Patented Medicine Prices Review Board

NEWSletter

Volume 3, Issue No. 3 July 1999

Since our last issue, April 1999 ...

Following are some of the key events which occurred over the last quarter:

May 4	Appointment of Dr. Ingrid Sketris
May 25	Dr. Robert G. Elgie, Chairperson, appeared before the Standing Committee on Health on the 1999-2000 Plans and Priorities. His remarks are available on our web site, under Publications, Speeches
May 27 & 28	Board Meeting
June 4 & 8	Wayne D. Critchley, Executive Director, gave presentations to the BCHS Pharmacy Business Practices Conference, Richmond, B.C. and PHARMAC '99 Conference, Toronto, Ontario
June 14	Release of the 1998 Annual Report
June 23 & 24	Meeting of the Working Group on Price Review Issues
July 5	Hoechst Marion Roussel Canada Inc. - Nicoderm: Hearing on the issue of the Board's jurisdiction.

Please contact us at our toll-free number: **1-877-861-2350** to obtain copies of any materials or consult our web site at: **http://www.pmprb-cepmb.gc.ca**.

Congratulations!

On June 11, 1999, the Workers' Compensation Section of the Canadian Bar Association (Ontario) presented Dr. Robert G. Elgie, Chairperson of the Patented Medicine Prices Review Board, with an award for his leadership and contribution in Worker's Compensation Law. Dr. Elgie was Chair of the Workers' Compensation Board of Ontario from 1985 to 1991 and part-time Chair of the Workers' Compensation Board of Nova Scotia from 1992 to 1996.

Guy Roberge, PMPRB's Technical Officer, celebrated 25 years with the federal Public Service on May 21, 1999. Guy joined the Department of Consumer and Corporate Affairs in May 1974 where he worked until he joined the PMPRB upon its creation on December 7, 1987.

PMPRB Web Site

If you want to know more about the PMPRB and you have access to the NET, look for our site at **http://www.pmprb-cepmb.gc.ca**

The 1998 Annual Report is available on our web site under **Publications**, **Annual Report**.

Inside...

1998 PMPRB Annual Report

Upon release of the Annual Report on June 14, 1999, Dr. Robert G. Elgie, Chairperson of the Board, stated that, "In the past year, the evolving role of the Board as an integral part of Canada's health care system, has been highlighted with the completion of our year-long public consultations, the release of the Board's *Road Map for the Next Decade* and the publication of the Auditor General's report on the PMPRB."

In 1998, the prices of patented drugs were virtually unchanged from 1997, falling by an average of 0.1%, as compared to the Consumer Price Index (CPI) which increased by 1.4%. Internationally, prices for patented drugs in Canada still ranked third lowest, just below the United Kingdom. Since 1987, Canadian prices for patented drugs have declined over 30% compared to foreign prices.

Total sales by manufacturers of all drugs in Canada are estimated to have increased over 11.4% to $7.8 billion in 1998, while sales of patented drug products increased by 18.9% to $4.3 billion. Patented drugs accounted for over 55% of the total sales of all drugs. Patentees

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. The PMPRB does not set prices.

"People are seeking more information to make more informed decisions about cost-effective therapies. The Board has an important role to play in meeting these needs. It is a role we take very seriously and one which we are committed to fulfill in the most responsive, effective and open manner possible."

Dr. Robert G. Elgie, June 14, 1999

reported $798.9 million in R&D expenditures, an increase of $73 million since 1997. For the 74 reporting firms, the R&D-to-sales ratio remained unchanged at 11.5%. Patentees reported expenditures of $146.8 million on basic research. Although spending on basic research increased by 4.6% from 1997, its share of total R&D declined from 20.7% in 1997 to 19.6% in 1998.

