Patented Medicine
Prices
Review Board
Since 1987

The mandate of the Patented Medicine Prices Review Board is to ensure that prices at which patentees sell their patented medicines in Canada are not excessive; and to report on pharmaceutical trends of all medicines and on R&D spending by patentees.

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.

PMPRB

Notice and Comment

June 2010

FASLODEX®, an AstraZeneca Canada Inc. product

Notice and Comment issued by the PMPRB: June 18, 2010

Canada

www.pmprb-cepmb.gc.ca

NOTICE

TAKE NOTICE that the Vice-Chairperson of the Patented Medicine Prices Review Board ("Board" or "PMPRB") proposes to accept a Voluntary Compliance Undertaking (VCU) in respect of the price of the medicine FASLODEX.

AND TAKE NOTICE that written submissions in respect of the proposed Voluntary Compliance Undertaking will be considered.

A. Purpose of this Notice

1. The purpose of this Notice is 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 in the form set out in **Attachment 1** with respect to the price proposed by AstraZeneca Canada Inc. ("AstraZeneca") for the patented medicine FASLODEX®.

B. Background

2. 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 5mL intramuscular injection.

3. Canadian Patent No. 2,351,004 pertaining to FASLODEX was granted to AstraZeneca AB, Sweden on February 18, 2003 and will expire on January 8, 2021. AstraZeneca is the patentee for the purposes of the PMPRB.

4. Health Canada issued a Notice of Compliance (NOC) to AstraZeneca for FASLODEX on February 17, 2004 (DIN 02248624). FASLODEX was first sold in Canada on February 1, 2006.

5. Pursuant to sub-section 85 (1) of the *Patent Act* (Act), and for purposes of determining whether the price of a patented medicine is excessive under section 83, the Board shall take into consideration the following factors, to the extent that information on such factors is available to the Board:

   a. the prices at which the medicine has been sold in the relevant market;
   b. the prices at which other medicines in the same therapeutic class have been sold in the relevant market;
   c. the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;
   d. changes in the Consumer Price Index; and
   e. such other factors as may be specified in any regulations made for the purposes of this subsection.

6. Based on the Board's previous Excessive Price Guidelines (pre-2010 Guidelines), the Human Drug Advisory Panel (HDAP) recommended that FASLODEX pre-filled syringes be classified as a category 3 new drug product (provides moderate, little or no therapeutic advantage over comparable existing drug products). The HDAP also identified the oral therapies TAMOFEN (tamoxifen), ARIMIDEX® (anastrozole), FEMARA (letrozole), AROMASIN (exemestane) and MEGACE (megestrol) as comparable drug products, as they share the same indication and are used in the treatment of patients with hormone-receptor positive advanced or metastatic breast cancer.

7. In considering whether the introductory price of a category 3 new drug product appears excessive, one of the tests under the PMPRB's pre-2010 Guidelines is whether it exceeds the prices of the comparable drug products in the same therapeutic class (Therapeutic Class Comparison (TCC) test). Based on the TCC test, the introductory maximum non-excessive (MNE) price was $161.1990 (**Attachment 2**).

8. A second test under the pre-2010 Guidelines is whether the Canadian price of the new drug product exceeds the prices of that drug in the countries listed in the *Patented Medicines Regulations* (Regulations).[1] FASLODEX is sold in all seven comparator countries. Prices in these countries at the time of introduction ranged from $616.3043 (Italy) to $962.7268 (United States). The median international price was $692.2303. The Canadian price was $600.00, lower than the price of FASLODEX in all seven of the PMPRB reference countries.

9. The introductory MNE price ($161.1990) based on therapeutically comparable drugs in Canada is considerably lower (73.4% lower) than the lowest price in the comparator countries listed in the Regulations. **Attachment 3** provides details of the international prices.

10. The price of FASLODEX in Canada has remained constant at $600.0000 since introduction in 2006.

11. FASLODEX is sold to a very small population of Canadian women to respond to their very specific needs. The market share of FASLODEX in Canada relative to the other hormonal therapies identified as therapeutic class comparators during the introductory period was very minimal (0.005%), and as units of sale have not increased measurably from the introductory period, its market share among the hormonal therapies has not grown appreciably during subsequent periods of sale (**Attachment 4**).

12. Section 85 of the Act identifies a comparison of the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada as one factor which the Board must take into account in its deliberation in contemplation of a remedial order.

