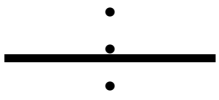
Top Selling Non-Patented Single Source Drug Products



International Price Comparison

1998/99

Prepared by the Patented Medicince Price Review Board for
Federal/Provincial/Territorial
Working Group on Drug Prices

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Executive Summary

- This study reports on an international comparison of ex-factory gate prices (manufacturers' price) of the top selling non-patented single source (NPSS) prescription drugs in Canada. Previous studies have shown that Canadian prices of these drugs are high relative to other OECD countries. This analysis updates previous analyses and provides further evidence and insight into Canadian price levels of non-patented single source drug products relative to international prices.

- In 1999, manufacturers' sales of non-patented drugs were $3.6 billion, growing at an annual rate of 7% over the last decade. In 1999, non-patented drugs represented 39% of all manufacturers' sales in Canada. Based on provincial drug plan data for six jurisdictions, British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia, non-patented single source drugs represented, on average 13% of all expenditures submitted to the drug plans.

- In this study, Canadian prices of these top selling NPSS drugs were compared to prices in the seven counties used by the Patented Medicine Prices Review Board (PMPRB) to regulate patented medicines: France; Germany; Italy; Sweden; Switzerland; the United Kingdom; and the United States.

- The study found that Canadian prices for these top selling NPSS drug products were, on average, substantially higher (28% when weighted by expenditures) than the median international prices of the seven countries. Comparing Canadian prices to a European median price (MEP) reveals that Canadian prices are on average approximately 75% above the MEP.

- The sensitivity analyses conducted on these results demonstrates the robust nature of these findings.

- This analysis suggests that had NPSS medicines been priced at median international levels, spending by the six provincial drug plans (BC, AB, SK, MN, ON, NS) would have been approximately $60 million or 20% less than the $300 million these plans spent on NPSS drugs in 1999/00.

- The top selling NPSS drug products were identified from the Ontario Drug Benefit (ODB) database. A total of 56 tablets and capsules (DINs) were included in the analysis. ODB prices were used to represent Canadian price and utilization patterns. The drugs included in this analysis represent approximately 50% of all non-patented single source drug products in the six provincial drug plans.

1. Introduction

1.1 Background

In March 1997, the Federal/Provincial/Territorial (F/P/T) Task Force on Pharmaceutical Prices prepared an overview paper that provided a description of the pharmaceutical sector in Canada. The paper contained a summary of existing information on drug prices, spending and mechanisms used by private and public payers for regulating and/or influencing pharmaceutical prices and expenditures.[1]

The Task Force has since further examined amongst other things, price and expenditure trends, price levels and cost drivers as they relate to prescription drugs reimbursed by six provincial drug plans. In April of 1999, the F/P/T Task Force conducted an international comparison of non-patented single source (NPSS) drug products. The analysis reported that prices for the top selling NPSS products in Canada where significantly higher than prices in the seven countries listed in *the Patented Medicines Regulations*. Specifically, the report concluded that Canadian prices in 1996 were, on average, 30% higher than the median international price (MIP) level for these products in that year.

As of June 1999, the F/P/T Task Force on Pharmaceutical Prices has been reconstituted as a working group of the F/P/T Pharmaceutical Issues Committee (PIC) and is now known as the *Working Group on Drug Prices.*[2] PIC is responsible for joint F/P/T activities on pharmaceutical issues.

1.2 Focus of Report

The contribution of this paper is to update previous analyses and to provide further evidence and gain increasing insight into Canadian price levels of non-patented single source drug products relative to international prices. The analysis included in this report updates and further investigates the relative cost to Canadians of purchasing these medicines and compares these costs internationally.

Accurate measurement of cross-national price differences for drugs is an important policy and research issue. Cross-national comparisons of drug prices are often used to evaluate the performance of different regulatory systems and to guide future policy options.[3] Reliable sources of publicly available prices, differences in market structures and distribution chains, regulation and utilization patterns can make measurement of inter-jurisdictional price comparisons challenging.

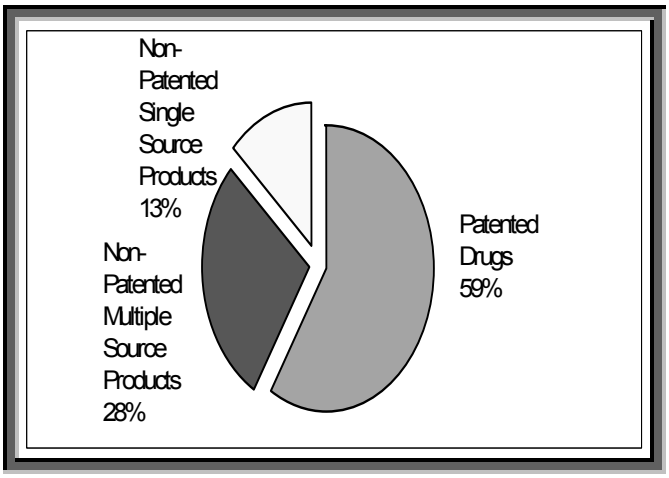
Different approaches are used to compare Canadian prices to international prices in this analysis. Canadian prices of 63 top selling NPSS drugs[4] are compared to a median international price. Canadian prices are also compared to prices in each jurisdiction directly. In addition, the analysis investigates the possible difficulties associated with calculating an accurate/representative U.S. price.[5] It examines the impact of product availability in the competitor countries on the international comparison statistics. Average median international prices are used in comparisons to Canadian NPSS price. The international price comparison is conducted with the inclusion of other brands and generics if they were available in that jurisdiction as well as direct brand to brand price comparisons.

1.3 Non-Patented Sales

Non-patented drug products include those drug products that were never patented or whose patent has expired and do not fall under the jurisdiction of the Patented Medicine Prices Review Board (PMPRB).[6] Single source drug products are defined as drugs containing a unique chemical, strength, dosage form and route of administration and sold by one manufacturer[7].

In 1999, Canadian manufacturers' sales of non-patented drugs were estimated to be $3.6 billion[8]. Between 1990 and 1999, manufacturers' sales of non-patented drugs have been growing at an average annual rate of 7%. In comparison, manufacturers' sales of patented drugs increased at an average annual rate of 16% while generics increased at 12% over the same period.

Figure 1-1 1999/00 Provincial Drug Plan Expenditures



In 1999, non-patented drugs represented 39% of all manufacturers' sales and 41% of provincial expenditures. Based on provincial drug plan data for six jurisdictions, British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia, non-patented single source drugs represented, on average, 13% of all prescriptions and expenditures submitted to the drug plans in 1999/00. The drugs included in this analysis represent approximately 50% of both volume and expenditures of these non-patented single source drug products.

2. Methodology

2.1 Drugs Included in the Analysis

Claims data from the Ontario Drug Benefits (ODB) database was used to identify an initial sample of approximately 100 top selling non-patented single source drug products in 1998/99. Of the top drugs chosen in the NPSS sample, only those that were tablets and capsules were included in the final analysis. This reduced the sample to 63 drug products; the sample was further reduced to 56 when only those products available in at least one international comparison were identified. The analysis was limited to tablets and capsules in order to ensure accurate unit price measurements at an international level. Oral, solid dosage forms offer the most reliable comparisons over entire markets of generic and brand products in many countries[9].

Non-patented drug products include those drug products that were never patented or whose patents have expired and do not fall under the jurisdiction of the Patented Medicine Prices Review Board (PMPRB). **[10]** Single source drug products are defined as drugs containing a unique chemical, strength, dosage form and route of administration and sold by one manufacturer**[11]**; in other words, a claim for a bioequivalent product was not made to the ODB in 1998/99. With notable exceptions, these are typically drug products with a relatively small market in which generic competition does not exist in Canada. Some single source drugs examined in this study have subsequently become multiple source drugs. Appendix D has a complete list of the drug products included in this analysis and identifies any products that have subsequent to the study become multiple sourced, i.e. offered by more than one manufacturer .[12]

2.2 Determining Ex-factory Gate Price in Canada and Internationally

Canadian ex-factory gate prices were derived from the claims data in the ODB database and verified by the ODB formulary list price for the same period**[13]**. Ex-factory gate prices for the seven comparison countries were derived from publicly available sources – refer to Appendix B for more detail. Unit dose or individually packaged tablets and capsules were excluded from the analysis if comparable packages of the same quantity were also available.[14] All bio-equivalent drug products were identified in each country and a unit price was calculated for each manufacture/brand name combination. [15]

Products that are single source in Canada were not necessarily single source in other countries, (see Table 3.1). If more than one bioequivalent drug product was found in a country, the product with the median unit price was used to represent the price in that country for most of the analysis.[16] An analysis using the comparable brand product was also presented in Appendix A. These products were identified abroad using both the manufacture and the brand name.[17]

Variation in pricing over package sizes was of particular concern because of the scope of this study. Prices were captured over all bio-equivalent brand and generic products from all distributors and manufacturers listed in the public sources used. The inclusion of multiple manufacturers increases the potential impact of price differences between package sizes on the final results. For example, generic and brand manufacturers may use different pricing strategies for different package sizes. This would not be a major issue for an analysis focusing solely on brand-to-brand price comparisons in different jurisdictions. The median package size price was used to get the most representative price for products that came in a variety of package sizes.**[18]** Sensitivity analysis showed that for brand-to-brand comparisons, mean and median package prices produce the same results.[19]

The analysis is based on ex-factory gate price comparisons. In order to derive an ex-factory gate price, relevant taxes, pharmacy mark-ups and wholesale mark-ups were removed where applicable.[20] Refer to Appendix C for background information on each of the countries included in this analysis as well as the methods used to derive the manufacturers' ex-factory gate price. Per unit prices were converted to Canadian dollars using the average exchange rate taken from the thirty-six month average.[21]

There were two sources of publicly available prices in the US, the Federal Supply Schedule (FSS), and the Red Book. In a large portion of

the analysis, the U.S. price is determined using an average of both of these prices. Where possible, the results were also presented separately both in the main text and in the Appendix. [22]

2.3 Calculating the Median International Price (MIP) and the Median European Price (MEP)

Once a foreign price was determined for each Canadian DIN (Drug Identification Number associated with each unique product), a MIP was calculated based on the prices in the countries where that drug product was available.[23] Canadian prices are excluded from the MIP. The average Canadian to MIP ratio was calculated using the geometric mean.[24] There were 56 products for which there was at least one country available for a price comparison; a sensitivity analysis was also conducted in order to investigate the impact of limited international product availability for constructing the price comparisons. An analysis was done on a smaller sample of products, 39, that were available in at least three[25] foreign countries. A sensitivity analysis based on ten products which were sold in all comparator countries was also conducted.

The average foreign to MIP ratio was also generated for each of the other seven countries. The MIP used to compare with each country was unique in that it contained the Canadian price, but not the price of the country it was being compared to. In this way each country was compared to at the very least Canada, as well as all other countries where that product was found.[26] Some analysis was also done using a subset of countries as opposed to a subset of products; specifically the analysis used the six European countries, but excluded the U.S. in the generation of a median international price.

The geometric average ratio, weighted by expenditure and quantity was also calculated using Canadian expenditure and utilization levels.[27] This was used to examine if the average price ratios changed if weighted according to Canadian utilization patterns.

In all of the analysis featuring the average Canadian to MIP ratio and the average foreign to MIP ratios for other countries, those countries with a significantly different ratio were identified. This was established by pair wise t-tests at a significance level of 0.05.[28]

Variations on the international comparison that were not incorporated into the main analysis are presented in the appendix. The appendix includes analysis based on only brand-to-brand comparisons, separation of the US price into FSS price and Red Book price.

Brand-to-brand price analysis, which excludes any unmatched manufacturers from the analysis, is presented in Appendix A1. The method for choosing the comparable brand name product in each country was outlined above.

Appendix A2 presents the analysis for the U.S. FSS and Red Book price separately. If only the FSS price was used to represent the U.S. price, the average foreign to MIP ratios would change for all countries including Canada. The same would be true if only the Red Book price was used. For this reason, the analysis using each of these possible U.S. prices, instead of the average of the two, is presented in Appendix A2. This is first done using the median available price from each country, and then again using only the most comparable brand name price, determined as outlined above.

The ten drug products with the highest Canadian to MIP ratios and the ten with the highest total expenditure levels are examined separately in Appendix A6.

2.4 Common Basket and Cost Analysis

An average foreign to MIP ratio is done for products found in all countries, removing the problem of missing prices. An analysis comparing the cost of a 'basket' of drugs at Canadian and foreign price levels is presented in section 3.9. The basket is the top selling NPSS products observed in the ODB database for fiscal year 1998/99. For the purpose of this analysis, the Canadian cost of 'the basket' is represented by the ODB utilization multiplied by the ODB price. The cost of the basket at a foreign price uses the same quantity multiplied by the foreign price. This gives a hypothetical expenditure and addresses the question: "What would be the 1998/99 ODB expenditure level for these products at foreign prices?" [29] Not all 56 top

selling products were available in each of the seven countries; an analysis comparing the total cost of the ten common drug products found in all of the countries as well as a country by country comparison was also conducted.[30]

2.5 Foreign To Canadian Price Comparisons

The number of Canadian observations below and above the foreign price was also determined for each country and an average foreign to Canadian price ratio was calculated using a geometric mean. The average ratio was initially taken over all possible products, i.e. all products found in each respective country. An average was also calculated for sub groupings of drugs used for calculating the Canadian to MIP ratio, (e.g. only products found in at least three countries or in all counties). An average weighted foreign to Canadian price ratio was also calculated using ODB expenditures and utilization. For each average foreign to Canadian price ratio a 95% confidence interval was examined and those ratios for which the confidence interval does not include the value "1.00" are identified.[31]

In some instances a probability associated with the number of observations below and above the foreign price was also determined. This represented the likelihood of the observed frequency of Canadian prices above and below the respective foreign prices assuming that either event was equally likely.[32]

3. Results

3.1 Non-patented Single Source Expenditure

In 1998/99, the total claimed spending in six provincial drug plans (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia) for NPSS products was approximately $300 million dollars. Expenditures on NPSS products represented 31% of total non-patented expenditures and 13% of total expenditures claimed for all products in the six publicly funded drug plans.

As described in Section 2, the analysis presented in this section is based on the top selling 56 tablet and capsule products that were found in at least one other country included in the international comparison. These products had a total claimed expenditure in Ontario of $61.1 million dollars. This represents 40% of ODB Plan's NPSS expenditure, 12% of non-patented spending and 5% of spending over all products.

3.2 Availability of International Competitors

The products selected for this analysis were sold by a single manufacturer in Canada, but may have been offered by multiple sources in the foreign markets.[33] This was often the case in Italy, Germany and the US.[34] In Italy, 37% of the products used in this analysis were produced by more than one supplier, with as many as 10 companies competing in the same market. Uniform pricing is a unique feature in the Italian market place.[35] Although Germany has a reference based pricing system, an active generic market and price competition exists.[36] In Germany, approximately 51% of drug products included in the analysis had more than one competing firm; as many as 15 companies in the same bioequivalent market were identified.

The U.S. also had an active generic market for the sample of drugs included in this study. There was more than one bioequivalent product listed in the U.S. FSS price list for 34% of the products and more than one bioequivalent product listed in the Red Book for 55% of the products. Regardless of how the U.S. price was defined, (i.e. FSS or Red Book or an average of both), there was a great deal of discrepancy between manufacturers prices at the bioequivalency level, (i.e. brand vs. generic prices). For drugs listed in the Red Book, there was up to 19 different bioequivalent products offered by different competitors.[37]

Table 3-1 and 3-2 below provide country specific summary data on the relative market size and the number of competing manufacturers for each of the products included in the analysis.

Table 3-1

1998/99 International Comparison Summary For DINs that are Top Non-Patented Single Source in Canada

Country	Share of Total Retail Market for Countries in this Analysis. [38]	N	DINs Used in This Study That are Multiple Source In Respective Countries	Average Number Of Competitors Within Multiple Source DINs	Maximum Number Of Competitors
Canada	4%	63	0	-	-
Italy	6%	32	12	3.3	10
France	9%	30	1	3.0	3
Sweden	2%	25	3	2.0	2
UK	6%	34	N/A	-	-
Switzerland	1%	29	2	3.5	4
Germany	12%	35	18	5.2	15
US (FSS)	61%	44	15	4.2	9
US (Red Book)		44	24	7.7	19

Table 3-2

Number of Countries Used in the Median International Price Comparison			
Number Of Countries Available for Comparison (i)	Number of DINs Found In (i) Countries	Number of DINs Observed In At Least (i) Countries	Number of DINs Observed in (i) Countries, Where One of the Country Was the US
1	9	56	8 of 9
2	8	47	7 of 8
3	8	39	4 of 8
4	5	31	4 of 5
5	6	26	4 of 6
6	10	20	7 of 10
7	10	10	10 of 10
Total			44 of 56
Average Number of Countries 4.1			

Fifty-six of the NPSS products had a comparable product in at least one of the seven countries used in the analysis. In those cases where the drug was available in only one of the countries, that country determined the international price. This was the case for nine drug products, eight of which had the U.S. as that single comparable price. If a comparable product is found in two other countries, then the international median price is the mean of the two available prices. Both countries, therefore, exhibit equal influence on the median international price. For eight of the drug products in this analysis, there were two comparable countries to generate the international price. For seven of these eight cases, one of the two prices was a U.S. price. This means that the Canadian to international price ratio heavily reflected the Canadian to U.S. price ratio for fifteen of the 56 observations, (27%). Due to the large relative effect of the U.S. on the international price, different methods of calculating the U.S. price greatly influence the Canadian price relative to the international price. This is seen in the variability amongst the various mean Canadian to international median price ratios presented below.

As stated in the methodology, further analysis was done to gain insight into the sensitivity of the results to the methodology used to calculate the U.S. price and its influence on international price calculations.

3.3 Canadian to Median International Price Level Comparison

The analysis presented in Table 3-3 illustrates that Canadian price for non-patented single source drug products were, on average, substantially higher than the median international price of the seven countries. For example, if the U.S. price is taken as the average between the FSS and Red Book prices, the overall unweighted ratio of Canadian prices to median international prices is 1.12[39]. In other words, Canadian prices for non-patented single source drugs were, on average, 12% higher than the median international prices. When the Canadian to median international price is weighted by expenditures, the relative premium paid by Canadians increases to 28% above the average international price for drug products included in the study.

Table 3-3 provides a summary of the instances where Canadian prices were the highest, lowest and above the median of the foreign prices. In most cases, 32 out of 56 or 57.1%, Canadian drugs were priced above the median international price. If Canadian prices were equally likely to be above or below the international price, the probability of observing 32 instances of the Canadian price above the international price would be 6%.[40] The number of cases where the Canadian price was the highest was 12 (21.4%). Canadian prices were

the lowest of all counties in 10 (17.9%) instances.

The average Canadian to foreign price ratio depends greatly on the way the foreign price is calculated and the U.S. price used. If the foreign price is taken as the median available foreign price, then the unweighted average Canadian to foreign international price ratio is between 1.05 and 1.26, depending on the U.S. price used. If the U.S. price is taken to be the average between the FSS price and Red Book price, Canadian prices are estimated to be 12% higher than the average international price.

If only the available brand products are used to determine the foreign prices, (excluding generics from the analysis), Canadian prices are estimated to be 7% higher than the average international price. Comparing only brand name products in Table 3-3, Canadians are paying the maximum price for 9 products, (16.1%), and the minimum price for 12 products, (21.4%). Canadian prices are above the international price for 30 products, (53.6%) and below the international price for 26 products, (46.4%).[41]

If the FSS price is used as the U.S. price, Canadians pay 26% more than the international price. If the Red book is used as the U.S. price, Canadians pay 5% more than the international price. If the analysis uses only brand name products, Canadians pay either 18% more than the international price using FSS prices for the US, or they pay approximately the international price if the Red Book is used.

If the analysis is repeated for European countries only, 48 drug products are included in the sample of drugs. When the U.S. is excluded from the international price, Canadians pay on average 46% more than the other six countries.

Table 3-3

1998/99 Top Selling Non-patented Single Source Drug Products
International Price Comparison
Drug Prices at the Ex-factory level

Comparison Information	Median Available Foreign Price Used								Available Brand Foreign Price Used							
US Price Used	FSS and Red Book		FSS		Red Book		US Excluded		FSS and Red Book		FSS		Red Book		US Excluded	
Total Number Of Drug Products Used	56		56		56		48		56		56		56		48	
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
Canadian Price Highest	12	21.4	17	30.4	9	16.1	26	34.2	9	16.1	12	21.4	8	14.3	26	54.2
Canadian Price Lowest	10	17.9	6	10.7	10	17.9	3	6.3	12	21.4	8	14.3	13	23.2	5	10.4
Canadian Price Above Median International Price	32	57.1	39	69.6	28	50.0	37	77.1	30	53.6	37	66.1	27	48.2	35	72.9
Canadian Price Below International Price	24	42.9	17	30.4	28	50.0	11	22.8	26	46.4	19	33.9	29	51.8	13	27.1
Canadian Price To Median International Price Ratio (Geometric Mean)	1.12		1.26		1.05		1.46		1.07		1.18		1.00		1.54	

The analysis presented in Table 3-3 is based on a sample of 56 products. For eight of the drug products, the MIP was entirely composed of the U.S. price as it was the only other price available. For seven of these products, the Canadian to MIP ratios were among the lowest in the sample. For an additional eight products, only two other countries were included in the price analysis (MIP), with the U.S. being one of the countries in seven cases. In the cases where the U.S. and only one other European comparator were available, the Canadian to MIP ratios were also relatively low. This raises the possibility that reduced availability of international comparisons is causing a bias that underestimates the overall average Canadian premium relative to the MIP.

The results presented in Table 3-4 limit the analysis to only those products for which an international median price can be generated with prices from no less than three of the seven countries. This ensures that the international price is more representative. Specifically, this eliminates the possibility of the MIP simply reflecting the U.S. price and greatly diminishes the importance of which price is accepted as the U.S. price in the overall calculation. In order for the international price to be influenced by the U.S. price (or any other single extremely high or low price), there must be at least one other country priced above and below it. This also, however, has the effect of lowering the number of products used in the analysis from 56 to 39; this is a 30% decrease in the sample size. If no less than three countries are used to generate the international price ratio, and assuming that the U.S. price is the mean of both the FSS and the Red Book price, Canadian prices are, on average, 25% higher than the international price. The Canadian price is the maximum price for 7 products, (17.9%), and is the minimum price for 2 products, (5.1%). The Canadian price is above the median international price for 25 products, (64.1%) and below the international median price for 14 products, (35.9%).[42]

If the U.S. price is assumed to be the FSS price, Canadians pay 30% more than the international price. If the U.S. price is assumed to be the Red Book price, Canadians pay 24% more than the international price. If only brand name products are used in the analysis, Canadian prices are between 22% and 25% above the international price depending on the U.S. price used. As stated above, the average Canadian to international median price ratio varies much less with changes in the methodology used to define the U.S. price is determined if at least three countries are used to generate the international price.

The data demonstrates that varying approaches to producing a cross-national price comparison patented single source products.

Table 3-4

1998/99 Top Selling Non-patented Single Source Drug Products
International Price Comparison, Minimum of Three Comparable Countries For Each Drug Product
Drug Prices at the Ex-factory level

Comparison Information	Median Available Foreign Price Used						Available Brand Foreign Price Used					
US Price Used	FSS and Red Book		FSS		Red Book		FSS and Red Book		FSS		Red Book	
Total Number Of Drug Products Used	39		39		39		39		39		39	
	#	%	#	%	#	%	#	%	#	%	#	%
Canadian Price Highest	7	17.9	10	25.6	6	15.4	6	15.4	7	17.9	6	15.4
Canadian Price Lowest	2	5.1	1	2.6	2	5.1	4	10.3	2	5.1	4	10.3
Canadian Price Above Median International Price	25	64.1	28	71.8	25	64.1	25	64.1	27	69.2	25	64.1
Canadian Price Below International Price	14	35.9	11	28.2	14	35.9	14	35.9	12	30.8	14	35.9
Canadian Price To International Median Price Ratio (Geometric Mean)	1.25		1.30		1.24		1.22		1.25		1.22	

3.4 Average Foreign to International Median Price Ratios

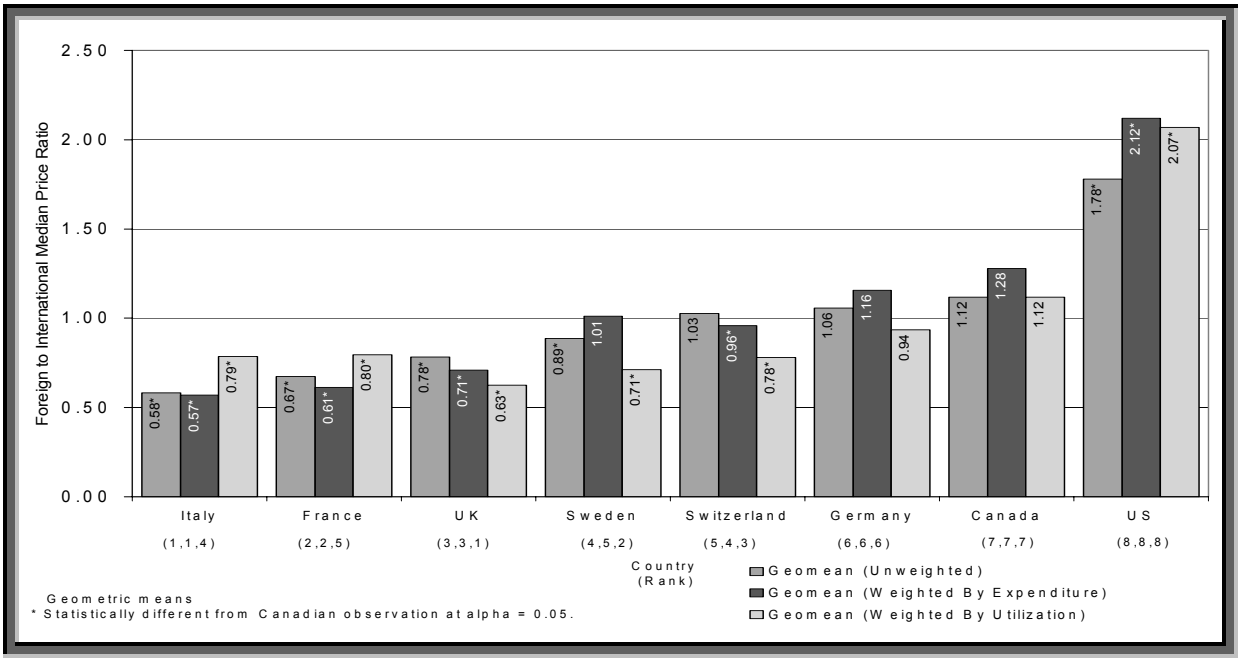
Figure 3-1 provides results comparing Canadian and foreign prices to the MIP.[43] Canada has the second highest unweighted average ratio, 1.12, lower only than the US. That is to say, Canadian prices are on average 12% above the MIP. If the averages are weighted by Canadian expenditure levels, Canadian prices are 28% above international prices.[44] The Canadian prices are the second highest regardless of the weighting strategy, and the U.S. remains the highest priced country for this sample of products.