The Board has recently established the Working Group on Price Review Issues, bringing together representatives of a cross section of our stakeholders to examine issues raised in the *Road Map*. In the coming months, the Working Group will begin reporting on the results of its review and analysis. ■

For information on the Nicoderm hearing, please contact Sylvie Dupont-Kirby, Secretary of the Board, at:

Toll-free number: 1-877-861-2350
Direct line:(613) 954-8299
Fax: (613) 952-7626
E-mail: sdupont@pmprb-cepmb.gc.ca

Once issued, the Board's decision will be posted on our web site: **http://www.pmprb-cepmb.gc.ca** under **Publications** and **Hearings & Decisions of the Board**.

Board members hear arguments on the Board's jurisdiction in the Nicoderm case

On April 20, 1999, the Chairperson of the Board issued a Notice of Hearing in the matter of Hoechst Marion Roussel Canada Inc. (HMRC) and the price of the nicotine patch Nicoderm, to determine whether, under the *Patent Act*, Nicoderm was sold at an excessive price.

On July 5, the Board received and heard evidence and argument on a motion by HMRC that the Board does not have jurisdiction in this matter. The Board is expected to issue its decision and reasons on jurisdiction shortly. ■

The Working Group on Price Review Issues holds its second meeting on June 23 & 24, 1999

At its meeting on June 23 & 24, the Working Group was joined by a new member, Dr. Luis Barreto of Pasteur Mérieux Connaught, who has replaced Joyce Groote, President of BioteCanada.

Summary of Minutes

1. The first day of the meeting was scheduled to finalize the review of the first issue, the appropriate use of U.S. Department of Veteran Affairs (DVA) prices in conducting international price comparisons (IPCs). The second day was scheduled to introduce and discuss the Price Review Process for New Patented Drug Products.

June 23 - U.S. DVA prices

2. The market for pharmaceuticals in the U.S., the role of U.S. Department of Veteran Affairs and sources of drug price information in the U.S. were reviewed.
3. Additional information requested by the Working Group at its previous meeting was provided and discussed.
4. The options for inclusion of the U.S. DVA prices were evaluated based on the Working Group's criteria. Consensus was reached on the preferred option. It was agreed that this option should be forwarded to the Board for its consideration. Certain concerns were also documented to be brought to the attention of the Board in the Working Group report.
5. It was agreed that the co-chairs would draft the Working Group report to the Board, based on the agreement described in paragraph 4, for review by the Working Group and that the Working Group would aim to finalize the report by early September 1999.
6. The impact of the preferred option for using U.S. DVA prices in conducting IPCs was reviewed at an aggregate level. The Working Group agreed that the Board should consider transition measures for those drug products whose prices would exceed the Guidelines.

June 24 - Price Review Process for New Patented Drug Products

7. The objective and scope of the Working Group were reviewed for the second issue, that is the Price Review Process for New Patented Drug Products. The objective of the second issue is to identify means to improve the transparency and accountability of the price review process for new patented drugs. The Working Group agreed to be guided by the principles outlined in the *Road Map for the Next Decade* in its review of the price review process. These are: transparency, efficiency and timeliness, high quality assessments and accountability. In addition, the Working Group agreed to add as a principle that the process should be forward looking in its approach.
8. A presentation was provided on the current price review process for new patented drug products.
9. The Working Group identified and prioritized items relating to the price review process and items not presently covered in the price review process. All items will be scheduled for discussion in subsequent meetings.

The next Working Group meeting is scheduled to be held in Vancouver on October 18 & 19, 1999. ■

For any additional information on the activities of the Working Group on Price Review Issues, please contact the co-chairs of the Working Group, at our toll free line 1-877-861-2350 or at their respective number:

Ron Corvari:
(613) 952-3305
rcorvari@pmprb-cepmb.gc.ca

Laura Reinhard:
(613) 952-7619
lreinhard@pmprb-cepmb.gc.ca

The Terms of Reference of the Working Group and all documents related to the *Road Map for the Next Decade* are available on our web site: **http://www.pmprb-cepmb.gc.ca**, under **Working Group on Price Review Issues** and **Publications**.

Breakthrough / Substantial Improvement Drugs

New Human Drug Products Identified as Category 2 Medicines in 1997 and in 1998

The PMPRB categorizes new patented drug products for price review purposes. An independent panel of experts, the Human Drug Advisory Panel, reviews submissions by patentees and other information in order to make recommendations on categorization. The categorization of a drug does not represent an endorsement by the PMPRB.