13. It is within the Board's discretion to ascribe the weight it deems appropriate to prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada when considering the particular circumstances of any matter upon which it is adjudicating. The pre-2010 Guidelines do not provide for the International Therapeutic Class Comparison (ITCC) test, but the Board Guidelines which were implemented January 1, 2010 do in the context of an investigation for information purposes.

14. In light of the circumstances of this case, Board Staff has recommended that it is appropriate to rely on a ratio approach ITCC test. The ratio approach ITCC test was previously used in the HUMALOG (insulin lispro) and VIREAD (temofovir disoproxil fumarate) cases in determining whether the prices were within the Guidelines.

15. Although MEGACE was the highest priced comparator in the domestic TCC test for FASLODEX, ARIMIDEX has the largest share of market sales and is also sold by AstraZeneca. As well, in two randomised clinical trials, ARIMIDEX has been compared to FASLODEX and determined to be clinically equivalent when used as second line hormonal therapy. Applying the median international ratio of FASLODEX to ARIMIDEX under the ITCC test to the price of ARIMIDEX in Canada would yield an introductory MNE price (now known as the maximum average potential price (MAPP)) of $521.2350 for FASLODEX (**Attachment 5**).

16. Board Staff and AstraZeneca are proposing that the ITCC test be used to set the introductory MNE price for FASLODEX at $521.2350, rather than using the TCC test result ($161.1990). On this basis, AstraZeneca and Board Staff have also agreed on a VCU (**Attachment 1**). Subject to the outcome of this Notice and Comment it is recommended that this VCU be accepted by the Vice-Chairperson.

1 France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States

C. Process for Submissions

17. All persons who wish to make representations in this matter shall file a written submission with the Board on or before **September 17, 2010**.
18. All submissions by the provincial and territorial Ministers of Health will be considered by the Board.
19. All submissions by other persons shall include a clear statement of the person's interest in this matter, and shall state the reasons why the Board should consider the submission.
20. All submissions shall be filed with the Director, Board Secretariat at Box L40, 333 Laurier Avenue West, Suite 1400, Ottawa, Ontario K1P 1C1. Further information on the role and process of the Board may also be obtained from the Director, Board Secretariat.
21. Board Staff and AstraZeneca will be given the opportunity to make written submissions to the Board in response to any written submissions received within fifteen (15) days thereafter, no later than **October 1, 2010**.
22. The Vice-Chairperson will consider all submissions in determining whether to accept the proposed Voluntary Compliance Undertaking.
23. The Vice-Chairperson's decision and all submissions will be posted on the PMPRB Web site.

Ottawa, June 11, 2010

D. Table of Contents

Attachment 1

Voluntary Compliance Undertaking

of

AstraZeneca Canada Inc.

to the

Patented Medicine Prices Review Board

1.0 Product Summary

1.1 FASLODEX® (fulvestrant) 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 as a pre-filled syringe with a strength of 50 mg/mL and is administered at monthly intervals as a single 5 mL intramuscular injection.

1.2 Health Canada issued a Notice of Compliance (NOC) to AstraZeneca Canada Inc. (AstraZeneca) for FASLODEX on February 17, 2004 (DIN 02248624). FASLODEX was first sold in Canada on February 1, 2006.

1.3 Canadian Patent No. 2,351,004 pertaining to FASLODEX was granted to AstraZeneca AB, Sweden on February 18, 2003 and will expire on January 8, 2021. AstraZeneca is the patentee for the purposes of the Patented Medicines Prices Review Board (PMPRB).

2.0 Application of the Excessive Price Guidelines

2.1 The PMPRB's Human Drug Advisory Panel (HDAP) recommended that FASLODEX be classified as a category 3 new drug product and identified oral hormonal treatments, namely, Tamofen (tamoxifen), ARIMIDEX® (anastrozole), Femara (letrozole), Aromasin (exemestane), and Megace (megestrol), as the most appropriate comparator drug products.

2.2 In accordance with the Board's *Excessive Price Guidelines* (Guidelines), a Therapeutic Class Comparison (TCC) test and an International Price Comparison (IPC) test were conducted. The result of the TCC test indicated that the introductory price of $600.00 appeared to exceed the Guidelines as it was above the maximum non-excessive (MNE) price of $161.1990. The result of the IPC test indicated that the Canadian price was lower than the corresponding prices of FASLODEX in all seven of the PMPRB reference countries outlined in the Regulations.