On average, Switzerland, Germany and the U.S. pay above international prices by 3%, 6% and 78% respectively; Italy, France, the UK and Sweden pay below international prices by 42%, 33%, 22% and 11% respectively. All of the countries except Switzerland and Germany have average foreign to MIP ratios that are statistically significantly different from Canada's.[45]

As stated above, Figure 3-1 also shows the average Canadian to international price ratio weighted by expenditure and (volume/quantity) utilization. When the ratio is weighted by Canadian expenditure levels, the Canadian price is on average 28% above the international median price.[46] When the foreign to international price ratio is weighted by Canadian expenditures, the average price seen in Germany changes from 6% above international prices to 16% above the MIP. The U.S. pays, on average 112% more for these products when weighted by expenditures. Italy, France, the UK and Switzerland pay 43%, 39%, 29% and 4% less than international prices when weighted by expenditures.

When the foreign to MIP ratio is weighted by utilization, the Canadian price is on average 12% higher than the median international price. This weighting scheme changes the ratios significantly enough to change the rank of many countries. For example, where Italy previously had the lowest average foreign to MIP ratio, when the ratio is weighting by utilization, Italy has the fourth lowest ratio. This puts Italian prices above those in the UK, Sweden and Switzerland.[47]

Figure 3-1 1998/99 - Average Foreign to Median International Price Ratio. The Results are Unweighted, Weighted by Canadian Expenditure and Weighted by Canadian Utilization.[48] Median Foreign Prices Used. Drug Prices at the Ex-factory level.



This suggests that had NPSS medicines been priced at median international levels, spending by the six provincial drug plans (BC, AB, SK, MN, ON, NS) would have been approximately $60 million less than the $300 million these plans spent on NPSS drugs in 1999/00.

3.5 Average Foreign to International Price Comparison - Sensitivity Analysis

The average foreign to MIP ratio was investigated further to gain confidence in the results ranking international price levels. Not all drug products are available in all countries, thus a different subset of the 56 DINs is used to formulate the average ratio for each country. In addition, a different group of countries is used to form the MIP for which the prices are to be compared to for each product.[49]

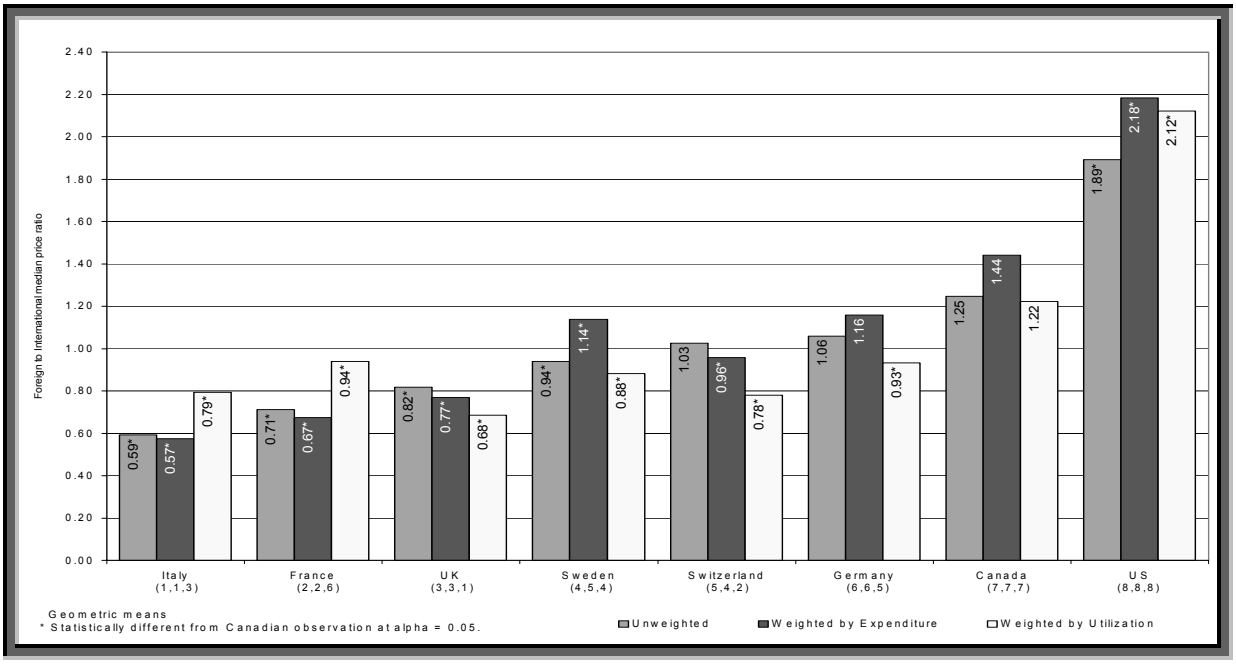
For 8 of the 56 DINs, the MIP price was composed solely of the U.S. price. For another seven DINs, the MIP was the arithmetic average between the U.S. and one other country. For this reason, Figure 3-2 shows the average foreign to MIP ratio, but restricts the analysis to MIP's that are generated by the prices from at least three countries. By limiting the analysis, the sample size is reduced to 39, but the MIPs reflect a more representative international price that is less susceptible to outliers. Similarly, analysis further restricting the sample of drugs based on international availability is presented in Section 3-9; this analysis is for a sample of 10 products for which a match was found in every country.

Figure 3-2 shows that if at least three countries are used to generate the MIP, the average Canadian prices increase to 25% above the MIP un-weighted, 44% if the ratio is weighted by expenditures and 22% if the ratio is weighted by utilization. The U.S. remains the country with the highest prices, but the unweighted premium on the U.S. price increases from 78% to 89%. All other countries remain at relatively the same price levels presented in Figure 3-1, with the possible exception of France and Sweden. The change in the Canadian and U.S. price ratios implies that the original ratios were in fact heavily affected because the countries were commonly being compared to each other. This had the effect of making both countries appear relatively lower priced.[50]

When the analysis was repeated using only

comparable brand products in each of the countries, the Canadian premium did not change significantly. Canadians are paying an average relative premium of 21% to 41% (also see Appendix Figure A.2). [51]

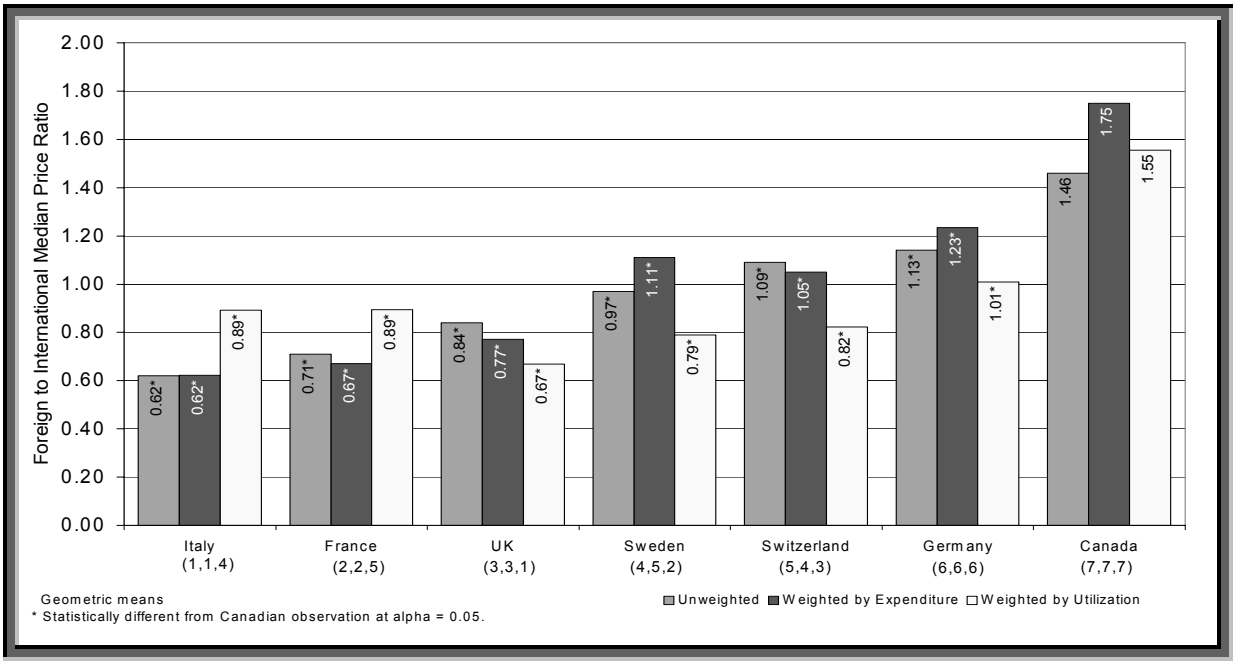
Figure 3-2 1998/99 - Average Foreign to Median International Price Using Only Those Drug Markets That Could Be Compared With At Least Three Other Countries. Median Foreign Prices Used.[52] Drug Prices at the Ex-factory level.



The countries included in calculating the median international price have a significant effect on the relative position of Canadian to international prices. From the previous discussion and analysis, the potential impact of relatively high U.S. prices may reduce the overall Canadian to international price difference reported. Comparing Canadian prices to median European prices also removes the concern about how to adequately capture U.S. price. Forty eight products are included in the Canadian to MEP analysis; these products tend to have comparators from a diverse selection of countries. The countries included in the European analysis have prices that are negotiated, regulated or are somehow otherwise restricted by the local government authorities.

Figure 3-3 presents information on the average foreign to MEP. Canadian prices are on average 46% higher than the MEP. This increases to 75% higher than the MEP if the average ratio is weighted by expenditure and 55% if the ratio is weighted by utilization. The average Canadian to MEP ratio is statistically different from all of the six European countries regardless of weighting scheme.[53] This shows that the U.S. price was greatly affecting the MIP and reducing the overall average Canadian premium. This lowered Canadian premium was seen even if FSS price (generally a lower U.S. price) alone was used to represent the U.S. price, (also see Appendix A.4). Prices in Switzerland and Germany are also above the MEP. If the comparison is weighted by expenditures, prices in Sweden are also above the median. Canada is the only one to be substantially higher than the MEP if the ratio is weighted by Canadian utilization. Prices in Italy, France, the UK and Sweden were on average below the MEP. Repeating this analysis using only the most comparable brand name product in each foreign country, resulted in an average Canadian premium relative to the MEP of 42%, (see Appendix Figure A.3). The German to MEP ratio is the only ratio to be substantially more than the values in Figure 3-3 when the analysis is based only on brand name products.

Figure 3-3 1998/99 - Average Foreign to Median European Price Ratios. Median Foreign Prices Used. Drug Prices at the Ex-factory level.



3.6 US Sensitivity Analysis

The U.S. pharmaceutical market is relatively dynamic and complex. In most of the analysis presented in the main text, three median prices are presented, the U.S. FSS price, the U.S. Red Book price and an average price comprised of both prices. The U.S. FSS prices are generally lower than the Red Book prices, and brand prices are generally higher than generic prices. As a result, the U.S. to median international price ratio varies greatly depending on the methodology used to generate it. Table 3-5 takes a closer look at the average U.S. to international price ratio.

If all bioequivalent drug products are used and the U.S. price is taken to be the average between the FSS price and the Red Book price, U.S. residents pay 78% more than the average international price. Using only brand name products, U.S. residents pay 93% more than the international price. These premiums drop to 13% and 30% for customers paying FSS price levels and the premiums increase to 131% and 144% for customers paying ex-factory prices derived from the Red Book.

Table 3-5

1998/99 Top Selling Non-patented Single Source Drug Products
International and U.S. Price Comparison
Drug Prices at the Ex-factory level

Comparison Information	Median Available Foreign Price Used						Available Brand Foreign Price Used					
US Price Used	FSS and Red Book		FSS		Red Book		FSS and Red Book		FSS		Red Book	
Total Number Of Drug Products Used	44		44		44		44		44		44	
	#	%	#	%	#	%	#	%	#	%	#	%
US Price Highest	30	68.2	20	45.5	38	86.4	34	77.3	25	56.8	39	88.6
US Price Lowest	2	4.5	11	25.0	2	4.5	2	4.5	8	18.2	1	2.3
US Price Above Median International Price	42	95.5	27	61.4	42	95.5	42	95.5	32	72.7	43	97.7
US Price Below International Price	2	4.5	17	38.6	2	4.5	2	4.5	12	27.3	1	2.3
US Price Above the Canadian Price	38	86.4	26	59.1	41	93.2	41	93.2	32	72.7	42	95.5
US Price To International Median Price Ratio (Geometric Mean)	1.78		1.13		2.31		1.93		1.30		2.44	

3.7 Foreign to Canadian Price Statistics Comparison by Country

The analysis presented thus far relate foreign to international price ratio and Canadian to international price ratios side by side, using the best possible median international price available. Another way to relate Canadian prices to another country is to look at the relationship between Canada and that country directly. This approach is presented in Table 3-6 and Figure 3-4. The analysis is this section compares prices to a common benchmark, i.e., the Canadian price. The relative standing of each country remained the same. Italy had the lowest average foreign to Canadian ratio, 0.50; thus Italians pay on average half of the Canadian price for the 30 top-selling non-patented single source products common to both countries. The Canadian price was higher than the Italian price for 93.8% of the sample.

France had the second lowest drug prices for the products included in this analysis; Canadian prices were on average 39% above prices in France. The Canadian price was higher than the French price for 80.0% of the drug products common to both countries. Average Canadian prices were 32% above prices in the UK. In 70.6% of the drug products common to both countries Canadian prices exceeded the price in the UK. Canadian prices were 24% higher than prices in Sweden, and were priced above Swedish products for 60.0% of the products found in both countries. Canadian prices were 21% higher then prices in Switzerland on average and Canadian prices were higher for 69.0% of the products common to both countries. Germany had the highest prices among the European countries, but still had prices that were on average 13% lower than Canadian prices, and was priced lower for 74.3% of the products. The average foreign to Canadian price ratio for all of these countries was significantly below 'one', (the value 'one' itself was not contained in the 95% confidence interval for these ratios, Figure 3-4).

When this analysis is done based on foreign brand name products, the average foreign to Canadian price ratio did not change substantially for all European countries other than Germany. (See Appendix Section A.3). The average German to Canadian ratio increased to 0.97, with only 62.9% of the products common to both countries being priced higher in Canada.[54]

Table 3-6 and Figure 3-4 provides information which relates the Canadian price to the U.S. FSS price, the U.S. Red Book price and the U.S. price taken as the average of the two. When the U.S. price is the average between the FSS price and the Red Book price, as it was in the analysis earlier in this study, the Canadian price is on average 46% below U.S. prices. The U.S. price was above the Canadian price for 93.2% of the products in this study.

The FSS price is the lower of the U.S. prices. In the analysis, the average FSS to Canadian price ratio is 0.93. The large confidence interval for

this value (0.73, 1.17), contained the value 1.00 and reflects the variability observed in the FSS to Canadian price ratios for each product. In addition, of the 44 drugs common to both Canada and the US, 59.1% had a FSS price above the Canadian price. Therefore, no conclusive statement can be made from this analysis as to whether or not Canadian top-selling non-patented single source tablets and capsule drug products are priced above or below FSS prices when generics are included in the analysis.

When only brand name products were used in the analysis, the average FSS to Canadian price ratio increased to 1.09. (See Appendix Table A.1 and Figure A.10) The 95% confidence interval for this average also included the value 1.00, (0.89, 1.34). The FSS price was above the Canadian price for 72.7% of the observations, and the probability of observing this under the hypothesis that Canada was equally likely to be above or below the FSS price would be only 1.2%.

The Red Book price is by far the highest of any in the study. Red Book prices were above Canadian prices for 93.2% of the products in this study. The Canadian price was, on average, 89% below the Red Book price. When only brand name products were used in the analysis, this average increased to 105%. (See Appendix Table A.1 and Figure A.12.)

Table 3-6

1998-1999 Top Selling Non-Patented Single Source Drug Products By Country
Comparing Canadian and Foreign Prices
Drug Product Prices At The Ex-factory Level

Foreign Country	# of Drug Products That Match	Canadian price Above		Canadian price Below		Average Price Ratio (Foreign/Canadian)
		#	%	#	%	
Italy	32	30	93.8	2	6.3	0.50
France	30	24	80.0	6	20.0	0.61
UK	34	24	70.6	10	29.4	0.68
Sweden	25	15	60.0	10	40.0	0.76
Switzerland	29	20	69.0	9	31.0	0.79
Germany	35	26	74.3	9	25.7	0.87
US(FSS)	44	18	40.9	26	59.1	0.93
US(FSS and Red Book)	44	6	13.6	38	86.4	1.46
US(Red Book)	44	3	6.8	41	93.2	1.89

The foreign to Canadian price ratios decrease slightly in Europe if the average ratio is weighted by Canadian expenditure levels. This implies that Canada spends the most money on the higher priced drug products. The U.S. Red Book average ratio stays relatively constant when weighted by Canadian expenditure levels.

The effect of weighting the average foreign to Canadian price ratio by Canadian utilization levels is mixed. For the two lower priced countries, Italy and France, the magnitude of the foreign discounts decreases. Thus, the Canadian price premium over Italian and French products is smaller on products used in Canada the most. The foreign to Canadian price ratio decreases for the UK, Sweden, Switzerland and Germany. This has the opposite implication. Weighting the European to Canadian price ratios by Canadian utilization changes the average ratios sufficiently enough to change the relative order of the countries (this information is presented in brackets in Figure 3-4). For example, the UK goes from being the third lowest priced country when the averages are not weighted, to being the lowest priced country when the averages are weighted by Canadian utilization; conversely, Italy goes from the lowest priced country to the fourth lowest.

The average U.S. to Canadian price ratio increases when weighted by Canadian utilization. The average FSS to Canadian price rises above 1.00 to 1.05 and the other U.S. price ratios increase.

Figure 3-4 – 1998/99 - Average Foreign to Canadian Price Ratio. The Results are Unweighted, Weighted by Canadian Expenditure and Weighted by Canadian Utilization.[55] Median Foreign Prices Used. Drug Prices at the Ex-factory level.

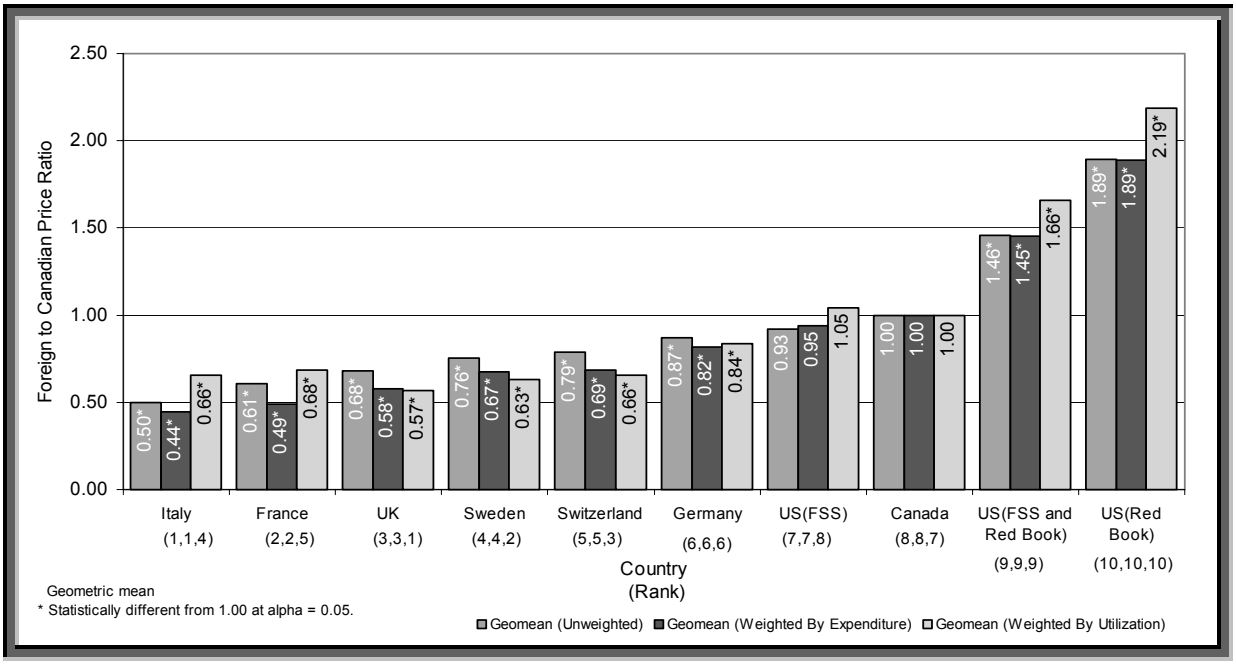
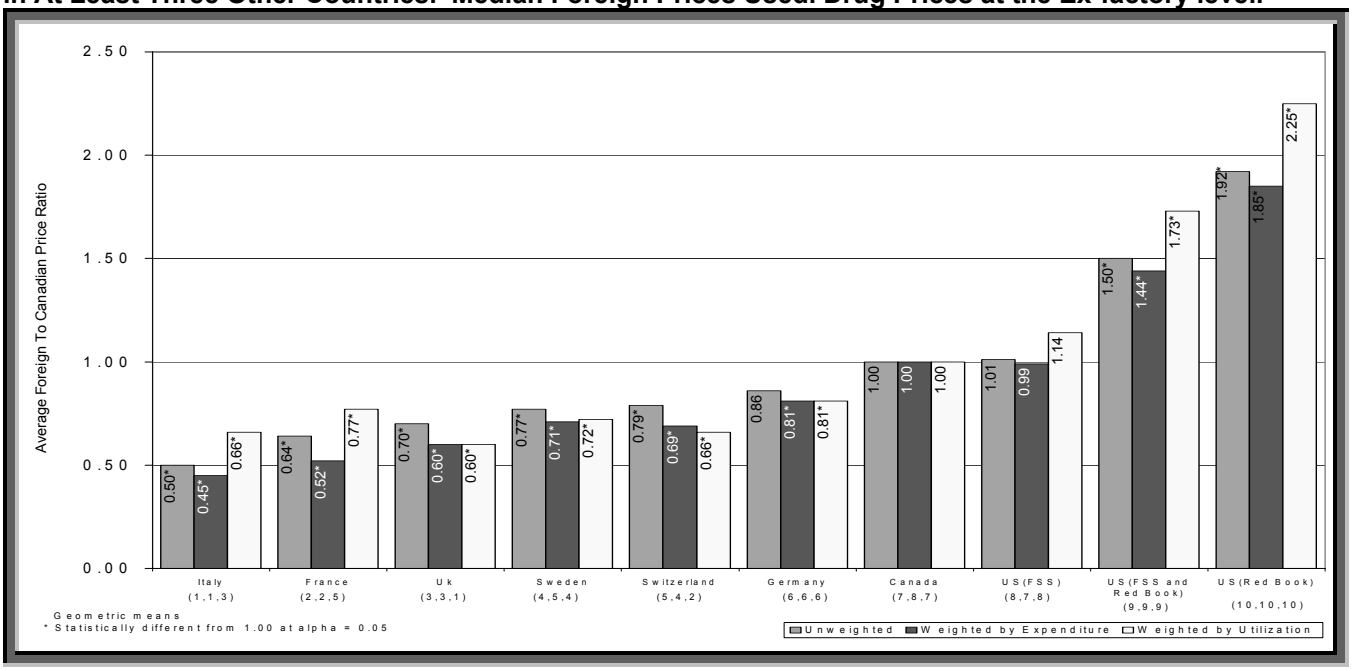


Figure 3-5 shows the average foreign to Canadian price ratios for the subgroup of products for which a bioequivalent product was available in at least three countries. The findings in this figure are very similar to Figure 3.4 (the average price ratios without the extra stipulation of three minimum comparator countries). Generally, this restriction does not have a significant effect on the final foreign to Canadian price ratios.[56]

The average foreign to Canadian price ratios calculated using only brand name products also showed little change if the drug product basket was restricted to the 39 tablets and capsules found in at least three countries. (See Appendix Figure A.12 and Figure A.13).

Previously, this sample of 39 products was also used to generate an average Canadian to MIP ratio in section 3.3. The restriction of products to those available in at least three countries was an attempt to compare Canadian prices to a more representative international price. This had the effect of significantly changing (increasing) the average Canadian premium paid. The similarity of the findings in Figure 3-4 and Figure 3-5 suggest that the 39 products are reasonably representative of the larger basket of 56 products.