1997

Aricept, Benefix, Camptosar, Crixivan, Eprex and Invarase were the 6 medicines (13 DINs) classified as breakthrough or substantial improvement products (category 2) in 1997.

ARICEPT (donepezil)
DIN 02232043 5 mg tablet
02232044 10 mg tablet
ATC N07AA

Indication: Symptomatic treatment of patients with mild to moderate dementia of the Alzheimer's type. ARICEPT has not been studied in controlled clinical trials for longer than 6 months.

Factors Considered: Aricept is the first drug product to be approved and sold in Canada that has demonstrated some efficacy in the treatment of Alzheimer's Disease.

Factors Not Considered: Aricept was not evaluated against tacrine (Cognex). There are no clinical trial data comparing the two drugs. Furthermore, tacrine has never been approved in Canada and is available only under the Special Access Program. Aricept was not evaluated against ginkgo biloba as the latter is not currently approved or sold as a drug product in Canada.

BENEFIX (coagulation Factor IX recombinant)
DIN 02231018 250 units/vial Injection
02231019 500 units/vial Injection
02231020 1000 units/vial Injection
ATC B02BD

Indication: Control and prevention of hemorrhagic episodes in patients with hemophilia B.

Factors Considered: Indirect evidence suggests that Benefix is as effective in controlling or preventing a hemorrhage as other factor IX products available on the Canadian market. Because of the purity of the product developed using recombinant technology, Benefix is, as stated in the product monograph, *inherently free from the risk of transmission of human blood-borne pathogens such as HIV, hepatitis viruses and parvovirus.*

Factors Not Considered: The risk of unpredictable recalls and supply interruptions due to contamination associated with the blood supply should be greatly reduced or eliminated with Benefix.

CAMPTOSAR (irinotecan) 20 mg/ml injection
DIN 02231622
ATC L01XX

Indication: Treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following 5-fluorouracil-based therapy.

Factors Considered: The Kaplan Meir estimates of median survival time for patients on the recommended starting dose of 125 mg/m^2 derived from three clinical trials discussed in the product monograph suggest that approximately 3/4 of patients exceeded the median survival among non-responders of 4.2 months . Median survival for all patients was 8.9 months (range 0.3 - 33.4 months) compared to a median survival time with 5-fluorouracil and leucovorin (5FU-L) of 11.5 months (Piedbois P et al. J Clin Oncol 1992; 10, 896-903). Given the improvement in survival time demonstrated in patients whose disease recurred or progressed following first-line 5-FU based therapy and the lack of alternative drugs possessing significant efficacy, Camptosar can be considered a substantial improvement in the treatment of colorectal cancer.

Factors Not Considered: Camptosar, which inhibits topoisomerase 1, has a different mechanism of action than 5-FU thereby offering an alternative approach to

A new patented drug product is classified as a category 2 drug product if it is the first drug product to treat effectively a particular illness or if it provides a substantial improvement over existing drug products.

The PMPRB publishes a list of the new patented drug products for human use which were categorized in the previous year as breakthroughs or drugs offering substantial therapeutic improvement over previously available medicines (category 2). The criteria for determining substantial improvement in therapeutic effect are set out in the Scientific Review Procedures in the PMPRB *Compendium of Guidelines, Policies, and Procedures*.

kill colorectal tumour cells. This factor alone is not adequate to classify Camptosar as a category 2 new medicine. Camptosar was not evaluated against raltitrexed (Tomudex) as there is no clinical evidence to suggest that the two drugs are comparable. Camptosar was not evaluated against topotecan (Hycamtin) as this topoisomerase inhibitor is only approved in Canada for the treatment of ovarian cancer.

CRIXIVAN (indinavir)
DIN 02219161 200 mg Capsule
02219196 400 mg Capsule
ATC J05AX

Indication: In combination with reverse transcriptase inhibitor nucleoside analogues for the treatment of adults with HIV-1 infection.