2.3 The price of FASLODEX in Canada has remained constant at $600.0000 since it was first sold in 2006.

2.4 The Board's Notice and Comment dated June 11, 2010 provides the details for the rationale and background information surrounding the application of the ratio approach International Therapeutic Class Comparison (ITCC) test for FASLODEX.

2.5 **ARIMIDEX** (anastrozole) has the largest share of market sales, is sold by AstraZeneca in Canada and is sold in all seven of the PMPRB reference countries. Applying the median international ratio of FASLODEX to ARIMIDEX under the ITCC test to the price of ARIMIDEX in Canada would yield an introductory MNE price of $521.2350. Cumulative excess revenues calculated by Board Staff as having been received by AstraZeneca as a result of selling FASLODEX at a price above the MNE price were $405,030.29 as of December 31, 2009.

3.0 Position of the Patentee

3.1 This Voluntary Compliance Undertaking (VCU) constitutes no admission by AstraZeneca that the price in Canada of FASLODEX is now, or was at any time since the date of the first sale of the medicine, excessive for purposes of the Patent Act.

3.2 AstraZeneca will not be bound by the undertaking herein unless this VCU is accepted by the Board.

4.0 Terms of the Voluntary Compliance Undertaking

4.1 In order to comply with the Guidelines, AstraZeneca agrees to undertake the following:

4.1.1 To agree that the MNE prices of FASLODEX are as follows:

2006	$521.2350
2007	$532.1809
2008	$544.6906
2009	$546.7755
2010	$558.7899

4.1.2 To reduce the price of FASLODEX within 30 days of the acceptance of this VCU so that it does not exceed the 2010 MNE price of $558.7899;

4.1.3 To offset the cumulative excess revenues received from February 2006 to December 31, 2009 by making a payment to Her Majesty in right of Canada in the amount of $405,030.29 within 30 days of the acceptance of the VCU;

4.1.4 To offset any excess revenues received during the period January 1, 2010 to the date of reduction of the price of FASLODEX as per 4.1.1 of this VCU by making a payment within 30 days of the filing of semi-annual price and sales data as required by the *Patented Medicines Regulations* in the amount of the excess revenues, as calculated by Board Staff, received as a result of selling FASLODEX at a price in excess of the 2010 MNE price set out in sub-paragraph 4.1.1 above;

4.1.5 Within 15 days of acceptance of this VCU, to provide notification to customers of the price reductions for FASLODEX and that this price reduction is the result of an undertaking to the PMPRB, to provide a reference to the PMPRB Web site for the complete text of the VCU, and to provide copies of such notifications to Board Staff;

4.1.6 To file evidence with Board Staff within 30 days of the acceptance of this VCU that the price of FASLODEX has been reduced in a manner consistent with the terms of this VCU; and

4.1.7 To ensure that the price of FASLODEX remains within the Guidelines in all future periods in which FASLODEX is under the PMPRB's jurisdiction.

AstraZeneca Canada Inc.

Signature: Original signed by

Company Officer: Marion E. McCourt

Position: President and CEO

Date: June 11, 2010

Attachment 2

Therapeutic Class Comparison

	Strength	Dosage Regime	Unit Price	Cost per 30 Day Treatment
Faslodex (fulvestrant)	250 mg/5 mL	1 vial every 30 days	600.0000[1]	600.0000
Tamofen (tamoxifen)	20 mg	1 tab daily x30 days	0.3500[2]	10.5000
Arimidex (anastrozole)	1 mg	1 tab daily x30 days	4.9500[2]	148.5000
Femara (letrozole)	2.5 mg	1 tab daily x30 days	4.9500[2]	148.5000
Aromasin (exemestane)	25 mg	1 tab daily x30 days	4.9500[2]	148.5000
Megace (megestrol)	160 mg	1 tab daily x30 days	5.3733[2]	161.1990
Megace (megestrol)	40 mg	4 tab daily x30 days	1.3430[2]	161.1600

Notes:

1 Publicly available ex-factory price as per *Patented Medicines Regulations*

2 Ontario Drug Benefit Formulary 2005 & September 2006

Highest allowable unit price based on cost per treatment $161.1990 of Megace 160mg