Figure 3-5 1998/99 - Foreign to Canadian Price Where Drug Product Must be Available for Comparison in At Least Three Other Countries. Median Foreign Prices Used. Drug Prices at the Ex-factory level.

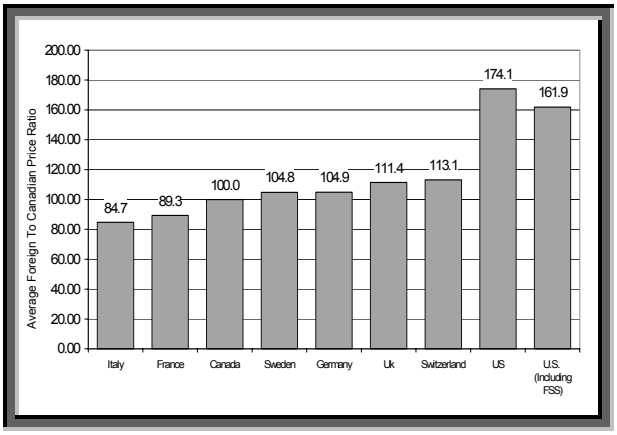


3.8 Comparison of International Prices of Non-patented Single Source Drugs and Patented Drugs

The PMPRB has published analyses of international price comparisons for the top selling patented drugs since 1992. In the first international price comparison for the top selling patented drug products, it was found that Canadians were often paying more for patented drug products than citizens in most other reference countries. The United States was the exception.

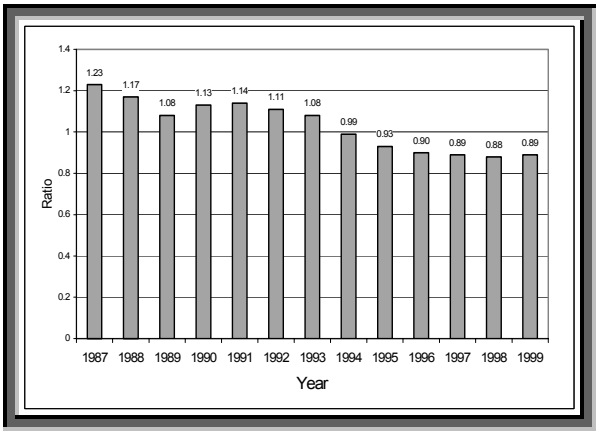
In 1994, the PMPRB amended its Guidelines to put greater emphasis on international price comparisons for new and existing drugs.

Figure 3-6 Average Foreign-to-Canadian Price Ratios. All Patented Drug Products in 1999.



(Source PMPRB - 1999 Annual Report)

Figure 3-7 Ratio of Canadian Prices of Patented Drug Products to Median International Price, 1987-1999. Weighted by Canadian Expenditures.



(Source PMPRB - 1999 Annual Report)

Figure 3-6 and 3-7 show that the relationship of non-patented single source drugs to foreign prices in 1998/99 is similar to the relationship of patented prices to foreign prices in the late 1980's and early 1990's.

In 1999, patented drugs were on average 11% below the international median price ranking as the third lowest priced country. For non-patented single source drugs, Canadian prices were on average 28% above the MIP.[57] For non-patented single source products, Canada ranked as the second highest price country after the U.S. in 1999; Canadian prices of patented products were third lowest compared to other countries.

3.9 Common Basket Analysis

Figure 3-8 shows the Canadian to MIP and foreign to MIP ratios for those products where a price was available in every country. This reduces the subset of drug products to ten, but it eliminates the potential bias of any missing observations and relieves many concerns about how representative the international price is. For these products, Canadian prices are 44% above the MIP. The U.S. is on average almost twice as high as the MIP. There were some changes also observed for the average ratio for several of the European countries; the average foreign to international price ratios for relatively lower priced countries decreases, whereas the relative prices in Sweden, Switzerland, and Germany increase.

If the analysis is restricted to brand name products, Canadian residents pay on average 40% more than the MIP on these ten products. (See Appendix Section A4, Figure A.14).

Figure 3-8 1998/99 - Average Foreign to International Median Price Ratios For a Common Basket 10 Products Found in Canada and All Seven Countries. Median Foreign Prices Used.[58] Drug Prices at the Ex-factory level.

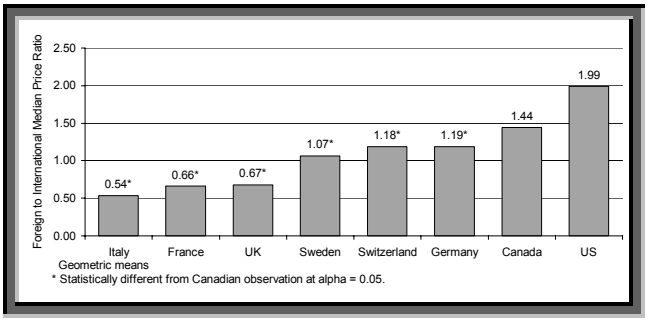
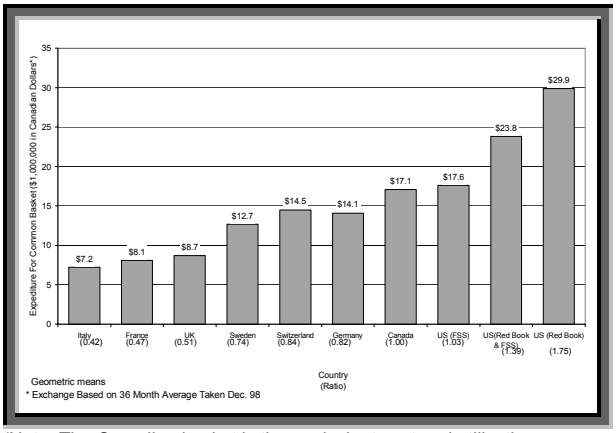


Figure 3.9 shows the cost of the ten drug products found in each of the seven-comparator countries. The basket is the equivalent to the utilization observed in the ODB database for 1998/1999. This addresses the question, "what would the cost to Canadians consumers be at foreign price levels. The cost of these brand name drug products at Canadian prices levels in 1998/99 was $17.1 million.[59] The cost would be as low as $7.2 million if Canadians paid Italian prices. Assuming the U.S. price to be the average between the FSS and the Red Book price, the cost of these products at U.S. prices would be $23.8 million. This is almost 40% more than the cost in Canada. This figure increases to $24.6 million if only brand name products were purchased in the US. (Appendix Figure A.19).

Figure 3-9 1998/99 - The Cost of a Common Basket of Drug Products At Canadian Utilization Levels. Foreign Median Prices Used. Drug Prices at the Ex-factory level.

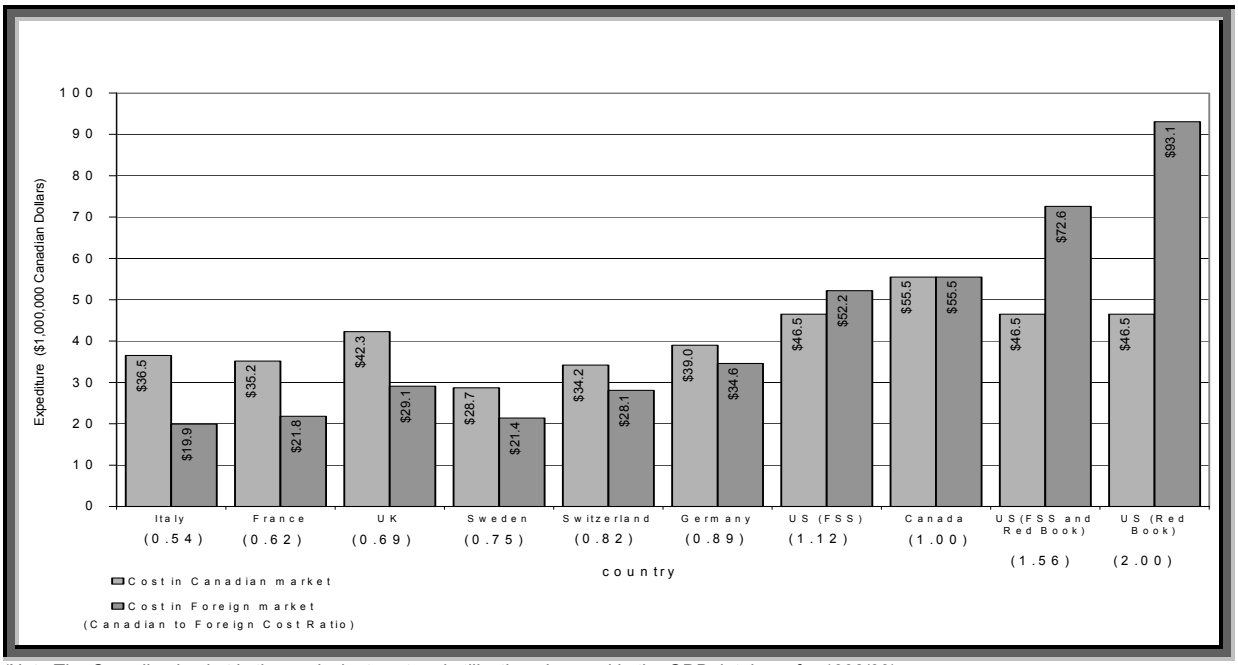


(Note: The Canadian basket is the equivalent cost and utilization observed in the ODB database for 1998/99)

Figure 3.10 shows the cost of the basket of drug products in the analysis that were common to each pair wise comparison .[60] For example, to purchase the 32 drug products found in Italy at Canadian prices and utilization levels costs $36.5 million. If these same products were purchased in the same quantities, but at Italian price levels, the cost in Canadian funds would be only $19.9 million. Canadians would therefore pay 46% less if they were paying Italian prices for this basket of Drugs. Canadians would pay 38% less for the 30 products found in France; 31% less for the 34 products found in the UK; 25% less for the 25 products found in Sweden; 18% less for the 29 products found in Switzerland and 11% less for the 35 products found in Germany. The products that were in this analysis and also found in the U.S. would cost more at U.S. prices, regardless of the U.S. price used. The total cost would be higher by 56% if the U.S. price was formed from both the FSS and the Red Book Price. The cost would be higher by 12% at FSS prices and 100% higher if only the Red Book price was used.

The same analysis using only brand name products is presented in the appendix (see Appendix - Figure A.18). The most significant changes were in the German and U.S. costs, both of which increased. In Germany, the cost of purchasing the same basket increased from $34.6 million to $38.4 million. The U.S. price (FSS and Red Book averaged), increased to $79.2 million, and became 70% higher than the Canadian price. The cost of the basket at FSS prices increased to $56.3 million (21% above Canadian costs), and at Red Book prices to $102.1 million, (119% above Canadian costs).

Figure 3-10 1998/99 - The Foreign Cost vs. Canadian Cost of Top Selling Non-Patented Single Source Drug Products. The Total Cost is For All Of the Top Products That Were Mutual To Both Countries. Foreign Median Price Used. Drug Prices at the Ex-factory level.



(Note:The Canadian basket is the equivalent cost and utilization observed in the ODB database for 1998/99)

Conclusion

The findings demonstrate that Canadian prices of top selling non-patented single source drugs are significantly higher than prices in six of the seven countries listed in the Patented Medicines Regulations. These findings are based on a comparison of ex-factory gate manufacturers' prices. These results were relatively robust with Canadian prices appearing to be substantially higher than the European countries (approximately 40%) and somewhat lower than the U.S. depending on which price is used to represent the U.S. market.

This analysis suggests that had these medicines been priced at median international levels, spending by the six provincial drug plans on NPSS drugs would have been reduced by approximately $60 million, or 20%.

A. Appendix A: Alternative Results Using Different Methodological Approaches – Ex-Factory Gate Price Analysis.

A1 Average Foreign to Median International Price Ratios at Brand Product Price Levels.

Figure A-1 1998/99 - Average Foreign to Median International Price Ratios Using Only Brand Products in Foreign Countries. Results are Unweighted, Weighted by Canadian Expenditure and Weighted by Canadian Utilization. The U.S. is Based on the Average of the FSS and Red Book Prices.

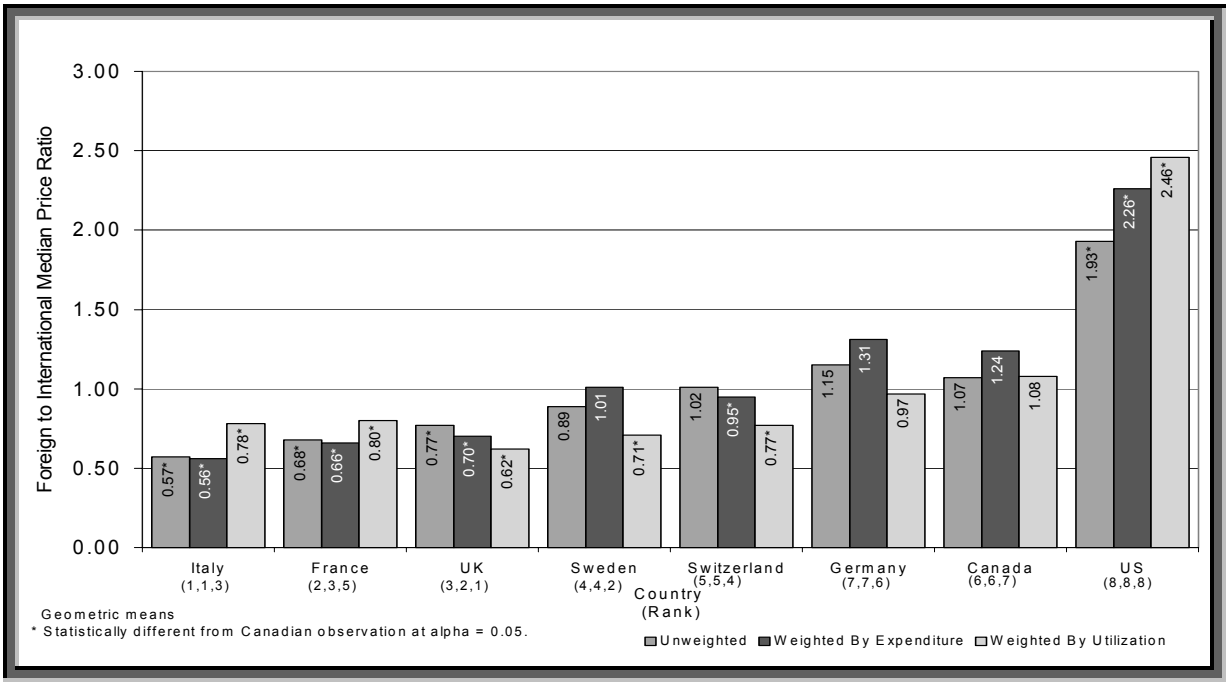


Figure A-2 1998/99 - Average Foreign to Median International Price Ratios Using Only Brand Name Products.^ A Minimum of Three Countries Required For Inclusion in Analysis. The U.S. Price is Based on the Average of the FSS and Red Book Prices.

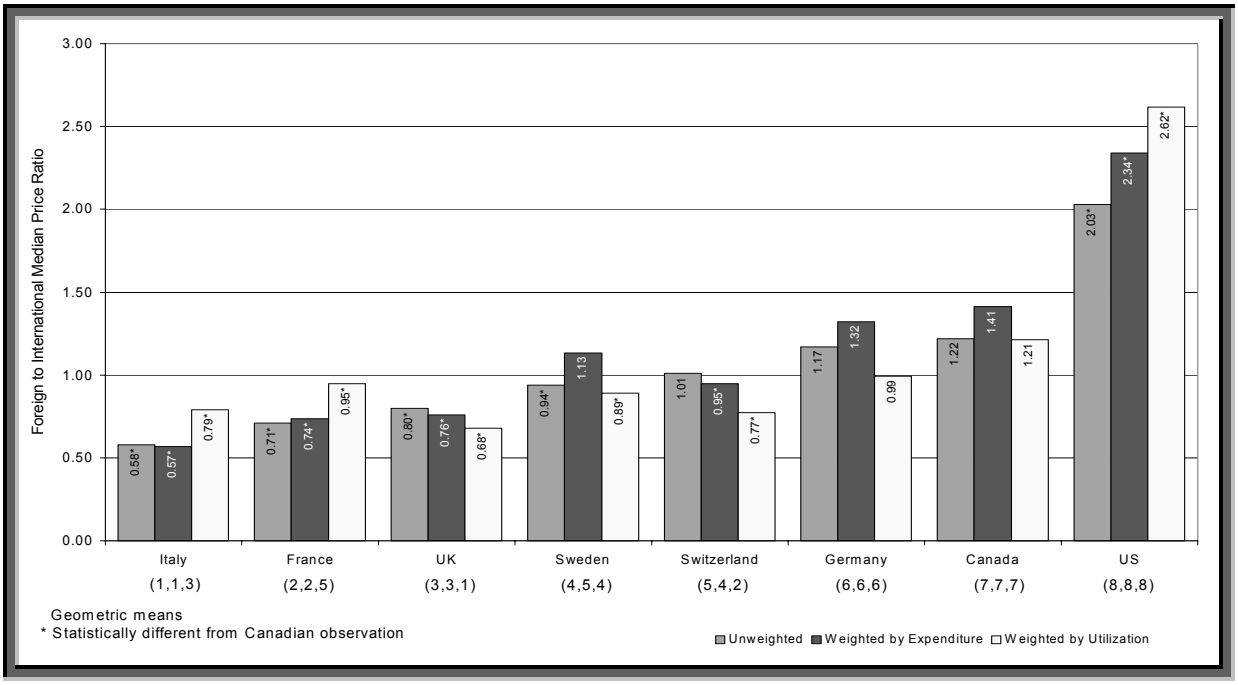
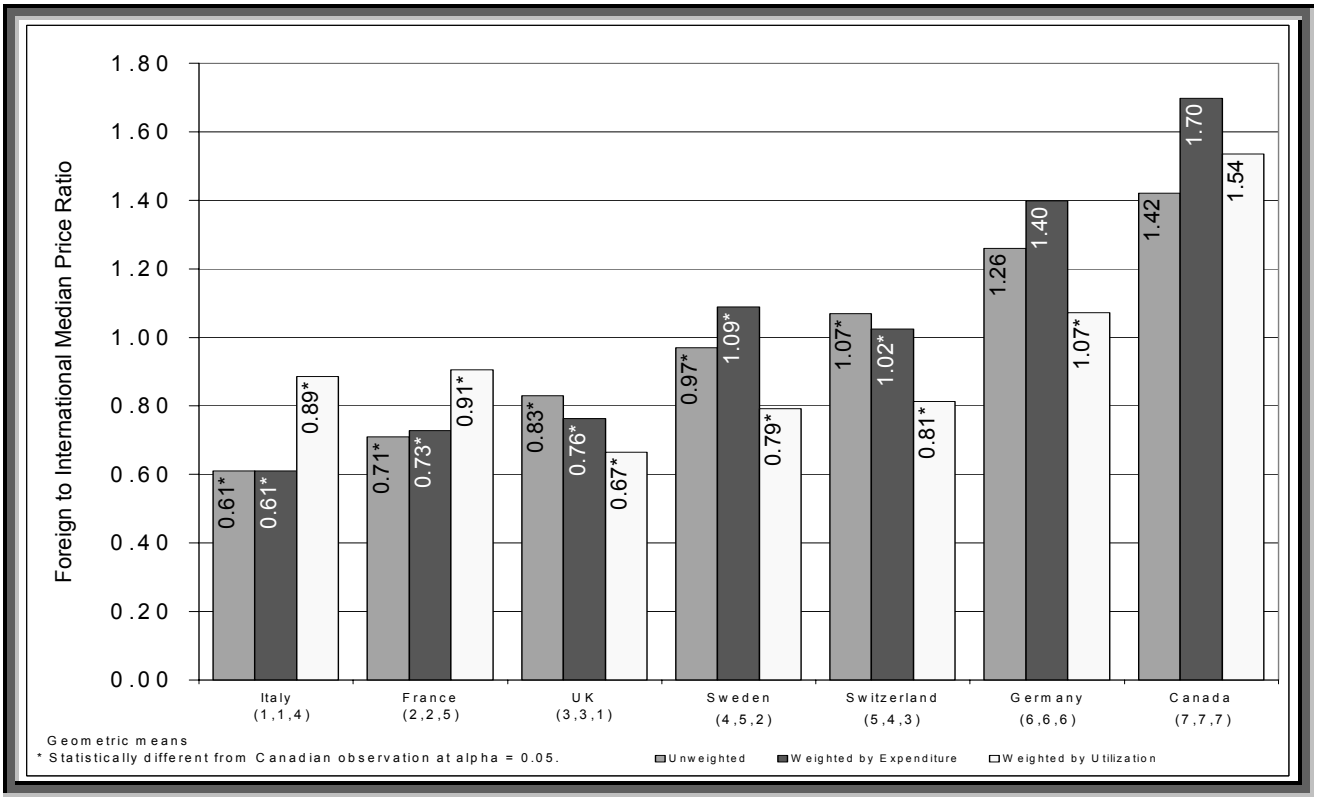


Figure A-3 1998/99 - Average Foreign to Median European Price Ratios Using Only Brand Products in Foreign Countries. U.S. Prices Are Excluded.



A2 Average Foreign to Median International Price Ratios; Presenting the U.S. Price FSS and Red Book Prices Separately

Figure A-4 1998/99 - Average Foreign to Median International Price. Results are Unweighted, Weighted by Canadian Expenditure and Weighted by Canadian Utilization. The U.S. Price defined as the FSS Price.

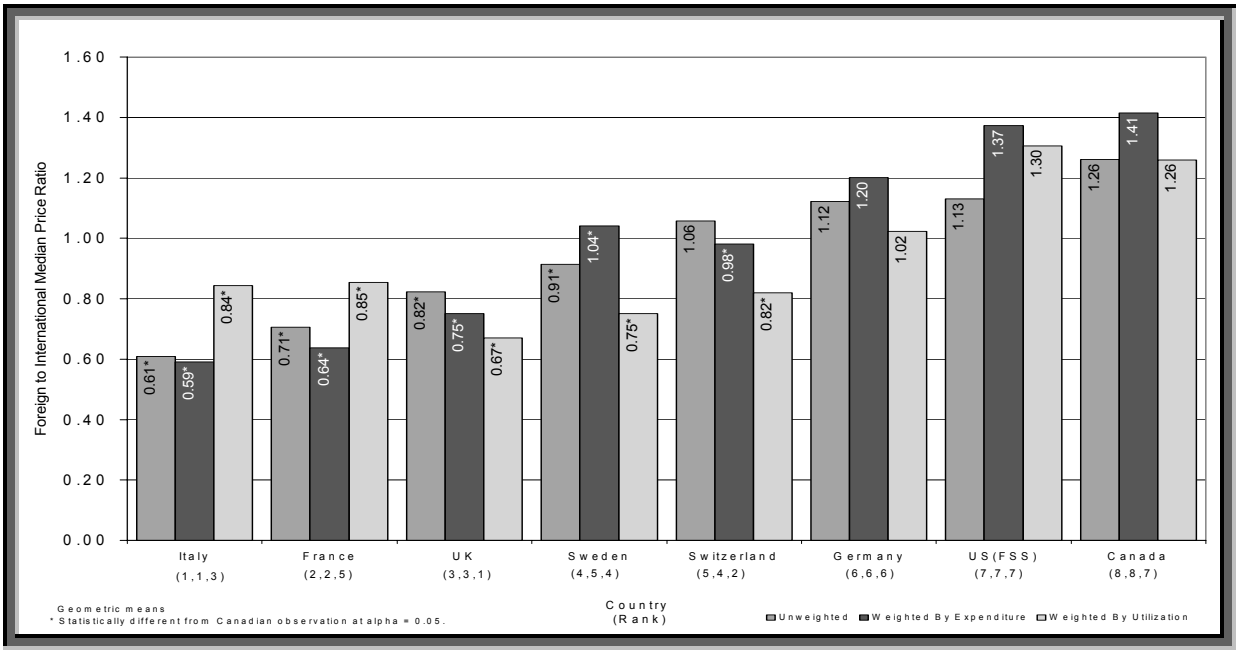


Figure A-5 1998/99 - Average Foreign to Median International Price Ratios . A Minimum of Three Countries Required For Inclusion in Analysis. The U.S. Price is the FSS Price.

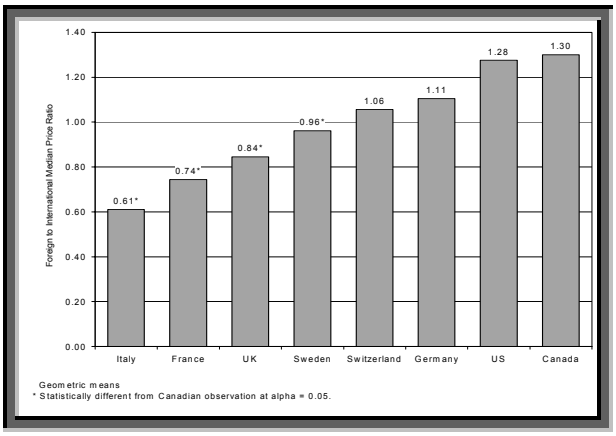


Figure A-6 1998/99 - Average Foreign to Median International Price. The U.S. Price is the Red Book Price.

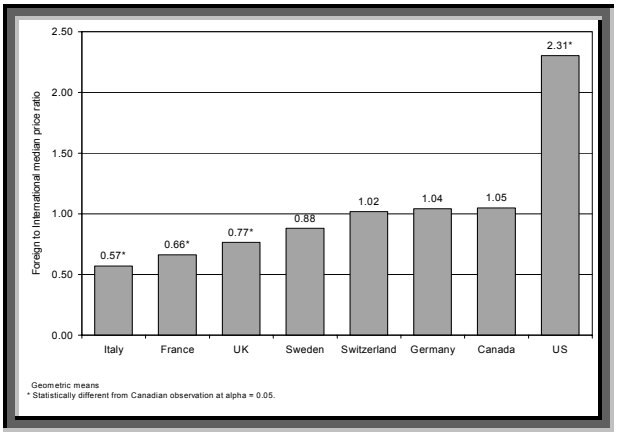


Figure A-7 1998/99 - Average Foreign to Median International Price. A Minimum of Three Countries Required For Inclusion in Analysis. The U.S. Price is the Red Book Price.