Factors Considered: Three protease inhibitors agents (ritonavir, indinavir, saquinavir) were introduced in Canada in 1996. Norvir (ritonavir) was the first of the three drugs to be patented and come under the jurisdiction of the PMPRB. When the introductory price of Norvir was reviewed in 1996, there was evidence to support that protease inhibitors in combination with reverse transcriptase inhibitor nucleoside analogues were a substantial improvement in the management of HIV disease. Although the protease inhibitors had not been compared head-to-head with the nucleoside analogues, the significant effect of protease inhibitors on viral load observed was considered a substantial reduction; this in combination with the increase in CD4 cell count and increase in short term survival in advanced HIV disease supported a category 2 classification of Norvir. Crixivan (indinavir) and Invirase (saquinavir) became patented drug products in 1997. Since the three drugs were introduced within weeks of one another in 1996, the PMPRB assigned the same category to Crixivan and Invirase as was assigned to Norvir.

Factors Not Considered: The clinical significance of the differences between the three protease inhibitors available on the Canadian market has not been evaluated in this review.

EPREX (epoetin alfa)
DIN 02126575 2000 IU/1 mL Vial
02126583 4000 IU/1 mL Vial
02126591 10000 IU/1 mL Vial
02206072 20000 IU/1 mL Vial
ATC B03XA

Indication: To elevate or maintain the red blood cell level and to decrease the need for transfusions. Treatment of anemia of chronic renal failure, in zidovudine-treated HIV infected patients and in cancer patients. Also indicated in elective surgery regimens to reduce allogenic blood exposure.

Factors Considered: Chronic anemias which are independent of a deficit of iron or vitamins were usually treated with repeated transfusions which entail bloodborne risks and require short-term hospitalization. The only other pharmacological therapy available to treat the targeted patient population would be the androgenic products (e.g. nandrolone); this latter class is, however, not commonly used for this indication. Epoetin is the only therapy directed to increase the number of red blood cells correcting anemia in 97% of cases.

Factors Not Considered: While the benefits of this drug are relatively clear for patients with chronic renal failure, anemia associated with AZT therapy and cancer patients, there is less evidence to support the use of epoetin in surgical patients. The recommendation for categorization is based on the clinical evidence available for the former patient groups, not the latter. Pharmacoeconomic analysis of the use of epoetin were not considered in this evaluation.

It should be noted that although Eprex has been on the Canadian market since 1993, it did not become a patented drug product and subject to the PMPRB's jurisdiction until May 1997.

INVIRASE (saquinavir) 200 mg Capsule
DIN 002216965
ATC J05AX

Indication: In combination with reverse transcriptase inhibitor nucleoside analogues for the treatment of advanced HIV infection.

Factors Considered: Three protease inhibitors agents (ritonavir, indinavir, saquinavir) were introduced in Canada in 1996. Norvir (ritonavir) was the first of the three drugs to be patented and come under the jurisdiction of the PMPRB. When the introductory price of Norvir was reviewed in 1996, there was evidence to support that protease inhibitors in combination with reverse transcriptase inhibitor nucleoside analogues were a substantial improvement in the management of HIV disease. Although the protease inhibitors had not been compared head-to-head with the nucleoside analogues, the significant effect of protease inhibitors on viral load observed was considered a substantial reduction; this in combination with the increase in CD4 cell count and increase in short term survival in advanced HIV disease supported a category 2 classification of Norvir. Crixivan (indinavir) and Invirase (saquinavir) became patented drug products in 1997. Since the three drugs were introduced within weeks of one another in 1996, the PMPRB assigned the same category to Crixivan and Invirase as was assigned to Norvir.

Factors Not Considered: The clinical significance of the differences between the three protease inhibitors available on the Canadian market has not been evaluated in this review.

1998

Levovist and Taxol were the two drugs (2 DINs) classified as breakthrough or substantial improvement products in 1998.

