization Information System (NPDUIS);
  - the 2003-04 to 2005-06 Strategic Plan.
- Received a briefing on:
  - the Common Drug Review (CDR) process, by Barbara Shea, Director of the Common Drug Review Committee. ■

The next Board meeting is scheduled for May 22-23, 2003.

For any additional information, please contact the Secretary of the Board at 1 877 861-2350, or (613) 954-8299, or sdupont@pmprb-cepmb.gc.ca.

Upcoming Events

May
22-23
Board Meeting, Ottawa

May
30
PMPRB 2002 Annual Report to the Minister of Health

June
18
Conference – *Drug Cost Management,* Toronto
Wayne D. Critchley

September
23
Conference – *Drug Patents-West,* Vancouver
Wayne D. Critchley

September
22-23
Board Meeting, Ottawa

December
8-9
Board Meeting, Ottawa

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Comments

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