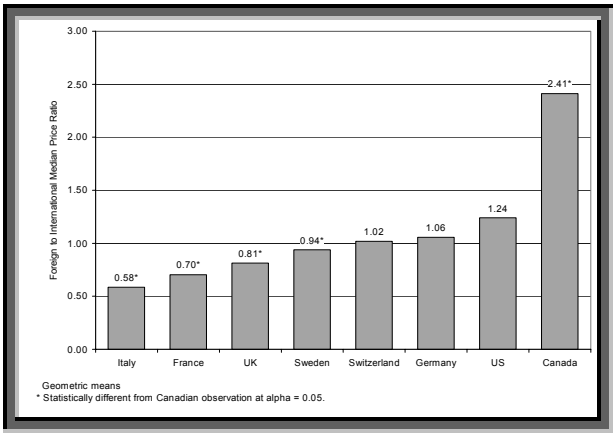


Figure A-8 1998/99 - Average Foreign to Median International Price Ratios Using Only Brand Products. The U.S. Price is the FSS Price.

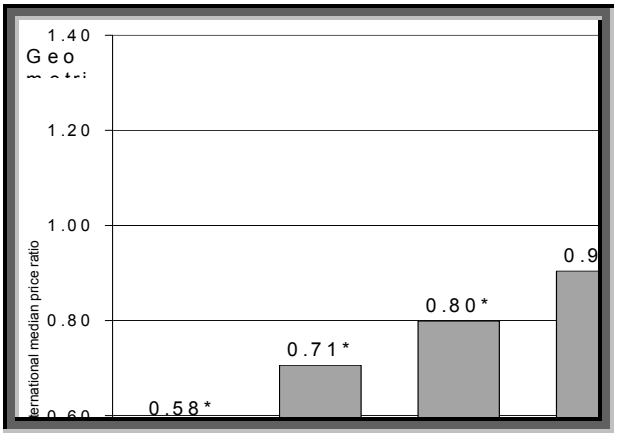


Figure A-9 1998/99 - Average Foreign to Median International Price Ratios Using Only Brand Products. A Minimum of Three Countries Required For Inclusion in Analysis. The U.S. Price is the FSS Price.

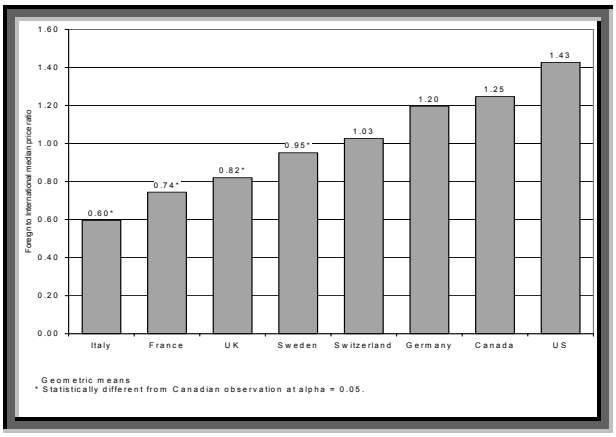


Figure A-10 1998/99 - Average Foreign to Median International Price Ratios Using Only Brand Name Products. The U.S. Price Used Was the Red Book Price.

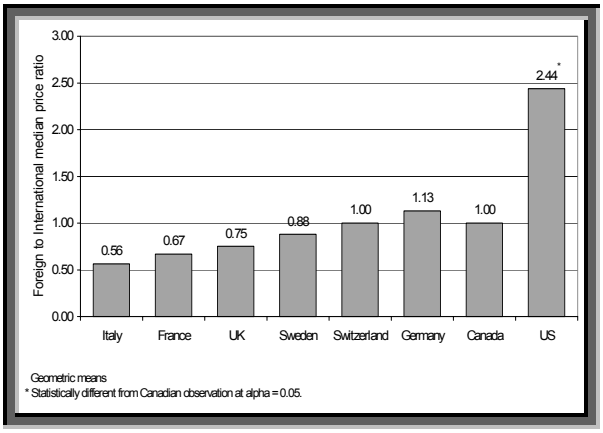
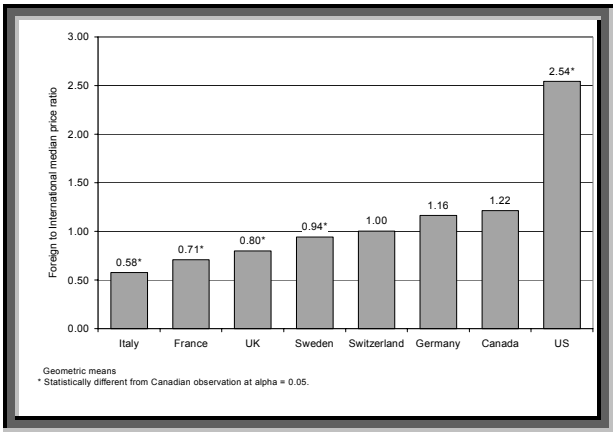


Figure A-11 1998/99 - Average Foreign to Median International Price Ratio Using Only Brand Name Products. A Minimum Of Three Countries Required For Inclusion Into the Analysis. The U.S. Price Used is the Red Book Price. Drug Prices at the Ex-factory level.



A3 Foreign to Canadian Price Statistics with Brand Product Price Levels.

Table A-1

1998/99 Top Selling Non-Patented Single Source Drug Products By Country Using Only Brand Name Products. Comparing Canadian and Foreign Prices

Foreign Country	# of Drug Products That Match	Canadian price Above		Canadian price Below		Average Price Ratio (Foreign/Can)
		#	%	#	%	
UK	34	24	70.6	10	29.4	0.68
Italy	32	30	93.8	2	6.3	0.50
France	30	24	80.0	6	20.0	0.62
Sweden	25	15	60.0	10	40.0	0.77
Switzerland	29	20	69.0	9	31.0	0.79
Germany	35	22	62.9	13	37.1	0.97
US(FSS)	44	12	27.3	32	72.7	1.09
US(Red Book)	44	2	4.5	42	95.5	2.05
US(Red and FSS)	44	3	6.8	41	93.2	1.62

Figure A-12 1998/99 - Average Foreign to Canadian Price Ratio Using Only Brand Name Prices. Results are Unweighted, Weighted by Canadian Expenditure and Weighted by Canadian Utilization

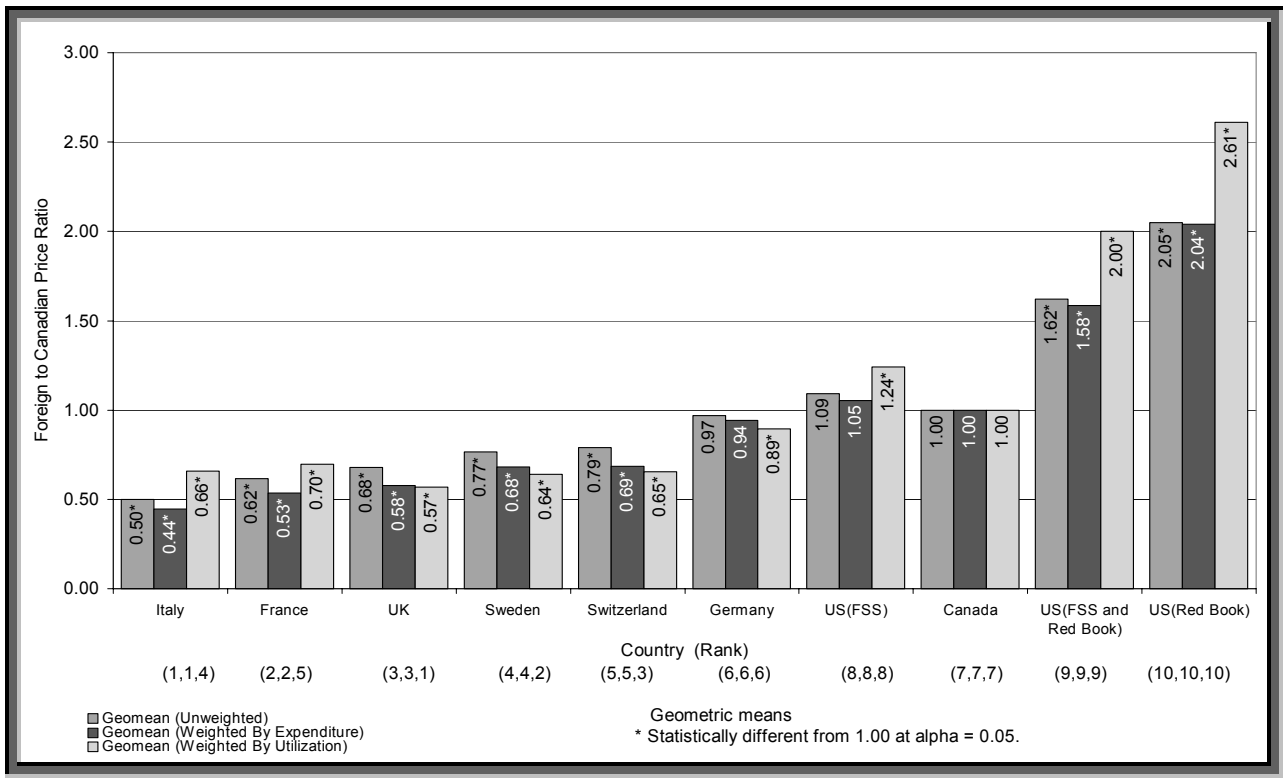
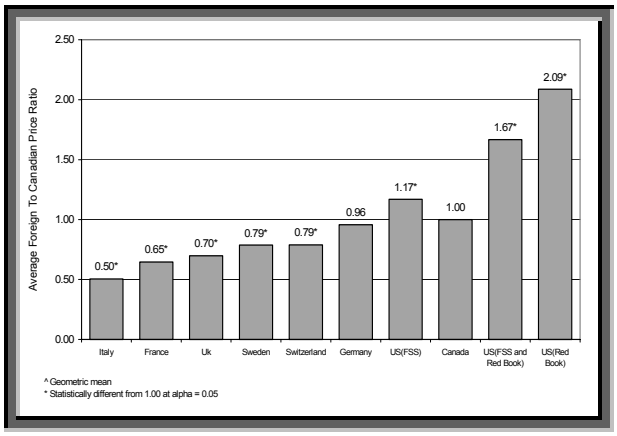


Figure A-13 1998/99 - Average Foreign to Canadian Price Ratio Using Only Brand Name Prices. Minimum of Three Countries Required to be Included in the Analysis.



A4 Common Basket Analysis with Brand Product Price Levels.

Figure A-14 1998/99 - Average Foreign to International Price Ratios Using Only Brand Name Products. Products Must be Available in All Seven Countries For Inclusion Into Analysis. The U.S. Prices are an Average of the FSS and Red Book Prices.

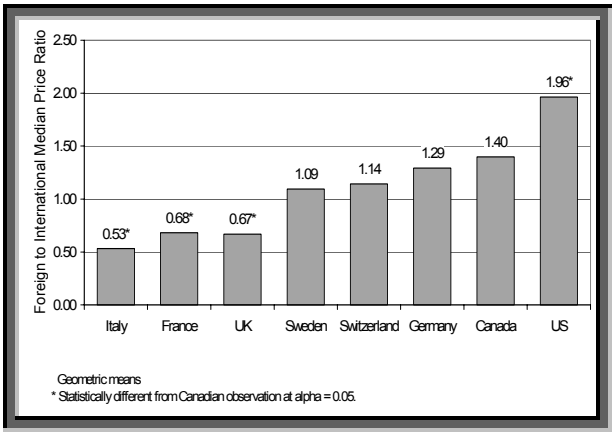


Figure A-15 1998/99 - Average Foreign to Median International Price Ratio. Products Must be Available in All Seven Countries For Inclusion in Analysis. Median Foreign Price Used. The U.S. Price Used is the FSS Price.

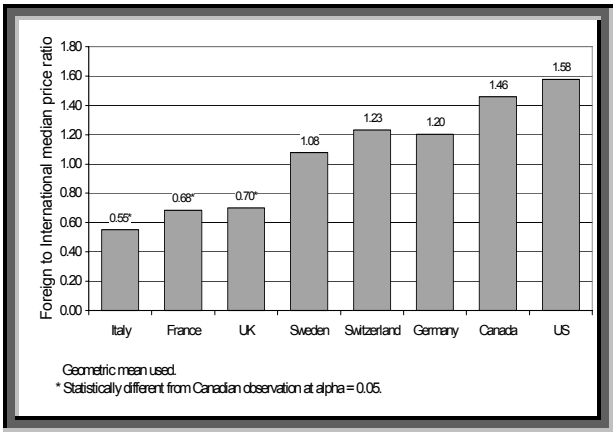


Figure A-16 1998/99 - Average Foreign to Median International Price Ratio Using Only Brand Name Products. Products Must Be Available in All Seven Countries to be Included in Analysis. The U.S. Price Used is the FSS Price.

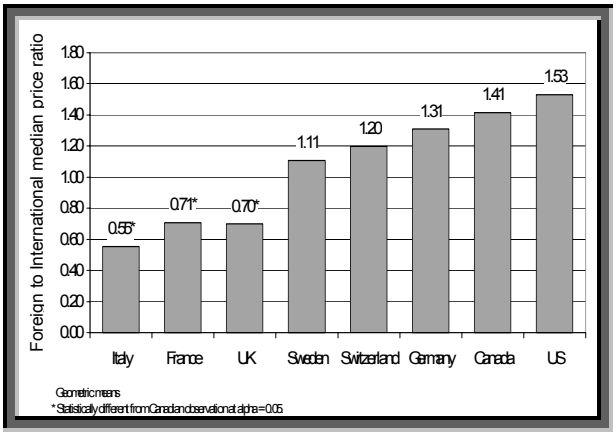


Figure A-17 1998/99 - Average Foreign to Median International Price. Products Must Be Available in All Seven Countries to be Included in Analysis. Median Foreign Prices Used. The U.S. Price Used is the Red Book Price.

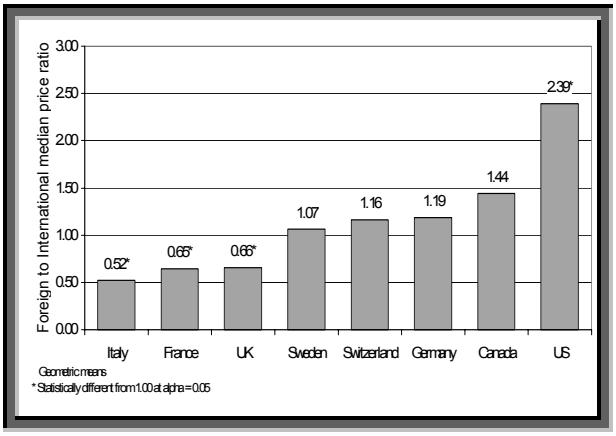


Figure A-18 1998/99 - Average Foreign to Median International Price Ratio Using Only Brand Name Products. Products Must be Available in All Seven Countries For Inclusion in Analysis. The U.S. Price Used is the Red Book Price.

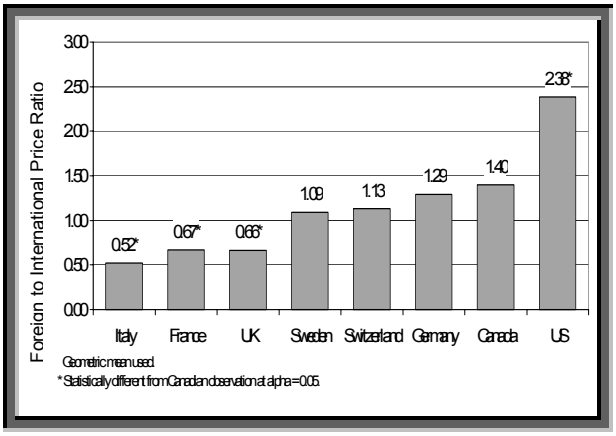
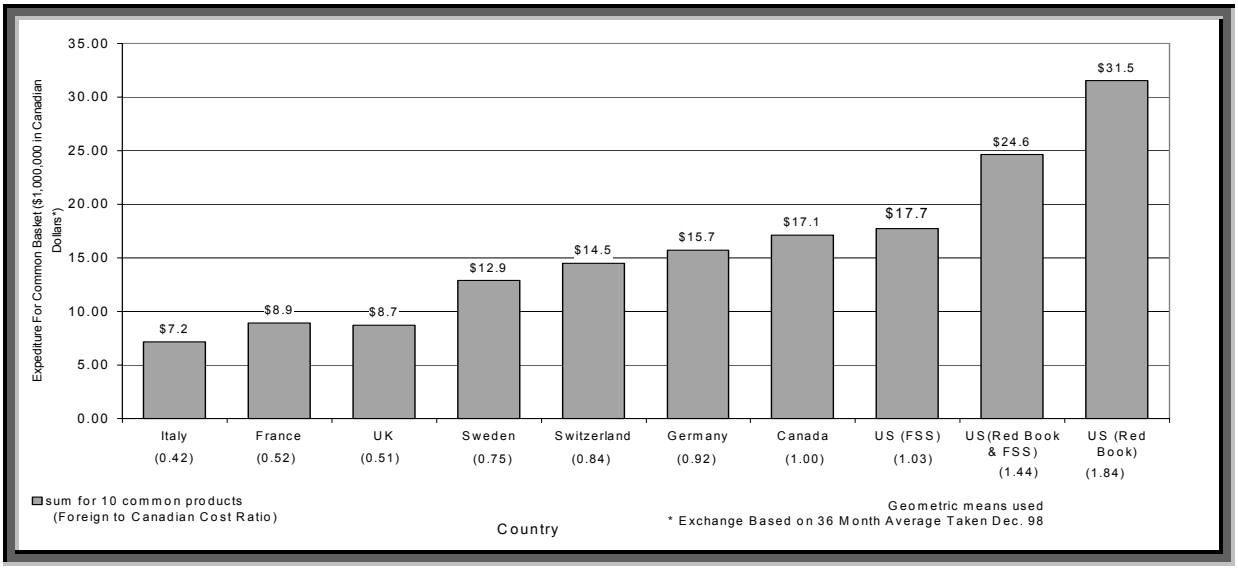
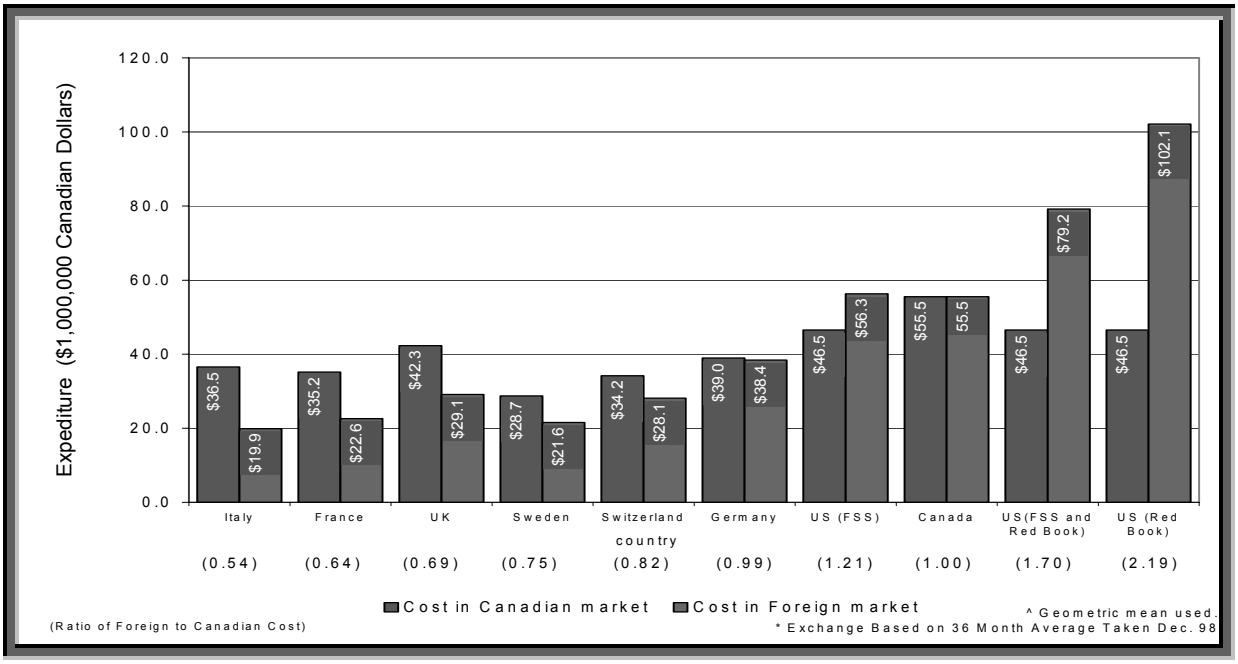


Figure A-19 1998/99 - Total Cost of a Common Basket of 10 Products Found In All Seven Comparator Countries. Only Brand Name Price Levels Used.



(Note: The Canadian basket is the equivalent cost and utilization observed in the ODB database for 1998/99)

Figure A-20 1998/99 - The Cost of the Drugs Common to Both the Foreign Country and Canada, at Canadian Utilization Levels. Only Brand Name Products Included in the Analysis.



(Note: The Canadian basket is the equivalent cost and utilization observed in the ODB database for 1998/99)

A5 Analysis Based on Brand Name Comparisons, With U.S. Prices Defined by the Red Book and Using Average (Mean) Package Size[61]

Table A-2

1998/99 Top Selling Non-patented Single Source Drug Products.
Comparing Canadian and Median International Prices Using the Methodology From the Previous Study. Only Brand Name Product Prices Used, the Average (Mean) Package Size Price is Used and the U.S. Price is the Red Book Price.
Drug Prices at the Ex-factory level.

Total # of Drug Products	56	
	Number	Percent
Canadian Price Highest	8	14.3%
Canadian Price Lowest	13	23.2%
Canadian Price Above Median International Price	27	48.2%
Canadian Price Below Median International Price	29	51.8%
Canadian Price/International Median Price (Geometric Mean)	**1.00**	

Figure A-21 Average Foreign to Canadian Price Ratio Using Methodology from the Previous Study. Only Brand Name Product Prices Used, the Average (Mean) Package Size Price is Used and the U.S. Price is the Red Book Price.

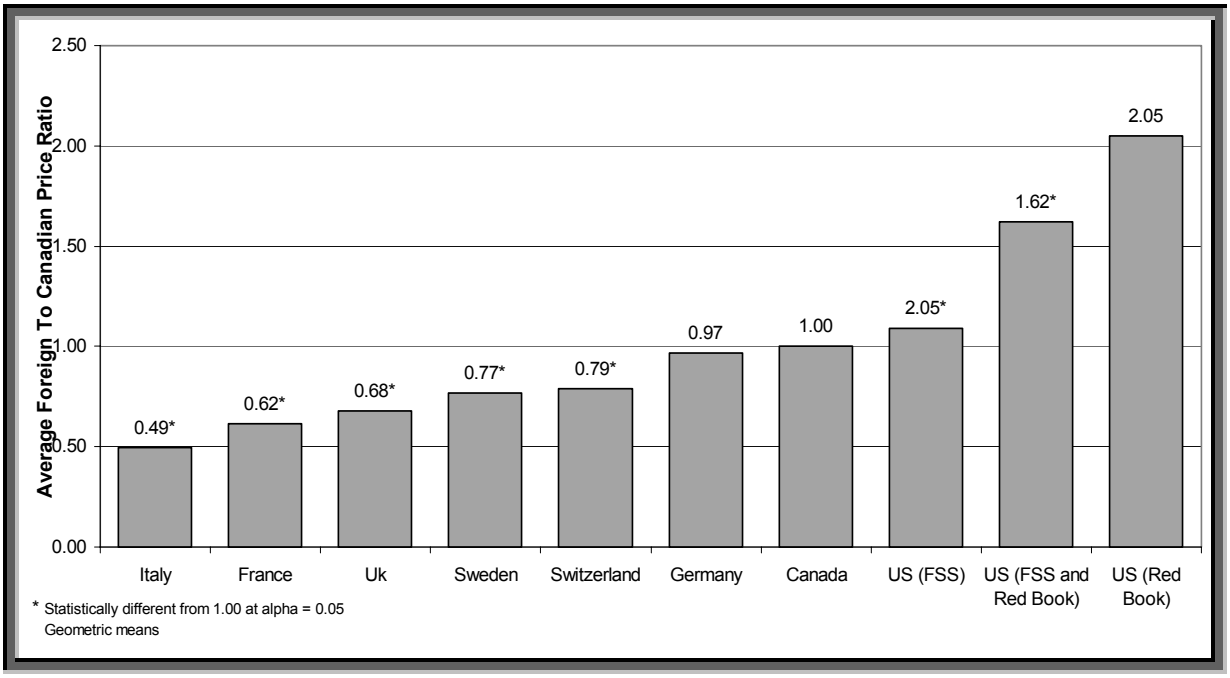


Table A-3

1998/99 Top Selling Non-Patented Single Source Drug Products By Country. Comparing Canadian and Foreign Prices With Only Brand Name Products, the U.S. Prices Defined by the Red Book and the Average (Mean) Package Size Used.