LEVOVIST (galactose/palmitic acid)
DIN 02227347 granules - 2.5 g
02229102 granules - 4.0 g
ATC V08DA

Indication: One- and two- dimensional Doppler sonographic blood flow imaging in patients with insufficient Doppler signal intensity; B-mode contrast echocardiography.

Factors Considered: Levovist is the first ultrasound contrast agent to be approved in Canada and therefore the first to be accepted by the Health Protection Branch as effective for this indication. As there is no clear evidence as yet that other agents are also effective, Levovist meets the criteria for classification as a category 2 new medicine. There is little or no evidence available at this time to assess the potential impact Levovist will have on clinical outcomes.

Factors Not Considered: According to the literature, several other agents or techniques for enhancing ultrasound signal strength are under investigation including Albunex (sonicated albumin microspheres), PESDA (perfluorocarbon exposed sonicated dextrose albumin), IDE (iodipamide ethyl ester particles), SF6 (sulfur hexafluoride microbubbles) and PFOB (perfluorooctyl bromide lecithin emulsion). Comparable efficacy between Levovist and these other agents was not considered in the categorization.

TAXOL (paclitaxel)
DIN 02016796 injection - 6 mg/mL
(5 mL, 16.7 mL and 50 mL vials)
ATC L01CD

Indication(s): Alone or in combination, for the treatment of carcinoma of the ovary or breast or lung.
For ovarian carcinoma: first-line therapy in combination with other chemotherapeutic agents; second-line treatment of metastatic carcinoma of the ovary after failure of standard therapy.
For breast carcinoma: second-line treatment of metastatic carcinoma of the breast after failure of standard therapy.
For lung carcinoma: first-line treatment of advanced non-small cell lung cancer.

Factors considered: For purposes of this review, the primary use was the treatment of ovarian cancer; this was the indication approved for Taxol in 1992. Taxol is now approved for use in ovarian, breast and lung carcinoma. Based on current treatment guidelines, paclitaxel plus cisplatin is considered first line treatment for ovarian cancer. There are data supporting that the addition of paclitaxel to cisplatin improves the survival in ovarian carcinoma by 40 to 58%. Paclitaxel adds potentially dangerous adverse effects, but these are of less importance than those seen with cyclophosphamide. Taxol offers the greatest therapeutic advantage in relation to alternative therapies for the same indication in a significant patient population.

Factors not considered: The therapeutic merit of Taxol in the treatment of lung cancer or breast cancer was not evaluated. Taxol (paclitaxel) was not compared to Taxotere (docetaxel), the other taxoid available in Canada. Taxotere was not available when Taxol was first introduced and is not approved for the treatment of ovarian cancer.

It should be noted that although Taxol has been on the Canadian market since 1993, it did not become a patented drug product and subject to the Board's jurisdiction until May 1998. ■

Patented Medicine Prices Review Board - May 27 & 28 Meeting

At the last Board meeting, the Chairperson introduced the two newly-appointed Board Members:

- Dr. Anthony Boardman, B.A. (hons.), Ph.D. - Professor of Strategic Management and Public Policy Analysis and Chair of the Policy Analysis Division, Faculty of Commerce and Business Administration, University of British Columbia.
- Dr. Ingrid Sketris, BSc(Phm), Pharm. D., MPA(HSA) - Professor, College of Pharmacy and School of Health Services Administration; Associate Professor, Department of Community Health and Epidemiology, Dalhousie University; consultant to the pharmacy department of the Queen Elizabeth II Health Services Centre, Halifax.

The Members of the Board:
- Reviewed the communications package for the 1998 Annual Report. The Report was submitted to the Minister on May 31, 1999 and tabled in Parliament on June 11, 1999.
- Received an oral briefing on the first meeting of the Working Group on Price Review Issues.
- Received an oral briefing on the work of Board staff in the context of the activities of the Federal/Provincial/Territorial Task Force on Pharmaceutical Prices.
- Received a status report on the Board's follow-up activities to the September 1998 Report of the Auditor General on the PMPRB.
- Received the final Compliance Report for the 1998 calendar year.

The next Board meeting is scheduled for September 23 & 24, 1999.