International Price Comparison

Faslodex (250mg/5mL Syringe)
International Prices[1]
January – June 2006
(Cdn $)[4]

Country	Price per 250mg/5mL Syringe
Canada	$600.0000
Germany	$693.6503
France	$692.2303
Italy	$616.3043
Sweden	$624.9171
Switzerland	$664.9642
UK	$737.3052
US[2,3]	$962.7268
Median	**$692.2303**

Country	Exchange Rate
Canada	1.00000000
Germany	1.53510000
France	1.53510000
Italy	1.53510000
Sweden	0.16695556
Switzerland	0.99106389
UK	2.24159444
US	1.25196111

1 Sources for Prices:

Canada: Publicly available ex-factory price as per *Patented Medicines Regulations*
Germany: Rote Liste, January 2006
France: Sempex, February 2006
Italy: L'informatore farmaceutico, June 2006
Sweden: Prislista, June 2006
Switzerland: Medwin website, January-June 2006
UK: Mims, June 2006
US: Federal Supply Schedule (FSS), January-June 2006
Thomson Micromedex Wholesale Acquisition Cost (WAC), April 2006

2 The methodology for deriving net backed-out price can be found in the study, "Verification of Foreign Patented Drug Prices 2000" available on the PMPRB Web site www.pmprb-cepmb.gc.ca under Other Publications; Study Series

3 For the US, there is no national drug formulary, nor regulated mark-ups. The Red Book publishes a Direct Price (DP); the Federal Supply Schedule (FSS) includes a drug formulary for purposes of several federal drug plans and represents the prices paid by the U.S. Government. Thomson Micromedex publishes a Wholesale Acquisition Cost (WAC). For purposes of this comparison, the U.S. price has been estimated by averaging the WAC and FSS.

4 Exchange rates based on 36-months ending June 2006 as per PMPRB Compendium Schedule 3

Attachment 4

Market Shares of Faslodex and its Comparators

Introductory Period

January – June 2006 Period

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	300.0	$169,000.00	$563.3333	0.005%
Tamofen 20mg/tab	270,000.0	$94,000.00	$0.3481	4.3%
Arimidex 1mg/tab	3,447,000.0	$17,577,000.00	$5.0992	54.6%
Femara 2.5mg/tab	1,878,000.0	$10,050,000.00	$5.3514	29.7%
Aromasin 25mg/tab	687,000.0	$3,541,000.00	$5.1543	10.9%
Megace 160mg/tab	36,000.0	$115,000.00	$3.1944	0.6%
Total	6,318,300.0	$31,546,000.00	$582.4809	100.0%

Note: IMS, June 2006

January – December 2006 Period

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	1,000.0	$647,000.00	$647.0000	0.007%
Tamofen 20mg/tab	528,000.0	$186,000.00	$0.3523	3.9%
Arimidex 1mg/tab	7,335,000.0	$37,416,000.00	$5.1010	54.6%
Femara 2.5mg/tab	4,032,000.0	$21,623,000.00	$5.3628	30.0%
Aromasin 25mg/tab	1,467,000.0	$7,585,000.00	$5.1704	10.9%
Megace 160mg/tab	60,000.0	$6,990,000.00	$116.5000	0.4%
Total	13,423,000.0	$74,447,000.00	$779.4866	100.0%

Note: IMS, December 2006

Market Shares of Faslodex and its Comparators for the 2007 to 2009 Periods

2007

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	1,600.0	$984,000.00	$615.0000	0.011%
Tamofen 20mg/tab	426,000.0	$153,000.00	$0.3592	2.8%
Arimidex 1mg/tab	8,265,000.0	$42,213,000.00	$5.1074	54.3%
Femara 2.5mg/tab	4,839,000.0	$26,169,000.00	$5.4079	31.8%
Aromasin 25mg/tab	1,662,000.0	$8,582,000.00	$5.1637	10.9%
Megace 160mg/tab	24,000.0	$131,000.00	$5.4583	0.2%
Total	15,217,600.0	$78,232,000.00	$636.4965	100.0%