Foreign Country	# of Drug Products That Match	Canadian price Above		Canadian price Below		Average Price Ratio (Foreign/Can)
		#	%	#	%	
UK	34	27	79.4	7	20.6	0.68
Italy	32	30	93.8	2	6.3	0.50
France	30	24	80.0	6	20.0	0.62
Sweden	25	15	60.0	10	40.0	0.77
Switzerland	29	20	69.0	9	31.0	0.79
Germany	35	22	62.9	13	37.1	0.97
US(FSS)	44	12	27.3	32	72.7	1.09
US(FSS and Red Book)	44	3	6.8	41	93.2	1.62
US(Red Book)	44	2	4.5	42	95.5	2.05

A6 Products with Top Ratio and Expenditure Levels

Table A.4 shows the top ten drug products with the highest Canadian to MIP ratios. Cordarone had by far the highest ratio and by far the highest expenditure level. The Canadian price was 3.23 times the MIP.[62] The next ratio was considerably lower at 2.59. Cordarone was available in all seven countries. The next two products were Bonamine chewable tablets, comparable only in the US, and Loxapac tablets, comparable only with a single product in France. After that, drug products with the highest Canadian to MIP ratio tended to have a MIP comprised of prices from numerous countries. Conversely, of the ten products with the lowest Canadian to international price ratio, seven of the

products with the lowest ten ratios were found outside of Canada only in the US, thus the international price is simply the U.S. price. In these instances, the U.S. price was between 1.5 and 2.5 the Canadian price. One additional product amount the lowest ratios were found only the U.S. and one other country.

The expenditure for Cordarone in 1998/1999 was $7.8 million, or 14.13% of the total expenditure of the 56 tablets and capsules used in the analysis. Of the other top ten products by ratio, only Uripas tablets were amongst the products with the greatest expenditure. However, most of the products with the top expenditure also have Canadian to MIP ratios above one.

This analysis was done at the bioequivalence level, were products of different strengths were analysed separately. Therefore, three Coumadin products were amongst the top-ten products by expenditure. Had all four Coumadin products been treated as a single drug, they would have collectively accounted for 13.28% of the total expenditure on the 56 products used in this analysis.

Considering only brand name products in the analysis did not greatly change the results. Cordarone is still the product with the highest Canadian to MIP ratio and the highest expenditure level.

Table A-4

The Top Ten Canadian to Median International Price Ratios. Median Foreign Prices Used. The U.S. Price is the FSS and Red Book Prices. Drug Prices at the Ex-factory Level.

DIN	Brand Name	Canadian to International Price Ratio	Number of Countries with Comparable Product	Canadian Price	Median International Price	US to Canadian ratio	Ingredient Cost (Without up charge)	Percentage of Expenditure on Top-Selling 56 Tablets and Capsules	Rank By Expenditure
2036282	Cordarone tab 200MG	3.23	7	2.06	0.64	1.26	$7,843,264	14.13	1
220442	Bonamine chewable tab 25MG	2.59	2	0.27	0.10	0.18	$557,148	1.00	31
2170132	Loxapac tab 25 MG	2.42	1	0.55	0.23	N/A	$250,853	0.45	53
846341	Sibelium cap 5MG	2.39	3	1.08	0.45	N/A	$416,573	0.75	40
4626	Leukeran tab 2MG	2.27	6	1.21	0.53	1.24	$319,909	0.58	47
465283	Hydrea cap 500MG	1.88	7	1.62	0.86	0.70	$1,169,715	2.11	14
728179	Urispas tab 200MG	1.87	5	0.49	0.26	N/A	$1,725,067	3.11	9
603716	Rythmol tab 300MG	1.68	7	1.20	0.71	1.60	$541,693	0.98	33
755583	Tegretol CR tab 400MG	1.66	7	0.60	0.36	1.48	$731,226	1.32	22
782327	Andriol cap 40MG	3.23	7	2.06	0.64	1.26	$7,843,264	14.13	1

Table A- 5

The Top Ten Canadian Expenditure Levels. Median Foreign Prices Used. The U.S. Price is the FSS and Red Book Prices. Drug Prices at the Ex-factory Level.

DIN	Brand Name	Canadian to International Price Ratio	Number of Countries with Comparable Product	Canadian Price	Median International Price	US to Canadian ratio	Ingredient Cost (Without up charge)	Percentage of Expenditure on Top-Selling 56 Tablets and Capsules	Rank By Ratio
2036282	Cordarone Tab 200MG	3.23	7	2.06	0.64	1.26	$7,843,264	14.13	1
632600	Cytotec tab 200MCG	1.12	7	0.45	0.40	1.83	$3,900,632	7.03	28
2123282	Coversyl - 4MG Tab	0.86	5	0.75	0.87	N/A	$2,491,813	4.49	43
1918311	Coumadin Tab 1MG	1.00	2	0.30	0.30	1.73	$2,425,577	4.37	32
1918338	Coumadin Tab 2MG	1.05	2	0.32	0.30	1.69	$2,379,171	4.28	30
603708	Rythmol tab 150MG	1.40	6	0.68	0.49	1.55	$2,182,974	3.93	17
1918346	Coumadin tab 2.5MG	0.82	2	0.26	0.31	2.17	$1,791,520	3.23	45
35319	Lanoxin tab 0.125MG	1.32	6	0.09	0.07	1.06	$1,781,298	3.21	23
728179	Urispas tab 200MG	1.87	5	0.49	0.26	N/A	$1,725,067	3.11	7
2015439	MS Contin SRT 15MG	1.20	2	0.60	0.49	0.96	$1,655,325	2.98	26

Table A-6

1998/99. The Top Ten Canadian to International Price Ratios. Ratios are Calculated With Only Brand Name Products. The U.S. Price Remains the Average of FSS and the Red Book Price.
Prices At the Ex-Factory Level.

DIN	Brand Name	Canadian to International Price Ratio	Number of Countries with Comparable Product	Canadian Price	Median International Price	US to Canadian ratio	Ingredient Cost (Without up charge)	Percentage of Expenditure on Top-Selling 65 Tablets and Capsules	By Expenditure
2036282	Cordarone tab 200MG	3.14	7	2.06	0.66	1.35	$7,843,264	14.13	1
220442	Bonamine tab 25MG chewable	2.92	2	0.27	0.09	0.09	$557,148	1.00	31
2170132	Loxapac tab - 25 MG	2.42	1	0.55	0.23	N/A	$250,853	0.45	53
4626	Leukeran tab 2MG	2.27	6	1.21	0.53	1.24	$319,909	0.58	47
846341	Sibelium cap 5MG	2.20	3	1.08	0.49	N/A	$416,573	0.75	40
465283	Hydrea cap 500MG	1.88	7	1.62	0.86	0.75	$1,169,715	2.11	14
728179	Urispas tab 200MG	1.87	5	0.49	0.26	N/A	$1,725,067	3.11	9
782327	Andriol cap 40MG	1.66	6	0.94	0.57	N/A	$1,239,498	2.23	12
2221799	Frisium tab 10MG	1.62	4	0.34	0.21	N/A	$545,651	0.98	32
755583	Tegretol CR tab 400MG	1.60	7	0.60	0.37	1.48	$731,226	1.32	22

Table A-7

1998/99 -The Top Ten Products with the Highest Expenditure. Ratios are Calculated With Only Brand Name Products. The U.S. Price Remains the FSS and Red Book Price. Prices At the Ex-Factory Level.

DIN	Brand Name	Canadian to International Price Ratio	Number of Countries with Comparable Product	Canadian Price	Median International Price	US to Canadian ratio	Ingredient Cost (Without up charge)	Percentage of Expenditure on Top-Selling 65 Tablets and Capsules	By Ratio
2036282	Cordarone tab 200MG	3.14	7	2.06	0.66	1.35	$7,843,264	14.13	1
632600	Cytotec tab 200MCG	1.12	7	0.45	0.40	1.83	$3,900,632	7.03	27
2123282	Coversyl - 4MG tab	0.86	5	0.75	0.87	N/A	$2,491,813	4.49	41
1918311	Coumadin tab 1MG	0.97	2	0.30	0.31	1.78	$2,425,573	4.37	32
1918338	Coumadin tab 2MG	1.02	2	0.32	0.31	1.75	$2,379,171	4.28	29
603708	Rythmol tab 150MG	1.40	6	0.68	0.49	1.55	$2,182,974	3.93	16
1918346	Coumadin tab 2.5MG	0.80	2	0.26	0.32	2.25	$1,791,520	3.23	45
35319	Lanoxin tab 0.125MG	1.32	6	0.09	0.07	1.89	$1,781,298	3.21	20
728179	Urispas tab 200MG	1.87	5	0.49	0.26	N/A	$1,725,067	3.11	7
2015439	MS Contin SRT 15MG	1.17	2	0.60	0.51	1.01	$1,655,325	2.98	25

B. Appendix B: Public Sources Used To Gather International Prices

US:	The Red Book and FSS prices from DVA web site: http://www.vapbm.org/PBM/prices.htm
UK:	Monthly index of Medical Specialties, (MIMS)
Italy:	L'Informatore Farmaceutico
France:	Sempex
Sweden:	Prislista
Switzerland:	Medwin
Germany:	Rote List

C. Appendix C: Pharmaceutical Regulation, Coverage and Distribution and Methodology Used for Calculation of Ex-factory Prices Based on Publicly Available Prices

C1 Background on the Pharmaceutical Coverage, Reimbursement, Distribution Mark-Up's and Policies For Seven Foreign Countries Used In Analysis[63]

Most countries regulate manufacturer prices for pharmaceuticals, either directly (France, Italy) or indirectly through controls on reimbursement (Germany, Japan) or profits (the UK). [64]

Canada is the world's tenth largest market for pharmaceuticals and is sixth out of the eight countries in this study. The Canadian pharmaceutical market at retail prices, excluding hospital use, was worth $11.3 billion or $7.8 billion U.S. in 1999. Public sources pay for approximately 43% of the total pharmaceutical expenditure. Canada has a national health care system run jointly by the federal and provincial governments; but in general this system does not cover pharmaceuticals. Those covered for pharmaceuticals in Canada may include senior citizens, veterans and/or social assistance recipients, but eligibility for coverage varies greatly from province to province. Private and employer sponsored insurance programs do exist, and they account for approximately 30% of healthcare spending, (compared with the 70% share of the government).

Only patented medications are subject to price controls in Canada. The Patented Medicine Prices Review Board (PMPRB) regulates prices at the factory-gate level. For breakthrough medications, a median international price is formulated and used to help determine a reasonable price level. The countries used are the same ones used in this study, (i.e. the UK, France, Italy, Sweden, Switzerland, Germany and the US). For drugs with comparable drug products already on the market, the maximum price of the therapeutically equivalent drug is used as a ceiling. Price increases are compared to increases in other consumer products, via the Consumer Price Index, CPI. Over the counter medications are subject to the PMPRB guidelines so long as they are patented, but generic products and non-patented products are not.

United Kingdom

The UK pharmaceutical market at retail price levels was worth £7.6 billion or $12.3 billion U.S. in 1999, excluding hospital use. Public sources pay for approximately 63% of total pharmaceutical expenditure. The National Health Service, (NHS), in the UK provides public health care free to all citizens, although 12% of the population is covered by private insurance. Under the public system prescription pharmaceuticals are dispensed directly from the pharmacy at no cost to the patient. Some citizens have to pay the flat dispensing fee.[65]

The UK uses rate-of-return regulation to control pharmaceutical prices. The Pharmaceutical Price Regulation Scheme (PPRS) regulates companies supplying branded products to the National Health Service by considering the return on capital employed or by considering the return on sales depending on the size of the company. Manufacturers submit trade prices to the Pharmaceutical Pricing Authority (PPA) each year and account for a regulated 12.5% wholesale mark-up.[66] These prices are the basis of the reimbursement program and do not account for supply, bulk or bundling discounts. The community pharmacies are reimbursed in full directly for brand name products at the manufacturers' list price available in the Monthly Index of Medical Supplies (MIMS). Government policy tries to encourage cost effective purchasing practices on the part of pharmacies with polices such as the discount claw-back program that allows pharmacies a share in the savings.[67]

Sales to hospitals and community primary care facilities are covered by the PPRS, but exports, non-prescription drugs and products sold under private prescriptions are not included in the scheme. Generic products are also not subject to the same profit controlling policies as brand name products, but they are only reimbursed at the price listed in the Drug Tariff list. The Drug Tariff list price is determined by the classification of drugs according to the supply and demand conditions for that product.[68] The generic market is larger in the UK than elsewhere in the European Union. Over 65% of the prescriptions are written generically, but they account for less than a quarter of the total pharmaceutical expenditure.

The prices in the UK are generally recognised as higher then the European average, but for the non-patented single source top-selling tablets and capsules in this analysis, the UK had the third lowest price levels of the six European countries used in the paper.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 69 products could be matched with bioequivalent products on the NHS list of reimbursed drug products; 42 of which were tablets and capsules used in the analysis.[69] Approximately half of the products matched in the UK were sold under the same brand name. Of the matched drugs, six had more then one comparable product found in the UK, although none of the six were tablets or capsules used in the analysis. Of the 45 drugs without UK equivalents, 19 had comparable products with the same active ingredients and dosage form, but a different strength level. For 13 of the 114 top selling non-patented single source drugs, neither the drug product nor the active ingredients were found on the NHS list.

Italy

The Italian pharmaceutical market at retail prices, excluding hospital use, was worth Lit27,882 billion or $12.8 billion U.S. in 1999. The Italian market is estimated to be the third largest pharmaceutical market in Europe and its size is generally attributed to high volume. Public sources pay for approximately 80% of pharmaceutical expenditure.[70] Universal national health coverage is provided by the Servizio Sanitario Nazionale (SSN), which is operated by the national Ministry of Health. Primarily regional governments administer the system, which then allocate funds to 240 local heath authorities (Aziende Sanitarie Locali, ASL). The ASL are responsible for purchasing pharmaceuticals, balancing the allocated funds and collecting additional revenue through taxation if required. ASL is also responsible for administering hospital and ambulatory care. There is private insurance in Italy, but it is a supplement used primarily by higher income brackets only and is held approximately by less than 10% of the population.

Over the counter pharmaceuticals and new prescription pharmaceuticals not seeking reimbursement are priced freely by the manufacturer, although all prescription drug price revisions must be reported in advance to the Ministry of Healths Drug Committee, Commissione Unica del Farmaco (CUF).

Reimbursed pharmaceutical products are subject to price controls administered by the CUF. Once a manufacturer applies for reimbursement, one of two different models may be used to establish an accepted ex-factory price. One method is the Average European Price scheme (AEP), introduced in 1994. This scheme uses a basket of four countries for which a comparable product must be available in no less then two of those countries, one of which must be a country with a price control policy.[71] The Italian ex-factory price accepted must not exceed the average European price calculated. In May of 1997 the Italian government initiated a program to establish ex-factory drug prices for innovative pharmaceutical products approved by the European Medicines Evaluation Agency (EMEA). These prices are negotiated between the marketing company and the CUF based on a procedure developed by the Comituto Interministeriale per la Programazione Economica (CIPE). The procedure is designed to consider the degree of innovation and the sales forecasted. The specific criteria allowed for in the procedure include cost/benefit ratios, the products price in other countries, sales forecasts (for products and through licensees), number of patients and financial factors such as industrial policy considerations.

In 1996 the government introduced a same price for the same drug policy. This policy was to insure that once a chemical compound, strength, dosage, etc., is accepted as reimbursable, there is one national price for all similar products. In 1998 the CUF revised the system, making it based more on homogeneous therapeutic groups of products. This was to facilitate monitoring and comparisons with other countries, but similar drug products are still reimbursed at the same price level.

Reimbursed generic products are also regulated and must be listed at 20% off the original drug product. The generic market in Italy is extremely small, and was less then 0.4% in 1999. Negotiated drug prices are ex-factory prices. There is a fixed 6.65% wholesale mark-up and a fixed 26.7% pharmacy mark-up.[72] Both of these percentages are based on the public retail price before tax. This means that the combined wholesale and pharmacy mark-up is 33.35% of the public retail price, or 50% of the ex-factory price negotiated. There is also a 10% value added tax applied to all pharmaceuticals.[73] The final retail price is listed in L'Informatore Farmaceutico, including all mark-ups and taxes.

Italian pharmaceutical prices are generally recognized as low, estimated as approximately 30% less than the EU average. This is consistent with the results of this study that found Italy to have the lowest price levels for the products and basket of countries used in this analysis.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 57 products could be matched with equivalent products on the list of reimbursed drug products listed in L'Informatore Farmaceutico, 35 of which were tablets and capsules used in the analysis. Many bioequivalent brand name products were often offered, although all would be listed at the same price. Of the matched drugs, 20 had more then one comparable product found in Italy, 15 of these were tablets or capsules used in the analysis. Brand name drug products in the L'Informatore Farmaceutico were generally listed at a single strength level and in a single package size. Of the 57 drugs without listed equivalents, 20 had comparable products with the same active ingredients and dosage form, but were offered only at a different strength level.

France

The French pharmaceutical market at retail prices was worth FFr133 billion or $20.4 billion U.S. in 1999, excluding hospital use. Public sources pay for 60% of the pharmaceutical expenditure bill. The French population is almost entirely covered, (99%), by the statutory health insurance, Assurance Maladie / Sécurité Sociale. This program is organized into approximately 20 funds for different occupational groups, but the top three funds cover 96% of the population. There is also not-for-profit insurance schemes and private insurance which most individuals have to cover co-payments.

Pharmaceutical companies are technically free to set new product prices but when they apply to be reimbursed under the national system, the price must be negotiated. Manufacturers who have developed a product they wish to have reimbursed must submit detailed information to the Transparency Commission, Commission de Transparence (CT) and the Economic Committee on Health Products, Comité Économique des Produits de Santé, (CEPS).[74] The submission requirements to the committees include information on the disease, efficacy and marketing. Improved clinical merit was formally the foundation of the system and is still heavily considered. The CT has members from the Ministry of Health and Social Affaires, Economy and Finance and members from the industry. The three largest insurance funds have a seat on the CT. The CT then negotiates a recommended price and a reimbursement level within its members. The recommended price and reimbursement levels are then given to the CEPS individual appointed for the given case, who then comprises a report. The report reveals the recommendations for the product from the CT and arguments to support or reject these recommendations. If the appointee rejects the price or reimbursement level, the report recommends an alternative. Both the CEPS and the manufacturermust agree upon the final price and reimbursement level; otherwise the company can choose to launch a product without having it reimbursed. More then half of the products are reimbursable, most at 35%. Reimbursement levels are based on the products medical benefit and the severity of the disease. Products for non-serious diseases are reimbursed at 35%. Products with major or moderate benefit for major diseases are reimbursed at 65%. Products of modest medical benefit for any disease are reimbursed at 35% if the product is deemed justifiably reimbursement. Products of insufficient medical benefit are not reimbursed. Additional provisions insure that hospital drugs and some other hospital products are 100% reimbursable and available to patients at retail pharmacies for diseases such as HIV or cancer.

Reimbursable generics have strict labelling laws and must be clearly marked generic. They are listed at a price level 30% below the original brand name product. Until recently approximately 75% of the pharmaceutical expenditure was on ingredients with no patents, but the generic market share was only around 2%. In June of 1999 pharmacies were given the right to generic substitution and in September pharmacy mark-up policies were changed in an agreement by pharmacists substitute in approximately 35% of eligible cases. The market share and volume share of generic products increased drastically. From January 1998 to January 2000, the market share of generic products went from 2.0% to 3.1% and the volume share when from 3.1% to 5.7%.

The prices negotiated in the process outlined above are ex-factory prices. Pharmacy and wholesale mark-up margins are fixed and regulated for reimbursable drug products. Until April 1999 the wholesale mark-up was 10.74% of the manufacture's price or 9.70% of the pharmacy purchase price for all reimbursable products.[75] This was modified such that most products are

subjected to the 10.74% mark-up, but the mark-up for products priced above FFr150 was lowered to 6% of the manufacturer's selling price.[76] Pharmacy mark-ups were also changed in September 1999. Previously pharmacy mark-ups were regressive and different for three price bands: FFr0-FFr10, FFr10-FFr200 and over FFr200. Under this strategy, 90% of reimbursable products fell under the central price band and were subject to a pharmacy mark-up of 26.42% of the ex-factory price. As of September 1999 there are only two price bands. All products are subject to a 26.1% pharmacy mark-up for the first FFr150. Any additional cost of a product priced above that is subjected to pharmacy mark-up of 10%.[77] In addition, pharmacists receive a flat fixed fee of FFr3.5 per reimbursable drug item for most products and a FFr5.5 flat fixed fee for additional 40 products requiring more involvement on the part of the pharmacies. This flat fixed fee is the result of a promise on the part of pharmacist to use the new generic substitution provisions in 35% of possible substitution cases.

The price at which the pharmacies purchase the reimbursed drug products and the price at which the pharmacies may sell them are both in a publication entitled Sempex. These listed prices exclude tax. There is a value-added tax charged on pharmaceutical products in France, but it is at a reduced rate. Reimbursable medications are charged 2.1% and non-reimbursable medications are charged 5.5%.[78]

French pharmaceutical prices are generally recognised as well below the European average. This is consistent with the results of this study that found France to have the second lowest price levels for the products and basket of countries used in this analysis.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 61 products could be matched with equivalent products on the Sempex list, 37 of which were tablets and capsules used in the analysis. Most products were listed in Sempex in a single package size. Of the matched drugs, 6 had more then one comparable product found in France, but only one of them was a tablet used in the analysis. Of the 53 drugs without listed equivalents, 23 had comparable products with the same active ingredients and dosage form, but were listed only at a different strength level.

Sweden

The Swedish pharmaceutical market at retail prices, excluding hospital use, was worth SKr29.6 billion or $3.5 billion U.S. in 1999. Public sources pay for approximately 71% of pharmaceutical expenditure. The Swedish national health insurance plan is compulsory for all residents with a heavy emphasis on quality, equality and preventative care. Prices are generally regarded as high, but volume is moderate and attitudes towards pharmaceuticals are cautious. Policy decisions and standards are set nationally, but the administering of the pharmaceutical coverage has been the responsibility of 26 regional counties and municipalities since January 1998. Almost half of the healthcare dollars are generated and collected locally through payroll taxes.

A pharmaceutical company is technically free to set there own price levels when launching brand, generic and over the counter products; However, if the company is applying to have this product reimbursed, the National Social Insurance Board, Riksförsäkringsverket, (RFV), sets the price. Specifically it is the Division of Drug Affairs of RFV that negotiates a wholesale price level with the manufacturer. The Federation of County Councils is involved in the discussions, but is not permitted in the final price approval part of the negotiations. Factors that are considered in negotiating price levels include both the medical and economic value, the medical and economic impact of the product, prices elsewhere in Europe, prices of similar products, projected sales, R&D and manufacturing cost. Generally, purposed launch prices are compared heavily to prices in other Nordic countries. New products are normally priced at the average level for products in that therapeutic class. Higher prices are allowed for substantial improvements over existing therapies. Sweden has a reference based pricing system for similar products. The listed reimbursable price of any product must be within 10% of the cheapest comparable brand or generic product. The generic market is small and generally not promoted in Sweden; In 1999 generics accounted for approximately 4% of the pharmaceutical market. Price revisions for reimbursable pharmaceuticals is permitted only during the RFV's annual price review of each companies prices. If a company is permitted to raise prices, it is usually a figure for the entire company based on the companies reimbursed sales. The company then has the freedom to alter the prices of individual products accordingly, although any product price increase

above 10% requires additional approval by the RFV.

The prices set by the RFV are wholesale prices to be offered by one of the two wholesale distributors. ADA, a public subsidiary of the National Corporation of Swedish Pharmacies, Apoteket (AB), controls most distribution. The other wholesaler is owned by a few large pharmaceutical manufacturers. Wholesale mark-ups are not fixed. They are generally negotiated between the wholesalers and the manufacturers and tend to be between 4% and 5% of the manufacturers selling price. In 1999 the general wholesale mark-up was approximately 4.2%.

AB has a monopoly on pharmacies and pharmacy margins are regulated. The Prilista publication lists the retail price at which pharmaceuticals are paid to the public, but it also lists the regulated pharmacy mark-ups. In February 2000 the price of all reimbursable pharmaceuticals was reduced by a flat fee of SKr2.60, the changes in pharmacy mark-ups are presented below. These mark-ups differ from those used in this study only by the SKr2.60 reduction.[79] After this change the RFV decided to renegotiate pharmacy margins every six months.

Table C-1 Fixed Pharmacy Mark-ups for Swedish Formulary in Prilista

Wholesale Price (WP)	Pharmacy Mark-up
WP. 34,25	(WP x 1.30) + 15.40
34,25. WP. 75,00	(WP x 1.18) + 19.60
75,00. WP. 300,00	(WP x 1.08) + 27.10
300,00. WP. 2.00,00	(WP x 1.07) + 30.10
2.000,00. WP	(WP x 1.01) + 150.10

Although the Swedish taxation rate of 25% applies to other products, there is not tax applied to reimbursed medicines.

With the exception of insulin's, patients pay for the entire cost of their medication for the first SKr900 in a given year.[80] At that point, patients start to share the cost with the national insurance program. For total accumulated spending between SKr901-SKr1,700 patients are reimbursed 50%; for total accumulated spending between SKr1,701-SKr3,300 patients are reimbursed 75%; for total accumulated spending between SKr3,301-SKr4,300 patients are reimbursed 90%; and for total accumulated spending above SKr4,300 patients are not required to pay anything.[81] This translates to a maximum total out-of-pocket spending of SKr1,800 for each patient. Patients are also responsible for any cost of a product above the reimbursable listed price in Prislista. This cost, if incurred, is not calculated as part of the patients' accumulated total pharmaceutical expenses.