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 ■

Exchange Rates

The methodology for calculating exchange rates for purposes of the PMPRB's International Price Comparison is described in Schedule 3 of the Compendium of Guidelines, Policies and Procedures.

Existing Drug Products

The simple average of the monthly average noon spot exchange rates for each country for the 36-month period ending June 1999 will be used in the review of prices for existing medicines in the first half of 1999.

The international prices of an existing drug product for the period January to June 1999 can be converted to Canadian currency for comparison purposes by multiplying the local currency price in each country by the corresponding simple average exchange rate.

36 Month Average Exchange Rates Ending June 1999

Period Ending	France	Germany	Italy	Sweden	Switzerland	United Kingdom	United States
June 99	0.24870556	0.83664722	0.00084583	0.18703611	1.01074722	2.34058154	1.43141719

We have received several requests for information on how to obtain the WHO's ATC [Anatomical Therapeutic Chemical Classification System of the World Health Organization].

Here is where you can inquire:

WHO Collaborating Centre for Drug Statistics Methodology
c/o NORSK MEDISINALDEPOT AS
P.O. Box 100, Veitvet
N-0518 Oslo
Norway
Tel: +47 22169811
Fax: +47 22169818
E-mail: whocc@nmd.no

New Drug Products

The following table provides the average 36-month exchange rates for new drug products introduced between June 1998 and November 1999.

Average Exchange Rates for New Drug Products Introduced between June 1998 and November 1999

Month of Introduction	France	Germany	Italy	Sweden	Switzerland	United Kingdom	United States
Jun 98	0.25896944	0.88461944	0.00084511	0.19218056	1.07077500	2.19176813	1.37429969
Jul 98	0.25807222	0.88066389	0.00084336	0.19184167	1.06738333	2.19594882	1.37522983
Aug 98	0.25663333	0.87438056	0.00084206	0.19140556	1.06037778	2.19877431	1.37547802
Sep 98	0.25528889	0.86860556	0.00084192	0.19128056	1.05317778	2.20376451	1.37697641
Oct 98	0.25443611	0.86435556	0.00084194	0.19131944	1.04789444	2.20950075	1.37931417
Nov 98	0.25342778	0.85975000	0.00084167	0.19118889	1.04209444	2.21565643	1.38176126
Dec 98	0.25246111	0.85552500	0.00084150	0.19108889	1.03669722	2.22324574	1.38528168
Jan 99	0.25201389	0.85336667	0.00084228	0.19112778	1.03382222	2.23407389	1.39029203
Feb 99	0.25197778	0.85253333	0.00084422	0.19121944	1.03236944	2.24666681	1.39502995
Mar 99	0.25221944	0.85230556	0.00084744	0.19121667	1.03182500	2.26042183	1.40057175
Apr 99	0.25210000	0.85118056	0.00084953	0.19084722	1.02980000	2.27271985	1.40574463
May 99	0.25208333	0.85044444	0.00085158	0.19042500	1.02861111	2.28570991	1.41054273
Jun 99	0.25196111	0.84950556	0.00085289	0.19018611	1.02691389	2.29727986	1.41478313
Jul 99	0.25148611	0.84726389	0.00085264	0.18985833	1.02409722	2.30627126	1.41816647
Aug 99	0.25098611	0.84505833	0.00085206	0.18935833	1.02114444	2.31671280	1.42239319
Sep 99	0.25033056	0.84257222	0.00085075	0.18870000	1.01776667	2.32598912	1.42595721
Oct 99	0.24957500	0.83981667	0.00084858	0.18791667	1.01435556	2.33396904	1.42853928
Nov 99	0.24870556	0.83664722	0.00084583	0.18703611	1.01074722	2.34058154	1.43141719

PMPRB List of Publications

Here are the latest additions to our Publications List:

- 1998 Annual Report
- Speech Series (1999)
  Chairperson's remarks before the Standing Committee on Health on the 1999-2000 Plans and Priorities, May 25, 1999.

To order call our toll-free number 1-877-861-2350

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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