Note: IMS, December 2007

2008

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	1,800.0	$1,098,000.00	$610.0000	0.011%
Tamofen 20mg/tab	345,000.0	$124,000.00	$0.3594	2.2%
Arimidex 1mg/tab	9,057,000.0	$46,393,000.00	$5.1223	57.2%
Femara 2.5mg/tab	4,626,000.0	$31,202,000.00	$6.7449	29.2%
Aromasin 25mg/tab	1,782,000.0	$9,194,000.00	$5.1594	11.3%
Megace 160mg/tab	21,000.0	$139,000.00	$6.6190	0.1%
Total	15,832,800.0	$88,150,000.00	$634.0051	100.0%

Note: IMS, December 2008

2009(1)

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	800.0	$553,000.00	$691.2500	0.009%
Tamofen 20mg/tab	147,000.0	$53,000.00	$0.3605	1.7%
Arimidex 1mg/tab	4,587,000.0	$23,560,000.00	$5.1363	53.3%
Femara 2.5mg/tab	2,997,000.0	$16,852,000.00	$5.6230	34.8%
Aromasin 25mg/tab	873,000.0	$4,500,000.00	$5.1546	10.1%
Megace 160mg/tab	–	–	–	–
Total	8,604,800.0	$45,518,000.00	$707.5244	100.0%

Notes: IMS, June 2009
Megace 160 mg was reported as having less than a 1000 units sold (—)
Megace 40 mg was not reported in IMS during any period.

Market Shares of Faslodex and Arimidex

January – December 2007 Period

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	1,600.0	$984,000.00	$615.0000	0.02%
Arimidex 1mg/tab	8,265,000.0	$42,213,000.00	$5.1074	99.98%
Total	8,266,600.0	$43,197,000.00	–	100.00%

January – December 2008 Period

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	1,800.0	$1,098,000.00	$610.0000	0.02%
Arimidex 1mg/tab	9,057,000.0	$46,393,000.00	$5.1223	99.98%
Total	9,058,800.0	$47,491,000.00	–	100.00%

January – June 2009 Period

	Units	Sales Revenue	Unit Price	% of Market Share
Faslodex 250mg/5mL syringe	800.0	$553,000.00	$691.2500	0.02%
Arimidex 1mg/tab	4,587,000.0	$23,560,000.00	$5.1363	99.98%
Total	4,587,800.0	$24,113,000.00	–	100.00%

Note: IMS, (Dec 2007, Dec 2008 & Jun 2009) information was used for this table, which captures Hospital & Pharmacy markets only.

Attachment 5

International Therapeutic Class Comparison

Faslodex 250 mg/mL (DIN 02248624)
Pricing Ratios in Canada and Other Countries[1]
Using Backed-Out[2] International Formulary Prices for Faslodex and Comparators
Cost per Treatment in Canadian Currency[3]
(Based on Date of First sale: February 2006)

	Canada	France	Germany	Italy	Sweden	Switzerland	UK	US	Equivalent Canadian Faslodex price
Faslodex 250 mg/mL	$600.0000	$633.5178	$694.8106	$605.6430	$638.8639	$694.4976	$709.1020	$1,028.5746	
Arimidex 1mg (30 mg)	$148.5000	$220.4640	$211.5360	$162.9060	$181.7700	$242.7780	$149.5620	$271.6770	$521.2350

Notes:

1 Sources for Prices:
All Faslodex and Arimidex prices taken from publicly available ex-factory price as per *Patented Medicines Regulations*. All comparators taken from public sources.

Canada: Ontario Drug Benefit Formulary, September 2006, Quebec February 2006
Germany: Rote Liste, January 2006
France: Sempex, February 2006
Italy: L'informatore farmaceutico, June 2006
Sweden: Prislista, June 2006
Switzerland: Medwin website, January-June 2006
UK: Mims, June 2006
US: Federal Supply Schedule (FSS), January-June 2006
Thomson Micromedex Wholesale Acquisition Cost (WAC), April 2006

2 The methodology for deriving net backed-out price can be found in the study, "Verification of Foreign Patented Drug Prices 2000" available on the PMPRB Web site www.pmprb-cepmb.gc.ca under Other Publications; Study Series

3 Exchange rates based on 36-months ending September 2005 as per PMPRB Compendium Schedule 3

September 2005 36-month Exchange Rates	
Country	**Exchange Rate**
Canada	1.00000000
Germany	1.58379444
France	1.58379444
Italy	1.58379444
Sweden	0.17323056
Switerland	1.03508056
UK	2.32690833
US	1.33759167