Swedish pharmaceutical prices are generally recognized as being relatively high within Europe. For the products and countries considered in this analysis, Swedish products were priced fourth lowest, or third highest in Europe.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 48 products could be matched with bioequivalent products listed as reimbursable pharmaceuticals in Prislista list; 31 of which were tablets and capsules used in the analysis. Most products were listed in Prislista in numerous package sizes. Of the matched drugs, 9 had more then one comparable product found in Sweden and 5 of those were tablets or capsules used in the analysis. Of the 66 drugs without listed equivalents, 21 had comparable products with the same active ingredients and dosage form, but were listed only at a different strength level.

Switzerland

The Swiss pharmaceutical market at retail level was worth SFr4.3 billion or $2.7 billion U.S. in 1999, excluding hospital use. Public sources pay for approximately 60% of pharmaceutical expenditure. Prices of pharmaceuticals have historically been seen as being high relative to other European countries, but price reduction measures have now made Swiss prices fall more in line. The Federal Law on Sickness Insurance (KVG), requires all Swiss residents to have medical and pharmaceutical insurance. Private insurance is predominant, (90%), but coverage and rates are heavily regulated by the KVG. Insurance funds are also required to insure that no funds collected and allocated to sickness funds are devoted to other sources or investments. This has the effect of making insurance funds not-for-profit. There are also publicly available sickness funds and subsidies to reduce the insurance premiums of individuals with lower incomes. The terms for health care are detailed, outlined and monitored at the federal level, as is the pricing and reimbursement schemes for pharmaceuticals. The 26 Swiss cantons that form the Swiss Confederation are each responsible for the funding and delivery of the healthcare

system to their residents.

If a manufacturerchooses to have their products reimbursed, the Federal Social Insurance Office, Bundesamt für Sozialversicherung, (BSV) sets the price. A new pharmaceutical product is categorized by the Intercantonal Office for the control of Medicines, Interkantonale Kontrollstelle für Heilmittel, (IKS) and only products in grouped as prescription or non-prescription but suitable for sale at only pharmacies or drugs stores are considered for reimbursement.[82] The BSV determines the reimbursement status of a new pharmaceutical based on advisement by the Federal Drugs Commission, Eidgenössische Arzneimittelkommission, EAK. This is a committee of experts that is intern divided into two subcommittees of experts: the economic subcommittee and the scientific subcommittee. The economic subcommittee considers various factors including the medical and financial value of the product, the efficacy and the R&D costs. This subcommittee will also consider the cost of this or similar products in Denmark, Germany and the Netherlands. The scientific subcommittee must then classify the product as indispensable, important, conditionally necessary or unnecessary. The reimbursement rates depend on this classification and the prices are set on a sliding scale. Products deemed as indispensable or important may be granted high prices, but approximately only 5% of all applications fall into these categories. Products demonstrating great advances over existing treatments may be allowed a price up to 40% higher.[83] Generics only are added to lists of reimbursable drugs if they are 25% below the original, but are labelled similar to brand products in Switzerland. The reimbursable price for a product is established at the ex-factory level, but wholesale and pharmacy mark-ups are regulated. The mark-ups for both pharmacies and wholesalers are both regulated and are set to change in 2001. Wholesale mark-ups from 1996 to 2001, were regressive, ranging from 10% to 15% of the ex-factory price, with a maximum of SFr51.[84] From 1996 to 2001, pharmacy mark-ups were also regressive, ranging from 37.5% of the retail price on lesser-priced products to 19% on more expensive products, with a maximum of SFr95. Both prescription and over the counter pharmaceuticals are subject to a reduced value added tax of 2.3%. The retail price at which products were sold from the pharmacy and the wholesale price at which they were sold to the pharmacy were both available in the publication Medwin.
All health insurance funds must charge patient co-payments set by the Federal Council. Insurance funds are not permitted to cover these expenses. Adult patients pay a fixed fee of SFr 230 plus 10% of further costs on reimbursable products up to a maximum of SFr 600. Children do not pay the fixed fee, but do pay the 10% share up to SFr 300, with an accumulative maximum of SFr 600 for all children in the family. The Federal Council may also reduce or remove the co-payment charges for the treatment of long-term or serious illness, or in the case of poverty. Products outside of the list of products recognized by the Federal Council as reimbursable may be insured, but a co-payment of at least 10% must be charged.

Swiss pharmaceutical prices are generally recognized as being relatively high within Europe, although recent policy changes are credited with bringing prices more inline with other European nations. For the products and countries considered in this analysis, Swiss products were priced fifth, lower then only Germany amongst the European countries.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 58 products could be matched with equivalent products list of reimbursable pharmaceuticals in Medwin, 36 of which were tablets and capsules used in the analysis. Most products were listed in Medwin came in a large and small package size. Of the matched drugs, 9 had more then one comparable product found in Switzerland and 4 of those were tablets or capsules used in the analysis. Price differences for similar products sold by competing manufacturers tended to be small to negligible. Of the 56 drugs without listed equivalents, 18 had comparable products with the same active ingredients and dosage form, but were listed only at a different strength level.

Germany

The German pharmaceutical market at retail level was DM 53.2 billion or $27.4 billion U.S. in 1999, excluding hospital use. This is the largest pharmaceutical market in Europe. Prices are high, but volume is within the European average. Public sources pay approximately 70% of the pharmaceutical bill. Most Germans (90%) use the statutory health insurance program, Gesetzliche Krankenversicherung (GKV). The GKV is comprised of 550 public sickness funds, Krankenkassen, funded by employees, employers and the state. The remaining 10% of the population are covered by private insurance plans, Private Krankenversicherung (PKV). In order to opt

out of the GKV in favour of PKV, an individual must be either self-employed or earn more than DM6,000.

Manufacturers are essentially free to set their own prices on all products, but if the product is priced above the reimbursed price patients must pay the difference.[85] Unlike other countries, Germany has not had a 'positive list' of reimbursable pharmaceutical products so much as a 'negative list' of products specifically deemed as non-reimbursable.[86] This generally resulted in a large group of reimbursable products. This changed in 1999 when the Federal Committee changed guidelines completely, and the policy is now that the mere licensing of pharmaceutical products is a necessary but not sufficient condition for reimbursement in the Social Health Insurance system.[87] In addition, the previous plan for the creation of a positive list in 1996 (that was scraped with a change in government) is again being promoted in Germany.

Germany has a reference based pricing system. Approximately 50% of the market (60% of prescriptions), are currently grouped were a maximum reimbursable price is assigned to that group. Products not grouped (and not on the negative list) are reimbursed in full. If a company does not lower their price they often lose their market share.[88] The reference group for a set of products may be based on three different levels of grouping: Level I Same active ingredients if therapeutically relevant; Level II products with pharmacologically and therapeutically comparable active ingredients (chemically related agents); Level III products with therapeutically comparable effects. Provisions must be made to insure: That level I and level II group prices are not so low as to impede/restrict the inclusion of medically necessary treatments.

Level II pricing should not be set for a patented product based on a new principle that is recognized to offer a significant therapeutic advantage.

The interpretation of this second provision changed at the beginning of 1996. Where as it used to be taken to mean that a reference level price could not be established for a level II grouping until the first product cam of patent, it is now taken to mean that a products can not be included into a level II or level III pricing group until it's patent has expired. Consequently, patented pharmaceuticals registered after December 31st 1995 are excluded from the grouping system until their patent expires. Where patent expiry is the trigger for including a product into a level II or level III reference groups, available generisized versions of a product on the market are necessary for establishing a level I grouping. In Germany generic versions of a product usually appear soon after patent expiry. The Federal Committee of Doctors and Sickness Funds, Bundesausschuss der Ärzte und Krankenkassen (BAK), establishes the reference groups or any subgroups and the average daily dose, (ADD). The purposed results are published in the Federal Report (Bundesanzeiger), an oral hearing is held. Representatives of the associations of pharmaceutical manufacturers and pharmacies are present and may raise issues, but individual manufacturers are not present and points concerning specific interests are not considered.

The standard pack is identified and is the one available from the most manufacturers.[89] The prices for the standard packages for each manufacturerare the pharmacy retail prices listed in official price list, Lauer Taxe. For Manufacturers offering the standard package size, a linear equation is derived to relating all packages to the standard. The equation relies on the regression equation coefficients from regression analysis accepted as best fitting the price relationship between all packages of all manufacturers offering the standard package. For manufacturers not offering the standard package size, a proxy standard package size is identified as the package closest to the standard package. A relative price for the proxy is calculated by taking the actual retail price of the proxy standard package is divided by it's estimated price using this package as derived using the linear equation derived for the manufacturers described above. A new linear equation is calculated to best fit all of the manufacturers not offering the standard package. The relative price of the fictitious standard package is normalized and again regression analysis is run again with prices of all packages expressed relative to the fictitious package and new coefficients determined.

Another process is required for grouping products at level II or level III as they contain products with different active ingredients. Instead of a simple dosage variable in the linear model, an active ingredient equivalent factor, Wirkstoffäquivalenzfaktoren (WÄF), is used. The WÄF is calculated as the dosage divided by an equivalent factor. The equivalent factor is in turn calculated as the ADD of an ingredient to be compared divided by the ADD of the active ingredient used as a reference for comparison.[90]

The Association of Sickness Funds, Spitzenverbände der Krankenkassen (SK), sets the maximum reimbursable price for the standard package of a group. The SK must unanimously decide on the standard price using their discretion and very few guidelines. The requirement is made that there must be adequate selection of products and manufacturers competing at or below the reference price. Generally SK accepts this condition as being met so long as 15-20% of the market within a group is covered by the reference price.[91] The SK establishes the reimbursable price for the standard package size at the pharmacy retail level and all other package sizes are related to this one by the regression equations outlined above.

Accommodations are made for varying cost structures if a pharmaceutical product included into the group is of a different form such as a drop, tablet, spray, etc. Incorporating 'dummy' variables into the regression model does this.

Manufacturers have four weeks to comment on the purposed reference prices before they are published in the Bundesanzeiger; but they have little recourse if they disagree with the final reference price or the assigned ADD. There is no official appeal process and legal action is limited.

Wholesale and pharmacy margins are fixed by law and both are regressive. Wholesale mark-ups range from 12% of the factory gate price to 21% on lesser priced items. This represents from 10.7% to 17.4% of the wholesale price. For products price above DM1,339.28, the mark-up is a flat DM 120.53 plus 3% of the manufacturers price. The pharmacy mark-ups range from 30% to 68% of the wholesale price, or from 23.1% to 40.5% of the pharmacy retail price. For products with a wholesale price above DM 1,063.8, the pharmacy mark-up is a flat DM 231.25 plus an 8.263% of the wholesale price. The normal tax rate of 15% also applies to pharmaceuticals.

The Rote List publishes the price of a product as well as the reference group price if applicable. Prices are listed at the pharmacy retail level including the value-added tax. The Rote Liste also identifies the relative size of a package, which is used as a code for patient co-payments. Package size classification is specific to the therapeutic class of a pharmaceutical product. For example, 20 tablets of a treatment used for chronic conditions may be a considered a 'small pack' while 20 tablets of a product used to treat a minor illness may be considered a medium package. The co-payment structure is designed to encourage larger and more cost effective prescribing habits by doctors. Since January 1st 1999 the co-payment structure has been DM8 for small packs, DM9 for medium packs and DM10 for larger packs. The total patient co-payment must not surpass the cost of the product(s) and there thresholds and exceptions for some residents.[92]
In addition to the pack size co-payment structure patients are responsible for any cost of the product that exceeds the reimbursed reference price. This is not common however, and in 1995 only 7% of the products insured had a price in excess of the reference price.

German pharmaceutical prices are generally recognized be high and for the products in this analysis Germany had the highest prices in Europe.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 62 products could be matched with bioequivalent products listed as reimbursable pharmaceuticals in Rote Liste; 40 of which were tablets and capsules used in the analysis. Most products were listed in Rote Liste came in more than one package size. Of the matched drugs, 32 had more then one comparable product found in Germany and 24 of those were tablets or capsules used in the analysis. Some of the products had as many as 15 competing firms. Of the 46 drugs without listed equivalents, 16 had comparable products with the same active ingredients and dosage form, but were listed only at a different strength level.

United States of America

The U.S. has by far the largest pharmaceutical market in the world. In 1999 the pharmaceutical sales, excluding hospital use, was $134 billion at retail prices. Public sources pay for approximately 14.7% of drug spending. There is no universal health care system in the U.S. Private firms offer insurance and there are public insurance funds covering specific sectors of society, (for example war veterans). It is estimated that approximately 15% of the population are uninsured. The two largest public funds are Medicare and Medicaid. Medicare is a federal plan for seniors, but does not cover out of hospital pharmaceuticals.[93] Medicaid is a state run program for patients below the poverty line. It does offer some drug coverage, but this coverage and the quality of coverage vary greatly from state to state.

There are generally no regulated controls on prices,

although there are some legislative measures in the form of discounts and rebates to try to ensure that public funds benefit from the best prices on the market. The retail cost of pharmaceutical products have been higher in the U.S. than to other countries. Insurance funds work in a variety of different fashions and so price containment measures vary greatly and plans are negotiated separately. Cash customers, (those individuals who pay for drugs themselves, or pay initially and seek reimbursement after), pay 15% more than the total cost of a product purchased by a third party insurer, (not including rebates).[94] This is up from 8% in 1996. The distribution of these price differences are drastically different for brand and generic products.[95] The gap between the retail price for cash and third party purchasers at the retail pharmacy increase to 20% for the most common drugs.[96]

The discrepancy in price for cash and third party payers would be increased if the estimated 2% to 35% manufacturers rebate commanded by third parties were included in the analysis. These rebates are an important part of third party insurance polices, but information on rebates for private funds are confidential and well protected. Public and third party insurance funds use large-scale purchasing either directly or through a pharmacy benefits manager, (PBM), to command competitive prices as competition for inclusion into formularies is fierce if numerous products are within the same therapeutic class.

In 1998, 90% of all out-of-hospital pharmaceutical sales were purchased at a retail pharmacy, but the wholesale/pharmacy margins and distribution chains vary greatly between types of funds. In April of 2000 the Department of Health and Human Services submitted a report to that was requested by (then) president Clinton. The report was called "Prescription Drug Coverage, Spending, Utilization and Prices. The following is a brief outline of the distribution and pricing for the different types of pharmaceutical coverage based on the finding of that report.

Retail Cash Customers:

Of the pharmaceutical prescriptions filled at retail pharmacies, cash customers purchased 25%. Cash customers include those who are uninsured and those who are indemnity covered were they pay for the products initially and seek reimbursement for the products after. Although the ultimate total of the cost of these drug products may be different for these two types of patients, the distribution chains of the products are similar. Price setting by the manufacturers to the wholesaler is free. For multi-source drug products manufacturers may offer discounts to the wholesalers in order to promote or create favour for their product, but this is not applicable for innovator or single source drugs. The manufacturers suggests a wholesale price to the wholesaler. This is the price listed in the Red Book as the "Average Wholesale Price" (AWP). Research by the Clinton report found that manufacturers prices are approximately 20% off the AWP, meaning there is a suggested 25% mark-up on the ex-factory price. The AWP is not generally reflective of the actual wholesale price.[97] The mark-up by wholesalers is believed to generally be small, between 2% and 4%.

Retail pharmacy mark-ups may have different strategies for different products. The Clinton report states that industry sources suggest the average retail mark-up between 20% and 25%. Pharmacies may also offer across the board discounts to certain groups such as seniors or patients who pay a member's fee to discount programs. Some insurers who also sell funds offering third party payment may have ways of allowing indemnity fund clients to benefit from negotiated discounts.

Third party payers:

In 1998, third party payers paid for 65% of the prescriptions filled at retail pharmacies. Funds of this kind can operate in two fashions. Some operate through a pharmacy benefits manager (PBM) and others purchase products directly from manufacturers.

If a fund purchases products through a PBM, they can use purchasing power to negotiate from both the manufacturerand the pharmacy.

For brand name products, the PBM may pay 13%-15% off of the AWP, plus a dispensing fee at around $2.50. This means that the general pharmacy mark-up may be 12% above the pharmacy acquisition cost, but in some cases the price demanded by the PBM may be so low as to not cover the cost to the pharmacy.[98]

Distributions in the U.S. for some generics are similar to brand name but with perhaps a slightly reduced dispensing fee in order to encourage the purchase of generics. For approximately 75% of the generic markets, PBM's pay a maximum allowable cost, (MAC). PBM's base this figure on

the cheapest equivalent generic available on the market and are generally 50% to 60% below the AWP.

PBM's also receive an additional discount in the form of a manufacture's rebate. This is a direct transaction negotiated between the PBM and the pharmaceutical company, but ultimately lowers the total cost of the drugs purchased by the PBM in the distribution chain outlined above. There are many form such rebates could take, but one of the simplest would be if a PBM reported the number of prescriptions for a given drug and received a set payment for each prescription filled. In return a PBM may exclude competing similar products for treatment of the same illness from its formulary, or charge higher co-payments for these products. Either the PBM or the pharmacy may also exert pressure on prescribers to prescribe formulary drugs.[99]

These rebates are private, highly confidential agreements between PBMs and drug companies. Estimation of these rebates is therefore very difficult. The Clinton report states that the Federal Employees Health Benefits Program estimates that manufacturers rebates offered a 5%-6% reduction in the total cost of drugs to them, (and therefore rebates were presumably slightly higher assuming PBMs didn't pass on the full rebate); But industry sources are reported as saying rebates can offer a reduction in the final price by up to 35%. The PBMs are required to pass on most of the rebates to the insurer or self-insured employer that they are in contract with. Industry sources are reported as stating that 70%-90% of the rebate is passed on. PBMs may receive non-cash rebates as well, for example a PBM may receive support for the development of disease management system and research activities. PBMs may receive cash rewards that are not associated with a particular drug product; for example PBMs may receive rewards in exchange for agreements about the content in communication with physicians. These benefits do not have to be passed on and some analysts believe these rewards may exceed the value of the other cash rebates.

Pricing for Favoured Private Purchasers such as Health Maintenance Organizations (HMOs) and Hospitals:

Some institutions such as hospitals or clinics that operate their own outpatient clinics, purchase their products directly from the drug manufacturers without a wholesaler or a PBM. Such purchasers are believed to represent 14% of the market. Not only do they not have to pay wholesale mark-ups, they may be able to command better prices than those attained by the wholesaler from the manufacturers. Because they purchase products directly from the manufacturers, it appears that rebates do not play as large of a part of their purchasing schemes as they do for those who use PBMs. Information on rebates and pricing is again, confidential and often unavailable. The sources used by the Clinton report estimated that these direct purchasers can attain products at approximately 33% off of the AWP price; but it also referenced evidence that some purchasers attain even lower prices.

Pricing for Federal Facilities and Agencies:

The Veterans Health Care Act of 1992 authorizes the Veterans Affairs Secretary to negotiate prices with drug manufacturers for products that are needed by the Department of Veteran Affairs (VA), as well as the Department of Defense, the Public Health Services (including Indian Health Service) and the Coast Guard.[100] These federal purchases represent less than 2% of the market.

The VA negotiates the Federal Supply Schedule prices with manufacturers using multi-year contracts and is believed to be one of the largest purchasing cooperatives doing so. Manufacturers must supply the VA with information on prices, discounts and rebates for non-federal customers along with descriptions of the terms and condition involved. Generally the FSS price can not exceed the best price offered by the drug company to non-federal purchaser's under similar terms and conditions.[101] The Clinton report cites evidence that the FSS price is generally 60% below the general ex-factory price or 52% below the AWP.

This low price represents the VA's ability to effectively negotiate low prices and vested interests the manufacturers may have in their drugs being available to federal facilities and agencies. For example, manufacturers are required to have drugs available to covered entities at FSS prices as a condition of eligibility for Medicaid reimbursement and there is a strategic interest in having their drugs used in VA hospitals that train large numbers of physicians. The VA started making prices available online in November 1997.

Pricing for the Medicaid Programs:

Medicaid pays pharmacies a fixed dispensing fee (approximately $2.50), plus a fixed cost. For brand name products without competition the fixed

reimbursement costs attempts to reflect the actual acquisition cost of the products to the pharmacy. For multiple source drugs, the pharmacy is paid a Maximum Allowable Cost, (MAC). The MACs are published every six months and are updated to reflect 150% of the lowest published price for any equivalent product.[102]

Under the Omnibus Budget Reconciliation Act of 1990, drug manufacturers are required to offer Medicaid a rebate. The rebate for single source or multi-source innovator drugs must be the difference between the average ex-factory price to the wholesalers and the manufacturers best ex-factory price, (not including the prices offered to federal purchasers). There is the additional requirement that the rebate on these products must be at least 15.1%. The Clinton report states that the average rebate is about 21%, but it uses the range 15.1% to 30% for illustrating examples. For non-innovator multiple source product the rebate is simply 11% of the average ex-factory price.

Products in the U.S. are generally regarded as high and this is consistent with the findings of this analysis. If prices were regarded without the incorporation of the generic products available on the market, prices in the U.S. were even higher.

Of the 114 drug products identified as top-selling non-patented single source in Canada, 79 products could be matched with bioequivalent products in the Red Book, 70 of which had the same brand name. Of the tablets and capsules used for the analysis, 53 of the 65 were found in the Red Book and 24 were offered by more than one competing firm. Some drug products had up to 19 firms offering bioequivalent products. All 53 tablets and capsules were also found in the FSS list of reimbursable products, 15 of which were offered by up to 9 firms competing in the same bioequivalent market. The FSS list generally contained the same brand name products as the Red Book, and a subset of the same generics. Both lists contained products of varying package sizes. Some products that were heavily genericized would have numerous products coming in moderate package sizes as well as firms offering an extremely large pack, (ex. 1000 tablets), with a relatively low unit cost and/or an extremely small package, (ex. 10 tablets) with an extremely high unit cost. Also, for heavily genericized products in both the Red Book and the FSS, the prices varied greatly even when package sizes did not, (sometimes in excess of 100%).

Most products were available in a large variety of strengths. This had been a problem for the European countries where comparable products with the same active ingredients and dosage form could not be matched because the product was only available at another strength. Frequently a divisible tablets or capsules would only be available at double or half of the strength found in Canada. Of the 40 products not found in the U.S. Red Book only 7 could not be matched because they were only offered at a different strength.

C2 Methodology For Backing Out Wholesale and Pharmacy Mark-ups to Ex-factory Levels.

UK

The price used was the NHS listed price in the Monthly Index of Medical Specialties. This price represents the price at which the National Health Services reimburses the pharmacies for the brand name prescription drug products dispensed to patients.[103]

There is a regulated wholesale mark-up charged by the pharmacies of 12.5% of the NHS price.[104] The UK ex-factory price was therefore estimated by multiplying the NHS list price by 0.875. (This represents (1 - 0.125)).

Italy

The price used was the retail price listed in the L'Informatore Farmaceutico. From this the VAT was removed by dividing the price by the listed price by 1.10.

The combined wholesale mark-up (6.65%), and pharmacy mark-up (26.7%) are on the retail price excluding tax is 33%. This translates to a 50% combined mark-up on the negotiated ex-factory price. Therefore dividing the retail price (excluding tax) by 1.50 can derive the ex-factory price. (This is mathematically equivalent to multiplying the retail price by 0.667)

France

The price used was the price at which the pharmacies purchase products available in the Sempex. Wholesale distribution was assumed and a wholesale mark-up of 10.74% of the ex-factory price or 9.7% of the pharmacy purchase price was used. Therefore, the ex-factory price was estimated

by dividing the pharmacy purchase price by 1.1074.[105]

Sweden

The price used was the reimbursable retail pharmacy-selling price listed in Prislista. The pharmacy mark-ups backed out where those described at the beginning of the Prislista publication. These mark-ups and the calculation to remove them are included in Table C.2.

Table C-2 Pharmacy Mark-ups and Removal From Prislista

Wholesale Price (WP), in Price Range:	Pharmacy Mark-up	Resulting Range in Retail Price (RP)	Calculation Used to Get Wholesale Price
WP ≤ 34,25	(WP x 1.30) + 18.00	RP ≤ 62,525	(RP – 18.00) / 1.30
34,25 ≤ WP ≤75,00	(WP x 1.18) + 22.20	62.615 ≤ RP ≤ 110.70	(RP – 22.20) / 1.18
75,00 ≤ WP ≤ 300,00	(WP x 1.08) + 29.70	110.70 ≤ RP ≤ 353.70	(RP – 29.70) / 1.08
300,00 ≤ WP ≤ 2.00,00	(WP x 1.07) + 32.70	353.70 ≤ RP ≤ 2172.70	(RP – 32.70) / 1.07
2.000,00 ≤ WP	(WP x 1.01) + 152.70	2172.70 ≤ RP	(RP – 152.7) / 1.01

Wholesale distribution was assumed for all products and a wholesale mark-up of 4.2% was used. Once the wholesale price was calculated, it was divided by 1.042.

Switzerland

The price used was the pharmacy-purchasing price listed in Medwin. The wholesale mark-ups backed out where those set in 1996 and used until 2001. These mark-ups used were described in later in this section ("Background on the Seven Foreign Countries"), and the calculation to remove them are included in Table C.3.

Table C-3 Calculation for Removing Wholesale Mark-ups from the Pharmacy Purchasing Price in Switzerland

Wholesale Price (WP) at Which Pharmacies Purchase	Calculation to Remove Wholesale Mark-up	
	Multiply By	Subtract
WP ≤ 12.49	0.85	-
12.49 < WP ≤13.74	-	1.87
13.74 < WP ≤ 64.74	0.8675	-
64.74 < WP ≤ 78.49	-	8.90
78.49 < WP ≤ 137.99	0.88	-
137.99 < WP ≤ 167.64	-	16.56
167.64 < WP ≤ 218.99	0.89	-
218.99 < WP ≤ 271.19	-	24.09
271.19 < WP ≤ 307.99	0.895	-
307.99 < WP ≤ 392.19	-	32.34
392.19 < WP ≤ 404.99	0.9	-
404.99 < WP ≤ 538.39	-	40.50
WP > 538.39	-	51.00

Germany

The price used was the pharmacy retail price listed in Rote Liste. The value-added tax of 16% was removed by dividing the available price by 1.16.[106] The pharmacy and wholesale mark-ups are regulated and found in Table C.4 and Table C.5.[107]

Table C-4 Regulated Pharmacy Mark-ups in Germany

Original Range in Wholesale Price (WP) in DM	Pharmacy Mark-up	Resulting Range in Retail Price (RP) in DM	Calculation Used to Get Wholesale Price
WP ≤ 2.40	68%	RP ≤ 4.03	RP / 1.68
2.41≤ WP ≤ 2.63	DM 1.63	4.04 ≤ RP ≤ 4.26	RP – 1.63
2.64 ≤ WP ≤ 7.60	62%	4.27 ≤ RP ≤ 12.31	RP / 1.62
7.61 ≤ WP ≤ 8.26	DM 4.71	12.32 ≤ RP ≤ 12.97	RP – 4.71
8.27 ≤ WP ≤ 14.28	57%	12.98 ≤ RP ≤ 22.42	RP / 1.57
14.29 ≤ WP ≤ 16.96	DM 8.14	22.43 ≤ RP ≤ 25.10	RP – 8.14
16.97 ≤ WP ≤ 23.75	48%	25.11 ≤ RP ≤ 35.15	RP / 1.48
23.76 ≤ WP ≤ 26.51	DM 11.4	35.16 ≤ RP ≤ 37.91	RP – 11.40
26.52 ≤ WP ≤ 38.00	43%	37.92 ≤ RP ≤ 54.34	RP / 1.43
38.01 ≤ WP ≤ 44.16	DM 16.34	54.35 ≤ RP ≤ 60.50	RP – 16.34
44.17 ≤ WP ≤ 57.00	37%	60.51 ≤ RP ≤ 78.09	RP / 1.37
57.01 ≤ WP ≤ 70.30	DM 21.09	78.10 ≤ RP ≤ 91.39	RP – 21.09
70.31 ≤ WP ≤ 1,063.81	30%	91.40 ≤ RP ≤ 1,382.95	RP / 1.30
1,063.82 ≤ WP	8.263% plus DM 231.25	1,382.96 ≤ RP	(RP – 231.25)/1.08263

Table C-5 Regulated Wholesale Mark-ups in Germany

Original Range in Ex-factory Price (EXP) in DM	Wholesale Mark-up	Resulting Range in Wholesale Price (WP) in DM	Calculation Used to Get Ex-factory Price
EXP ≤ 1.65	21%	WP ≤ 2.00	WP / 1.21
1.66 ≤ EXP ≤ 17.3	DM 0.35	2.01 ≤ WP ≤ 2.08	WP – 0.35
1.74 ≤ EXP ≤ 3.33	20%	2.09 ≤ WP ≤ 4.00	WP / 1.20
3.34 ≤ EXP ≤ 3.42	DM 0.67	4.01 ≤ WP ≤ 4.09	WP – 0.67
3.43 ≤ EXP ≤ 5.02	19.5%	4.10 ≤ WP ≤ 6.00	WP / 1.195
5.03 ≤ EXP ≤ 5.15	DM 0.98	6.01 ≤ WP ≤ 6.13	WP – 0.98
5.16 ≤ EXP ≤ 7.14	19%	6.14 ≤ WP ≤ 8.50	WP / 1.19
7.15 ≤ EXP ≤ 7.34	DM 1.36	8.51 ≤ WP ≤ 8.70	WP – 1.36
7.35 ≤ EXP ≤ 11.81	18.5%	8.71 ≤ WP ≤ 14.00	WP / 1.185
11.82 ≤ EXP ≤ 12.14	DM 2.19	14.01 ≤ WP ≤ 14.33	WP – 2.19
12.15 ≤ EXP ≤ 17.80	18%	14.34 ≤ WP ≤ 21.00	WP / 1.18
17.81 ≤ EXP ≤ 21.36	DM 3.20	21.01 ≤ WP ≤ 24.56	WP – 3.20
21.37 ≤ EXP ≤ 86.96	15%	24.57 ≤ WP ≤ 100.00	WP / 1.15
86.97 ≤ EXP ≤ 108.71	DM 13.04	100.01 ≤ WP ≤ 121.75	WP – 13.04
108.72 ≤ EXP ≤ 1,339.28	12%	121.75 ≤ WP ≤ 1,500.00	WP / 1.12
1,339.29 ≤ EXP	3% plus DM 120.53	1,500.00 ≤ WP	(WP – 120.53)/1.03

The United States of America

The FSS price represents an ex-factory price and no further calculations are required. The Red Book list price is called the "Average Wholesale Price", (AWP). This is not the actual wholesale, but a wholesale price suggested by the manufacturerof the product. Some products, (usually brand name products,) also have a "Direct Price" (DP), provided. If a DP is provided, it is the ex-factory price offered to those pharmacies that purchase directly from the manufacture. If this price was available it was used as an ex-factory price. Otherwise the ex-factory price is estimated as 80% off the AWP and so the AWP was multiplied by 0.80. This represents a 25% mark-up on the ex-factory price to the AWP.

D. Appendix D: Product Information and Product List

The analysis was done on bioequivalent products, defined as products sharing the same combination of active ingredient(s), dosage form, route of administration and strength. As a result, there was some distinct products in the analysis which were similar drugs but at different strengths. They are summarized in Table D-1.

Table D-1 Summary of Products with Common Active Ingredient(s), Dosage Form and Route of Administration Combination, but Were Distinguished as Different Products Based on Strength

Number of Distinct Strength Levels	Number of Active Ingredient(s), Dosage Form and Route of Administration Combinations	Distinct Products in the Analysis
Found in One Strength	24	24
Found in Two Strengths	11	22
Found in Three Strengths	2	6
Found in Four Strengths	1	4
Total	**38** Active Ingredient(s), Dosage Form and Route of Administration Combinations	**56** Bioequivalent Products in Analysis

Table D-2 Top-Selling Non-Patented Single Source Drug Products

Top-Selling Non-Patented Single Source Drug Products That Were Tablets Or Capsules Used In The Analysis			
DIN	Brand	Manufacture	Active Ingredient(s)
582352	Accutane cap 40MG†	Hoffman-LaRoche Ltd.	Isotretinoin
2221861	Anandron – tab 50MG	Hoechst-Roussel Canada Inc.	Nilutamide
782327	Andriol cap 40MG	Organon Canada Ltd.	Testosterone Undecanoate
220442	Bonamine tab 25MG (chewable)	Pfizer Canada Inc.	Meclizine Dihydrochloride
1958100	Cardura-1*	Astra Pharma Inc.	Doxazosin Mesylate
1958097	Cardura –2*	Astra Pharma Inc.	Doxazosin Mesylate
1958119	Cardura –4*	Astra Pharma Inc.	Doxazosin Mesylate
2036282	Cordarone tab 200MG*	Wyeth-Ayerst Canada Inc.	Amiodarone Hydrochloride
1918311	Coumadin tab 1MG†	Du Pont Pharma	Warfarin Sodium
1918346	Coumadin tab 2.5MG†	Du Pont Pharma	Warfarin Sodium
1918338	Coumadin tab 2MG†	Du Pont Pharma	Warfarin Sodium
2007959	Coumadin tab 4MG	Du Pont Pharma	Warfarin Sodium
2123274	Coversyl - 2MG tab	Servier Canada Inc.	Perindopril Erbumine
2123282	Coversyl - 4MG tab	Servier Canada Inc.	Perindopril Erbumine
2018160	Cyclomen cap 200MG †	Sanofi Canada Inc.	Danazol
632600	Cytotec tab 200MCG†	Searle Canada Inc.	Misoprostol
813966	Cytotec(Misoprostol) tab 100MCG	Searle Canada Inc.	Misoprostol
2182866	Dalacin C – cap 300MG *	Pharmacia & Upjohn	Clindamycin Hydrochloride
30570	Dalacin C cap 150 MG* †	Pharmacia & Upjohn	Clindamycin Hydrochloride
1924516	Dexdrine tab 5MG	SmithKline Beecham Pharma Inc.	Dextroamphetamine Sulfate
1997629	Didronel tab 200MG	Proctor and Gamble Pharmaceuticals Canada Inc.	Disodium Etidronate
22780	Dilantin cap 100MG†	Parke-Davis, Division Warner-Lambert Canada Inc.	PhenyToin Sodium

Top-Selling Non-Patented Single Source Drug Products That Were Tablets Or Capsules Used In The Analysis			
DIN	Brand	Manufacture	Active Ingredient(s)
125121	Dilaudid tab 4MG*	Knoll Pharma Inc.	Hydromorphone HCL
786543	Dilaudid tab 8MG	Knoll Pharma Inc.	Hydromorphone HCL
2221799	Frisium tab 10MG*	Hoechst-Roussel Canada Inc.	Clobazam
465283	Hydrea cap 500MG†	Squibb	Hydroxyurea
731269	Lanoxin tab 0.0625MG	Glaxo Wellcome	Digoxin
35319	Lanoxin tab 0.125MG†	Glaxo Wellcome	Digoxin
4685	Lanoxin tab 0.25MG	Glaxo Wellcome	Digoxin
4626	Leukeran tab 2MG	Glaxo Wellcome	Chlorambucil
2170132	Loxapac tab - 25 MG*†	Wyeth-Ayerst Canada Inc.	Loxapine Succinate
2015439	MS Contin SRT 15MG†	Purdue Frederick, Inc.	Morphine Sulfate
2014327	MS Contin SRT 200MG†	Purdue Frederick, Inc.	Morphine Sulfate
2022389	Neptazane tab 50MG	Lederle Cyanamid Canada Inc.	Methazolamide
2084279	Neurontin cap 300MG	Parke-Davis, Division Warner-Lambert Canada Inc.	Gabapentin
2084287	Neurontin cap 400MG	Parke-Davis, Division Warner-Lambert Canada Inc.	Gabapentin
633836	Nizoral tab 200MG*	Janssen Pharmaceutica Inc.	Ketoconazole
582247	Pondocillin tab 500MG	Leo Pharma Inc.	Pivampicillin
2043394	Premarin tab 0.3MG	Wyeth-Ayerst Canada Inc.	Conjugated Estrogenic Hormones
386464	Prolopa cap 100-25	Hoffman-LaRoche Ltd.	Benserazide HCL and Levodopa
632775	Ritalin-SR TAB 20MG	Novartis Pharmaceuticals Canada Inc.	Methylphenidate Hydrochloride
603708	Rythmol tab 150MG†	Knoll Pharma Inc.	Propafenone HCL
603716	Rythmol tab 300MG†	Knoll Pharma Inc.	Propafenone HCL
2065819	Sabril tab 500MG	Marion Merrell Dow Canada	Vigabatrin
846341	Sibelium cap 5MG†	Parmascience Inc.	Flunarizine Hydrochloride
2172089	Synthroid - TAB 0.075MG	Knoll Pharma Inc.	Levothyroxine Sodium
2172119	Synthroid - TAB 0.125MG	Knoll Pharma Inc.	Levothyroxine Sodium
2137984	Talwin – tab 50MG	Sanofi Canada Inc.	Pentazocine Hydrochloride
773611	Tegretol CR tab 200MG*†	Novartis Pharmaceuticals Canada Inc.	Carbamazepine
755583	Tegretol CR tab 400MG*†	Novartis Pharmaceuticals Canada Inc.	Carbamazepine
2049988	Tenoretic 100/25MG tab	Zeneca Pharma	Atenolol and Chlorthalidone
2049961	Tenoretic 50/25MG tab	Zeneca Pharma	Atenolol and Chlorthalidone
2106280	Trandate 200MG tablets	Roberts Pharmaceutical of Canada Inc.	Labetalol Hydrochloride
2014165	Uniphyl SRT 400MG	Purdue Frederick, Inc.	Theophylline
2014181	Uniphyl SRT 600MG	Purdue Frederick, Inc.	Theophylline
728179	Urispas tab 200MG†	Parmascience Inc.	Flavoxate Hydrochloride

* No longer Single Source in the Ontario Drug Benefit Formulary/Comparative Drug Index No.37, effective March 7th, 2001. (Sibelium, DIN: 846341 is single source in formulary, but was multiple source on the April 16th , 1999, update A)

† Were in previous 1996 Top-Selling Non-Patented Single Source Drug Product Study.

E. Appendix E: In Depth Review of Four Non-Patented Single Source Drugs.

Executive Summary

- This work was carried out under a Memorandum of Understanding (MOU) between the Board and the Minister of Health. Under the direction of the F/P/T Pharmaceutical Issues Committee Working Group on Drug Prices (WGDP), four non-patented drug products were identified as warranting a price analysis by the PMRPB.

- The international price comparison of top selling non-patented single source (NPSS) drugs found that in 1998/99 Canadian prices were, on average, 28% above the median international price of seven other countries (France, Germany, Italy, Sweden, Switzerland, UK, and U.S.). Had NPSS medicines been priced at median international levels, spending by six provincial drug plans (BC, AB, SK, MN, ON, NS) would have been approximately $60 million or 20% less than the $300 million these plans spent on NPSS drugs in 1999/00.

- The Patented Medicine Prices Review Board's (PMPRB) Excessive Price Guidelines served as the basis of analysis. This study is a case study of four NPSS drugs chosen for analysis by members of the WGDP. Members of the WGDP identified warfarin sodium (Coumadin), isotretinoin (Accutane), progesterone (Prometrium), and digoxin (Lanoxin) based on either recent concern relating to price changes or as a result of ongoing concerns relating to the budget impact and cost of the products to the drug plans.

- During the introductory period, the price of two strengths of warfarin (3mg and 5mg), the price of progesterone and two strengths of digoxin (0.25 mg and 0.0625 mg) appeared to exceed the PMPRB's Excessive Price Guidelines. By 2000, the 5mg strength of warfarin was priced within the Guidelines. The remainder of the drugs continued to exceed the Guidelines and most notably, the price of all strengths of digoxin exceeded the Guidelines by approximately 100%.

- Overall, for the products that had a price in excess of the Guidelines, the prices exceeded the maximum non-excessive (MNE) by a range of 0.4% to 238.7% in the introductory period and 12.9% to 215.9% in 2000. Had the prices of these products been limited to the MNE price, the total annual savings to the six provincial drug plans would have been approximately $7.4 million.

E1 Purpose

The purpose of this report is to provide a price assessment of four non-patented single source products identified by F/P/T Pharmaceutical Issues Committee Working Group on Drug Prices (WGDP). The review was conducted by assessing the prices of the identified products based on the Patented Medicine Prices Review Board's (PMPRB's) Excessive Price Guidelines (the Guidelines). In 2000/01 warfarin sodium (Coumadin), isotretinoin (Accutane), progesterone (Prometrium), and digoxin (Lanoxin) were identified by members of the WGDP based on either recent concern relating to price changes or as a result of ongoing concerns relating to the budget impact and cost of the products to the drug plan.

E2 Background

At their June 17 and 18, 1999 meeting, F/P/T Deputy Ministers of Health approved a recommendation that the federal Minister of Health, in collaboration with his provincial/territorial counterparts, request the PMPRB to undertake analytical work to support drug benefit plans to better understand and manage public spending on medicines and to provide greater transparency to the public on the prices and cost drivers that face provincial drug plans.

In response to this request, the PMPRB and Health Canada entered into a Memorandum of Understanding (MOU). The MOU specifies that the PMPRB will conduct the following type of analysis:

1. Annual price and expenditure trend analysis
2. Annual cost driver analysis
3. An annual inter-provincial drug price comparison
4. Annual comparisons of Canadian and foreign prices of NPSS drugs
5. Reviewing and reporting in detail of up to five (5) non-patented drugs identified as warranting a detailed review
6. Annual overview report.

This report is an informal review of four non-patented drugs identified by members of the F/P/T Working Group on Drug Prices as warranting a detailed review by PMPRB staff.

E3 Non-patented Single Source Products - In General

In 1999, manufacturers' sales of non-patented drugs were $3.6 billion, growing at an annual rate of approximately 7% over the decade. In 1999, non-patented drugs represented 39% of all manufacturers' sales in Canada. Based on provincial drug plan data for six jurisdictions[108], British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia, non-patented single source (NPSS) drugs represented, on average, 13% of all expenditures submitted to the drug plans.

Based on an analysis of top NPSS drug products in 1998/99, Canadian prices had been found to be, on average, 28% above median foreign prices in countries used by the PMPRB to review prices of patented medicines. In contrast, in 2000, Canadian prices for patented medicines were 8% below median foreign prices.

Canadian prices for NPSS drugs are among the highest priced countries, second only to the U.S. In 1999 and 2000 Canada ranked as the third lowest priced country after Italy and France for patented drug products. Had all non-patented single source medicines been priced at the median international levels, spending by the six provincial drug plans would have been approximately $60 million less than the $317.7 million these plans spent on NPSS drug products in 1999/00. This represents about two percent of the $2.5 billion spent on drugs by the six provincial drug plans in that year.

E4 Considerations

The non-patented drugs identified by the F/P/T WGDP were selected on the basis that they are not or will not come under the jurisdiction of the PMPRB. As part of its statutory mandate, the PMPRB is to ensure that the prices charged by manufacturers of patented medicines in Canada are not excessive. The review by PMPRB staff of the non-patented singe source drugs contained in this report was conducted pursuant to the terms of the MOU and section 90 of the

Patent Act. The report should not be relied upon for any purpose other than its stated purpose as defined in the MOU and is considered non binding upon the manufacturers and the Board.

Furthermore, the drugs referred to in this report and the various comparators used were selected for the purpose of conducting an analysis and preparing a report on the price assessment of the said non-patented single source drugs as per the terms of the MOU. Any reference to a drug in the report is not to be interpreted as an endorsement, recommendation or approval of any such drug nor is it intended to be relied upon as a substitute for seeking appropriate advice from a duly qualified health care practitioner.

Under the Patent Act, patentees are required to report all patented drugs to the PMPRB and to file detailed information of the prices and sales of those drugs every six months. Those filings ordinarily form the basis of the price review conducted by Board Staff and remedial action when necessary.

In the case of the non-patented drugs identified by the F/P/T WGDP, the PMPRB review was based on price information available from public sources, including provincial formularies and foreign formularies. The manufacturers involved have not been consulted nor provided an opportunity to comment.

It should also be noted that the Human Drug Advisory Panel (HDAP)[109], was not consulted in the review of the non-patented drugs included in this report.

The report has not been reviewed or approved by the members of the Board and should not be seen as binding the PMPRB in any way.

E5 Methodology

PMPRB's Excessive Price Guidelines[110]

The Patent Act, s.85(1), stipulates those factors that the Board must take into consideration when determining whether a medicine is being or has been sold at an excessive price. These factors are:

- The prices at which the medicine has been sold in the relevant market
- The prices at which other medicines in the same therapeutic class have been sold in the relevant market
- The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada
- Changes in the Consumer Price Index (CPI)
- Such other factors as may be specified in the regulations

Under the Guidelines, price is measured at the Drug Identification Number (DIN) level and is expressed as the price per unit in which that DIN is sold.

The Guidelines differentiate between "new" and "existing" drug products. Drug products are considered new in the year during which they are introduced. New drug products are divided into three categories for the purpose of applying the Guidelines: Category 1 drugs are line extensions of an existing drug product, category 2 represent drugs that are a breakthrough or substantial improvement over an existing product, and category 3 products offer moderate, little or no improvement over existing drug products.

The introductory price of a new drug product is determined by calculating the average price of the DIN during the benchmark period. The benchmark period is determined from the date of first sale to the end of the six-month regulatory reporting period (June 30 or Dec 31), provided the period is greater than one month.

The following is a list of price tests under the Guidelines:

The ***Reasonable Relationship*** **(RR)** Test considers the association between the strength and price of the same medicines in the same or comparable dosage forms. This test is usually the primary test for drugs classified as category 1.

The ***Therapeutic Class Comparison*** **(TCC)** Test compares the price of the DIN under review

with the price of DINs that are clinically equivalent. This test is usually the primary test used for drugs classified as category 3.

The *International Price Comparison (IPC)* Test compares the average transaction price of the DIN under review with the publicly available ex-factory prices of the same medicines sold in countries listed in the Regulations[111]. An international median price comparison is usually the primary test used for category 2 drugs.

The price of an **existing** drug is presumed to be excessive if it exceeds the benchmark price of the DIN adjusted for the cumulative change in the CPI from the benchmark period to the pricing period under review. In addition, the price increase in any year can not exceed 1.5 times the change in the annual CPI.

In addition, the price of a new or existing drug product, regardless of its category, is presumed to be excessive if it exceeds the prices of the same medicine sold in all countries listed in the Regulations.

E6 Application of Guidelines to the Four NPSS Drugs

As outlined in section 2, the test applicable to the introductory price of a **new** DIN is dependent upon the category of the drug. It was not practical to conduct an explicit scientific review for the purpose of categorizing the drugs included in this study.

The tests under the PMPRB guidelines were applied based on the principle of feasibility and appropriateness. Generally speaking, the RR test was used as the primary test line extension drugs introduced after 1995. A TCC test was conducted if it was feasible and appropriate to do so. If not, the median international price test was used.

In addition, the price of a new or existing drug product was presumed to be excessive if it exceeded the prices of the same medicine sold in all countries listed in the Regulations[112], i.e. the price could not exceed the highest IPC test.[113]

As the review and application of the Guidelines was conducted retrospectively, i.e. these were not "new" drugs the year 1995 was used as the base year for establishment of the benchmark price. The year 1995 was chosen as the base year for the retrospective analysis because it provided a sufficient length for the review while ensuring accuracy and accessibility of national and international pricing information for the drugs included in the study. The year of introduction for drugs introduced subsequent to 1995 became the benchmark period for those drugs.

In the case of progesterone (Prometrium), the year of introduction onto the Canadian market was December 31, 1995; the price in 1996 was used to establish the benchmark price.

The Ontario Drug Benefit (ODB) price in December 1995 was used to as the Canadian average transaction price (ATP), or the manufacturers' ex-factory gate price, in that year.

In the final year of analysis, 2000/01, prices and utilization trends submitted by the six provincial drug plans were used to estimate the "excess" revenue, i.e. the difference between the MNE, and the provincial manufacturer's unit price, multiplied by quantity of the drug product[114].

E6.1 Warfarin Sodium (Coumadin)

The Medicine

Warfarin is an anticoagulant agent used for prophylaxis and treatment of venous thrombosis and its extension, prophylaxis and treatment of pulmonary embolism, prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement, and as an adjunct in the treatment of coronary occlusion. Warfarin sodium also is used to reduce the risk of death, reinfarction, and thromboembolic events such as stroke or systemic embolization following myocardial infarction.

Warfarin is marketed in Canada by DuPont Pharma in multiple doses, 1 mg, 2mg, 2.5mg, 3mg, 4mg, 5mg and 10mg tablets. The drug was first offered for sale in Canada in 1957.

Patent Status

The best information available is that warfarin was not a patented drug during the time period under study. Warfarin is an old molecule first patented in the U.S. in 1947.

The Results

There are seven strengths of warfarin currently available on the Canadian market. In 1957, the 1, 5, and 10 mg strengths were introduced in Canada; the 2.5 and 4 mg strengths came on the market in 1992, the 2 mg strength was first marketed in 1993 and most recently, the 3 mg strength was introduced in 1999.

Concern regarding inter-provincial price differences for Warfarin prompted members of the F/P/T WGDP to request an examination of the price of this non-patented product. Table E-1 and Table E-2 provide a summary of the application of the Guidelines for warfarin and a summary of provincial prices.

Table E-1 Warfarin Analysis

Application of Guidelines for Warfarin, Sold by DuPont Pharma 1995-2000

Year	1mg/tab (DIN 01918311)		2mg/tab (DIN 01918338)		2.5mg/tab (DIN 01918346)		3mg/tab (DIN 02240205)		4mg/tab (DIN 02007959)		5mg/tab (DIN 01918354)		10mg/tab [115] (DIN 01918362)	
	MNE	ATP	MNE	ATP	MNE	ATP	MNE	ATP	MNE	ATP	MNE	ATP	MNE	ATP
1995	0.2829	0.2829	0.2992	0.2992	0.2395	0.2395	-	-	0.3709	0.3709	***0.2396***	***0.2400***	0.4306	0.4306
1996	0.2886	0.2829	0.3052	0.2992	0.2443	0.2395	-	-	0.3783	0.3709	0.2444	0.2400	0.4392	0.4306
1997	0.2905	0.2829	0.3073	0.2992	0.2460	0.2395	-	-	0.3809	0.3709	0.2465	0.2400	0.4422	0.4306
1998	0.2905	0.2829	0.3073	0.2992	0.2460	0.2395	-	-	0.3809	0.3709	0.2465	0.2400	0.4422	0.4306
1999	0.2903	0.2829	0.3070	0.2992	0.2457	0.2395	***0.3610***	***0.4186***	0.3805	0.3709	0.2462	0.2400	0.4418	0.4306
2000*	0.2945	0.2829	0.3115	0.2992	0.2493	0.2395	***0.3707***	***0.4186***	0.3861	0.3709	0.2498	0.2400	0.4483	0.4306

**2000 - IPC includes the* Federal Supply Schedule (FSS) *price in the U.S. price*

The Canadian price was estimated based on the Ontario Drug Benefit (ODB) Plan price and set the average transaction price (ATP) in December 1995. No comparators were identified; therefore, the median IPC was the primary test for all strengths on the market in 1995. For the 3 mg strength, the RR test was used in the introductory period in 1999.[116]

The introductory prices of warfarin 1 mg, 2 mg, 2.5 mg, 4 mg and 10 mg tablets were determined to be within the Guidelines. These strengths passed the median IPC test (which was the primary test used). After the introductory period (between 1996 and 2000), these strengths continued to be within the Guidelines, i.e. the rate of price increase did not exceed the CPI and in all years the Canadian prices were below the highest IPC[117].

In the introductory period, warfarin 5mg tablet failed the median IPC test by a small margin, however in the following year, 1996 and in subsequent years, the price of this strength was within the Guidelines. Warfarin 3mg/tablet was introduced in 1999[118]; as it was a new strength

of an existing drug, it was treated as a line extension and a RR test was conducted; warfarin 3 mg failed the RR test, but passed the highest IPC test.

As a result, the price of the 3 mg strength exceeded the Guidelines by approximately 15% at introduction in 1999 and in 2000.

Inter-provincial Analysis Results[119]

Inter-provincial price differences were identified by WGDP members as the primary price issue for this drug. Table E-2 is a summary of price information provided by participating jurisdictions for the purpose of this analysis. The prices presented for Alberta, Saskatchewan, Manitoba and Ontario are manufacturers list prices submitted to the drug plans; the prices presented for the other two drug plans represent a maximum allowable claimed price which may include a distribution margin, thus some caution should be used in interpreting the inter-provincial unit prices presented below.

Based on the most current price information available from the drug plans, the price in Ontario is the lowest among the six jurisdictions by approximately 35%. In all the six jurisdictions, the public plan prices declined in 2001 as compared to 2000, however, the decline on the ODB plan was consistently the highest for all the DINs.[120] The recent availability of a generic alternative may explain this trend.

In 2000, there did not appear to be any significant price differences between the six jurisdictions. In 2001 prices on the ODB plan were the lowest, however, significant price variations were not found among the other jurisdictions and for all the jurisdictions the prices appear to be within, or relatively close to within, the Guidelines.

Table E-2[121]

Current Provincial Unit Prices for Warfarin (2001)								
Jurisdiction	Date	DIN: 1918311	DIN: 1918338	DIN: 1918346	DIN: 2240205	DIN: 2007959	DIN: 1918354	DIN: 1918362
British Columbia	Unit Cost March 2001	0.3080	0.3250	0.2690	0.4040	0.4060	0.2660	0.4920
Alberta	Unit Cost April 2001	0.3041	0.3216	0.2575	0.3987	0.3987	0.2580	0.4629
Saskatchewan	Unit Cost July 2001	0.2829	0.2992	0.2395	0.3709	0.3709	0.2400	0.4306
Manitoba	Unit Cost July 2001	0.2829	0.2992	0.2395	0.3709	0.3709	0.2400	0.4306
Ontario	Unit Cost June 2001	0.1980	0.2094	0.1676	n/a	0.2956	0.1680	0.3014
Nova Scotia	Unit Cost April 2001	0.3067	0.3259	0.2764	0.4129	0.4116	0.2721	0.4300

Conclusion:

All strengths, with the exception of the 3mg tablet would be considered within Guidelines in 2000 based on the 2000 ODB price. The 5 mg strength failed the primary price test (median IPC) in the introductory period, 1995, but was within the Guidelines by 1996. Between 1996 and 2000, all the strengths, other than the 3mg strength, were priced within the CPI adjusted maximum established price. The 3mg strength failed the initial price review by 16%, and exceeded the Guidelines by 12.9% in 2000.

E6.2 Isotretinoin (Accutane)

The Medicine

Isotretinoin is a nodular inflammatory and conglolate acne therapy. Isotretinoin is used in the treatment of severe recalcitrant cystic acne. Isotretinoin has been used in the treatment of cutaneous disorders of keratinization that are resistant to treatment with other agents. It has been used, alone and in combination, with a psoralen and UVA light in the treatment of psoriasis. It also has been used in a limited number of patients in the prevention, treatment and adjunctive treatment of various cutaneous and extracutaneous malignant neoplasms.

Isotretinoin is marketed in Canada by Hoffman-La Roche in multiple doses, 10 mg/cap and 40mg/cap. The drug was first offered for sale in Canada in 1983.

Patent Status

Isotretinoin was first patented in 1972; the patent holder was Roche of Switzerland. Two Canadian patents were granted with respect to Accutane (Isotretinoin). Patent No. 967484 was granted on 13 May 1975 and expired on 13 May 1992. Patent No.914202 was granted on 7 November 1972 and expired on 7 November 1989.

The Results

The price of isotretinoin was found to be within the Guidelines and not excessive. A median IPC test was used as the primary price test as an appropriate therapeutic comparator at the 4th level of WHO's Anatomical Therapeutic Chemical (ATC) classification system[122] could not be identified. A 4th level of the ATC classification system is a standard process used by the PMPRB as a starting point in identifying appropriate therapeutic comparators for the purpose of conducting a TCC test. As a TCC test could/was not conducted, the IPC test was the primary test for both strengths of the drug.

Both strengths of isotretinoin were first marketed in Canada in 1983, thus 1995 was set as the benchmark period. As the IPC test was the primary test in the introductory period, the median international price level was used to set the MNE. Both strengths were within the median IPC, therefore the ODB price, which is used to set the Average Transaction Price, became benchmark price for 1995.[123] Canada ranked the 4th highest priced country for this drug.

Between 1996 and 2000, the ATP of isotretinoin 10mg and 40mg remained unchanged. The CPI adjustment factor and the highest IPC test were applied in every year of analysis. Based on these test, both strengths of the product were considered to be within the Guidelines over the entire period of analysis (see Table E-3), i.e. the price did not exceed the established MNE.

Table E-3 Isotretinoin Analysis

Application of Guidelines for Isotretinoin, sold by Hoffman-La Roche (1995 to 2000)				
Year	10mg/cap (DIN 00582344)		40mg/cap (DIN 00582352)	
	MNE	ATP Price	MNE	ATP Price
1995	1.4766	1.4766	3.0133	3.0133
1996	1.5061	1.4766	3.0736	3.0133
1997	1.5165	1.4766	3.0947	3.0133
1998	1.5165	1.4766	3.0947	3.0133
1999	1.5150	1.4766	3.0916	3.0133
2000	1.5371	1.4766	3.1368	3.0133

2000 - IPC includes FSS price in the US price

Inter-Provincial Analysis

WGDP members identified this product as worthy of examination due to concerns regarding the overall cost of this drug to provincial drug plans. Table E-4 is a summary of price information provided by participating jurisdictions for the purpose of this analysis. The prices presented for Alberta, Saskatchewan, Manitoba and Ontario are manufacturers' list prices, and the prices presented for the other drug plans represent a maximum allowable claimed price which may include a distribution margin, thus some caution should be used in interpreting the inter-provincial unit prices presented below. Taking distribution margins into account, Ontario appears to have the lowest price which is within the MNE ceiling; however, the price in the other provinces appears to be marginally higher than the MNE.

In all jurisdictions, other than Saskatchewan and Ontario, the price increased by over 10% in the last year of analysis, with the average per unit price exceeding the MNE (which is based on the ODB price in 1995) by approximately 7.5%.

Table E-4

Current Provincial Price Isotretinoin			
Jurisdiction	Date	DIN: 582344	DIN 582352
British Columbia	Unit Cost March 2001	1.7130	3.5190
Alberta	Unit Cost April 2001	1.6500	3.3667
Saskatchewan	Unit Cost July 2001	1.6500	3.3667
Manitoba	Unit Cost August 2000	1.6500	3.3667
Ontario	Unit Cost June 2001	1.4766	3.0133
Nova Scotia	Unit Cost April 2001	1.6929	3.4606

Conclusions:

Based on the analysis described above, both strengths would be considered within the Guidelines in 2000. However, as can be seen in Table E-4, the prices in the other jurisdictions are higher than the ODB price based on the most current public plan information; these prices are marginally above the MNE.

E6.3 Progesterone (Prometrium)

The Medicine

Progesterone is indicated in women with intact uteruses as an adjunct to postmenopausal estrogen replacement therapy to significantly reduce the risk of endometrial hyperplasia and carcinoma.

Progesterone is marketed in Canada by Schering Canada in a single dose, 100mg/cap. The drug was first offered for sale in Canada in 1995.

Patent Status

The best information available to the PMPRB is that Progesterone is not a patented drug.

The Results

A scientific review of this product by PMPRB staff identified possible therapeutic comparators for Progesterone and thus the TCC test was used as the primary test in establishing a MNE price. As the TCC was the primary test, the secondary test performed on this drug was the highest IPC. The drug failed the TCC test but passed the highest IPC test.

Table E-5 is a summary of the results. As the product was introduced in the last month of 1995, 1996 was used as the benchmark period for the purpose of the price tests.

Table E-5 Progesterone Analysis

Application of Guidelines for Progesterone, sold by Schering Canada (1996 to 2000) 100mg/cap (DIN 02166704)		
Year	MNE	ATP Price
1996	0.1260	0.4268
1997	0.1281	0.4268
1998	0.1303	0.4268
1999	0.1322	0.4268
2000	0.1351	0.4268

ATP = PPS (July 1996)

Medroxyprogesteron acetate (Provera), produced by Pharmacia and Upjohn, was identified as the relevant comparable medicine in conducting the TCC test. The comparable dosage regimen used was 2.5mg daily[124]. The result of the TCC test indicates that the price during the introductory period exceeds the cost of treatment with the comparable drug product. The daily cost per treatment of Progesterone was $0.4268 compared with the cost per treatment for Provera at $0.1260.

An IPC based on the highest international price was also conducted for all periods. Progesterone passed this test in all periods of

analysis. Canada ranked 2nd highest, above the median.[125] After the introductory period the MNE was adjusted by the appropriate CPI, the ATP continued to exceed the MNE over the period of analysis.

Inter-Provincial Analysis

WGDP members identified this product as worthy of examination due to concerns regarding the overall price level of this drug to provincial drug plans. Table E-6 is a summary of price information provided by participating jurisdictions for the purpose of this analysis.

The prices presented for Alberta, Saskatchewan, Manitoba and Ontario have been submitted by the drug plans as manufacturers' list prices, and the prices presented for the other drug plans represent a maximum allowable claimed price which may include a distribution margin, thus some caution should be used in interpreting the inter-provincial unit prices presented below. Taking distribution margins into account, the average price of Progesterone exceeds the MNE significantly, by 273%. If this product was priced at the MNE, the savings to the six provincial drug plans would have been approximately $1.2 million in 2000/01[126].

Table E-6

Current Provincial Price Progesterone		
Jurisdiction	Date	DIN: 2166704
British Columbia	Unit Cost March 2001	0.5320
Alberta	Unit Cost April 2001	0.498
Saskatchewan	Unit Cost July 2001	0.4983
Manitoba	Unit Cost July 2001	0.4980
Ontario	Unit Cost January 2001	0.5254
Nova Scotia	Unit Cost April 2001	0.4974

Conclusion:

Progesterone failed the initial price review by 238.7% and continued to exceed the Guidelines up to and including 2000. In 2000, Prometrium exceeded the Guidelines by 215.9%.

Based on current provincial data, Prometrium continues to exceed the MNE in 2001.

E6.4 Digoxin (Lanoxin)

The Medicine

Digoxin is a cardiac glycoside. Cardiac glycosides are used principally in the prophylactic management and treatment of heart failure and to control the ventricular rate in patients with atrial fibrillation or flutter. The drugs also are used to treat and prevent recurrent paroxysmal atrial tachycardia.

The drug was first offered for sale in Canada in 1936. Digoxin was marketed in Canada by Glaxo Wellcome in multiple doses, 0.25mg/tab, 0.125mg/tab, and 0.0625mg/tab. In 2001, the marketing of Lanoxin in Canada has been transferred to Virco Pharmaceuticals (Canada) Inc.

Patent Status

The best information available to the PMPRB is that digoxin is not a patented drug.

The Results

Digoxin had been on the market well before the benchmark period established in this analysis, thus, the publicly available Ontario Drug Benefit (ODB) price was used to establish the average transaction price (ATP) in 1995. A therapeutic assessment of this product could not produce an appropriate and relevant comparator thus it was not feasible to conduct a TCC test. The median IPC test served as the primary test to establish the MNE in 1995.

Table E-7 Digoxin Analysis

Application of Guidelines for Digoxin sold by Glaxo Wellcome 1995 to 2000						
Year	0.25mg/tab (DIN 00004685)		0.125mg/tab (DIN 00035319)		0.0625mg/tab (DIN 00731269)	
	MNE	ATP	MNE	ATP	MNE	ATP
1995	$0.0855	$0.0858	$0.0858	$0.0858	$0.0694	$0.0945
1996	$0.0872	$0.0858	$0.0875	$0.0858	$0.0708	$0.0945
1997	$0.0881	$0.0858	$0.0881	$0.0858	$0.0717	$0.0945
1998	$0.0881	$0.0858	$0.0881	$0.0858	$0.0729	$0.0945
1999	$0.0880	$0.0858	$0.0880	$0.0858	$0.0743	$0.0945
2000	$0.0893	$0.0858	$0.0893	$0.0858	$0.0756	$0.0945

2000: IPC includes DVA

Table E-7 provides a summary of the analysis conducted in assessing the price level of digoxin. The 0.25 mg strength tablet failed the initial (1995) median IPC test, however after the benchmark period, this DIN was found to be within the guidelines. Between 1996 and 2000 this strength passed the highest IPC and the price listed in the ODP did not change. The 0.125 mg strength passed both the initial median IPC test and continued to be within the Guidelines over the period of analysis. The only strength that failed the initial IPC test and subsequent CPI tests was the 0.0625 mg strength. Between 1995 and 2000 the ODB price for all strengths remained the same.

Between 1996-2000 all strengths passed the IPC (highest) test.

Inter-Provincial Analysis

WGDP members identified this product as worthy of examination due to concerns regarding the recent price increase submitted to provincial drug plans by the new manufacturer. The ODB current list price does not reflect this increase. The Formulary price has not changed for this product but pharmacies can submit a cost to operator claim for the acquisition cost of the product if the cost is greater than the drug benefit price plus 10%.

Table E-8, provides a summary of price information provided by participating jurisdictions for the purpose of this analysis. The prices presented for Saskatchewan, Manitoba and Ontario are manufacturers' list prices, and the prices presented for the other drug plans represent a maximum allowable claimed price which may include a distribution margin, thus some caution should be used in interpreting the inter-provincial unit prices presented below. Taking distribution margins into account, the recent price increase seen by provincial drug plans for this product exceeds the MNE by over 100%. The increase in the price in excess of the MNE represents an annual cost to the six provincial drug plans of approximately $6 million.[127]

Table E-8

Current Provincial Price Digoxin				
Jurisdiction	Date	DIN: 4685	DIN: 35319	DIN: 731269
British Columbia	Unit Cost April 2000	0.0920	0.0920	0.1020
British Columbia	Unit Cost March 2001	0.1990	0.1990	0.2010
% change		**116.7%**	**116.7%**	**97.5%**
Alberta	Unit Cost April 2000	0.0883	0.0883	0.0973
Alberta	Unit Cost April 2001	0.1887	0.1887	0.1994
% change		**113.7%**	**113.7%**	**104.9%**
Saskatchewan	Unit Cost June 2000	0.0945	0.0945	0.0945
Saskatchewan	Unit Cost June 2001	0.1994	0.1994	0.1994
% change		**111.0%**	**111.0%**	**111.0%**
Manitoba	N/A	N/A	N/A	N/A
Manitoba	Unit Cost June 2000	0.1994	0.1994	0.1994
% change		**N/A**	**N/A**	**N/A**
Ontario	Unit Cost 2000/01	0.0858	0.0858	0.0945
Ontario	Unit Cost June 2001	0.0858	0.0858	0.0945
% change		**0.0%**	**0.0%**	**0.0%**
Nova Scotia	Unit Cost April 2000	0.0897	0.0892	0.0982
Nova Scotia	Unit Cost April 2001	0.1982	0.2001	0.2061
% change		**121.0%**	**124.3%**	**109.9%**

Conclusion:

In 2000, both the 0.125mg/tab and 0.25mg/tab strengths would be considered within the Guidelines. The 0.25mg/tab strength exceeded the Guidelines in the initial price test by 0.4%, but was within the Guidelines in subsequent periods. The 0.0625mg/tab strength exceeded the Guidelines in the initial price test by 36.2% and continued to exceed the Guidelines up to and including 2000; the excess in 2000 was 25%.

As can be seen in the Table E-8 above, in 2001, based on the most current provincial price information, every provincial drug plan included in this analysis, other than Ontario (ODB), has experienced a significant price increase for all strengths. The current price for five out of six jurisdictions exceeds the MNE price by approximately 100% for all the strengths. The increase in the price in excess of the MNE price represents an annual cost to the six provincial drug plans of approximately $6 million.

E7 General Conclusions:

Table E-9 below provides a summary of the tests conducted in establishing a MNE price for those products identified by the WGDP members for analysis. A TCC test was used to establish the MNE price in the introductory period for progesterone. A RR test was conducted for the 3 mg strength of Warfarin. For all other products and strengths, the median IPC test was used to establish the MNE price in the introductory period. Over the period of analysis a CPI adjustment and the highest IPC test were conducted for all non-introductory periods.

During the introductory period, the price of two strengths of warfarin (3mg and 5mg), the price of progesterone, and two strengths of digoxin (0.25 mg and 0.0625 mg) exceeded the MNE price. By 2000, the 5mg strength of warfarin and the 0.0625 mg strength of digoxin were priced within the MNE price ceiling and the remainder of the drugs continued to exceed the MNE price.

It is important to note, that in 2001, the price of digoxin for all strengths increased significantly. This increase was not reflected in the publicly available ODB formulary; however, all other jurisdictions reported increases for digoxin of approximately 100%.

Overall, for the products that had a price in excess of the established MNE, the prices exceeded the MNE by a range of 0.4% to 238.7% in the introductory period and 12.9% to 215.9% in 2000. Had the price of the products with prices in excess of the MNE price been limited to the MNE price, the total annual savings to the six provincial drug plans would have been approximately $7.4 million.

Table E-9 Summary of PMPRB Review

DIN (Strength)	Introductory Period			2000		
	TCC/RR	IPC Median	IPC Highest	CPI	IPC Highest	Median Canadian[128] to International Price
Warfarin Sodium (Coumadin)						
01918311 (1mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.738280
01918338 (2mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.789107
01918346 (2.5mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.578557
02240205 (3mg)	RR-Not Within the Guidelines	NA	Within the Guidelines	Not Within the Guidelines	Within the Guidelines	0.811693
02007959 (4mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.467433
01918354 (5mg)	NA	Not Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.844061
01918362 (10mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.659604
Isotretinoin (Accutane)						
00582344 (10mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	1.033293
00582352 (40mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	0.355173
Progesterone (Prometrium)						
02166704 (100mg)	TCC-Not Within the Guidelines	NA	Within the Guidelines	Not Within the Guidelines	Within the Guidelines	0.854454
Digoxin (Lanoxin)						
00004685 (0.25mg)	NA	Not Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	2.251226
00035319 (0.125mg)	NA	Within the Guidelines	NA	Within the Guidelines	Within the Guidelines	2.167142
00731269 (0.0625mg)	NA	Not Within the Guidelines	NA	Not Within the Guidelines	Within the Guidelines	2.832386

E8 Sub-Appendix -- Prices in Canadian Dollars in Different Countries

Table E-9 Prices in Canadian Dollars in Different Countries

Prices in Canadian Dollars in Different Countries										
Year	Brand	DIN	Canada	Germany	France	Italy	Sweden	Switzerland	U.K	U.S.A
1995	Accutane	582344	1.4766	2.825	1.0743	1.0391	.	1.698	.	4.4712
1995	Accutane	582352	3.0133	.	.	.	.	.	.	6.1602
1996	Accutane	582344	1.4766	3.0996	1.1293	0.9732	.	1.8618	.	4.6437
1996	Accutane	582352	3.0133	.	.	.	.	.	.	6.398
1997	Accutane	582344	1.4766	3.1833	1.1158	1.1069	.	1.8349	.	4.9016
1997	Accutane	582352	3.0133	.	.	.	.	.	.	6.7528
1998	Accutane	582344	1.4766	3.1944	1.0826	1.1127	.	1.757	.	5.8636
1998	Accutane	582352	3.0133	.	.	.	.	.	.	8.0785
1999	Accutane	582344	1.4766	3.1009	1.047	1.3165	.	1.6272	.	6.9896
1999	Accutane	582352	3.0133	.	.	.	.	.	.	9.6298
2000	Accutane	582344	1.4766	2.9763	1.0061	1.3028	.	1.5859	.	6.8562
2000	Accutane	582352	3.0133	.	.	.	.	.	.	9.4459
1995	Digoxin	4685	0.0858	0.1948	0.0855	0.1201	0.0795	0.0621	0.0327	0.1498
1995	Digoxin	35319	0.0858	0.1434	.	0.1089	0.0679	0.0322	0.0327	0.1751
1995	Digoxin	731269	0.0945	.	.	0.1061	.	.	0.0327	.
1996	Digoxin	4685	0.0858	0.2043	0.0942	0.1259	0.0841	0.0668	0.0337	0.171
1996	Digoxin	35319	0.0858	0.1504	.	0.1145	0.0726	0.0346	0.0337	0.1967
1996	Digoxin	731269	0.0945	.	.	0.1116	.	.	0.0337	.
1997	Digoxin	4685	0.0858	0.1755	0.0931	0.1327	0.0847	0.0659	0.0346	0.179
1997	Digoxin	35319	0.0858	0.1326	.	0.1186	0.0799	0.0341	0.0346	0.2032
1997	Digoxin	731269	0.0945	.	.	0.1158	.	.	0.0346	.
1998	Digoxin	4685	0.0858	0.166	0.0903	0.1334	0.0838	0.0631	0.0362	0.2535
1998	Digoxin	35319	0.0858	0.1254	.	0.1192	0.079	0.0327	0.0362	0.2878
1998	Digoxin	731269	0.0945	.	.	0.1164	.	.	0.0362	.
1999	Digoxin	4685	0.0858	0.1612	0.0873	0.13	0.0804	0.0608	0.0376	0.2739
1999	Digoxin	35319	0.0858	0.1219	.	0.1162	0.0758	0.0315	0.0376	0.3109
1999	Digoxin	731269	0.0945	.	.	0.1134	.	.	0.0376	.
2000	Digoxin	4685	0.0858	0.1547	0.0839	0.1192	0.0732	0.0592	0.0375	0.2223
2000	Digoxin	35319	0.0858	0.117	.	0.1059	0.0687	0.0307	0.0375	0.2396
2000	Digoxin	731269	0.0945	.	.	0.1033	.	.	0.0375	.
1996	Prometrium	2166704	0.4268	.	0.2958	.	.	0.4796	.	.
1997	Prometrium	2166704	0.4268	.	0.2923	.	.	0.4726	.	.

Prices in Canadian Dollars in Different Countries										
Year	**Brand**	**DIN**	**Canada**	**Germany**	**France**	**Italy**	**Sweden**	**Switzerland**	**U.K**	**U.S.A**
1998	Prometrium	2166704	0.4268	0.6162	0.2836	.	.	0.4526	.	.
1999	Prometrium	2166704	0.4268	0.5982	0.2742	.	.	0.4359	.	0.6857
2000	Prometrium	2166704	0.4268	0.5742	0.2635	.	.	0.4248	.	0.714
1995	Warfarin	1918311	0.2829	.	.	.	.	.	0.0182	0.7025
1995	Warfarin	1918338	0.2992		0.0706	.	.	.	.	0.7459
1995	Warfarin	1918346	0.2395	.	.	.	0.1112	.	.	0.7688
1995	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.7613
1995	Warfarin	1918354	0.24	0.3618	.	0.1173	.	.	0.0344	0.7805
1995	Warfarin	1918362	0.4306	.	0.1794	.	.	.	.	1.1923
1996	Warfarin	1918311	0.2829	.	.	.	.	.	0.0188	0.7153
1996	Warfarin	1918338	0.2992	.	0.0743	.	.	.	.	0.7563
1996	Warfarin	1918346	0.2395	.	.	.	0.1219	.	.	0.7794
1996	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.7752
1996	Warfarin	1918354	0.24	0.3795	.	0.1231	.	.	0.0354	0.7913
1996	Warfarin	1918362	0.4306	.	0.1887	.	.	.	.	1.2141
1997	Warfarin	1918311	0.2829	.	.	.	.	.	0.0602	0.7476
1997	Warfarin	1918338	0.2992	.	0.734	.	.	.	.	0.7804
1997	Warfarin	1918346	0.2395	.	.	.	0.1227	.	.	0.8045
1997	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.8101
1997	Warfarin	1918354	0.24	0.3752	.	0.1327	.	.	0.1167	0.8159
1997	Warfarin	1918362	0.4306	.	0.1864	.	.	.	.	1.2411
1998	Warfarin	1918311	0.2829	.	.	.	.	.	0.0628	0.7973
1998	Warfarin	1918338	0.2992	.	0.0712	.	.	.	.	0.832
1998	Warfarin	1918346	0.2395	.	.	.	.0.1279	.	.	0.858
1998	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.864
1998	Warfarin	1918354	0.24	0.3992	.	0.1334	.	.	0.1219	0.87
1998	Warfarin	1918362	0.4306	.	0.1809	.	.	.	.	1.3237
1999	Warfarin	1918311	0.2829	.	.	.	.	.	0.0976	0.8605
1999	Warfarin	1918338	0.2992	.	0.0686	.	.	.	.	0.8979
1999	Warfarin	1918346	0.2395	.	.	.	0.1227	.	.	0.9263
1999	Warfarin	2240205	0.4186	.	.	.	.	.	0.1443	0.9299
1999	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.9325
1999	Warfarin	1918354	0.24	0.3732	.	0.1217	.	.	0.2335	0.9387
1999	Warfarin	1918362	0.4306	.	0.175	.	.	.	.	1.4289
2000	Warfarin	1918311	0.2829	.	.	.	.	.	0.0974	0.7004
2000	Warfarin	1918338	0.2992	.	0.0659	.	.	.	.	0.7236
2000	Warfarin	1918346	0.2395	.	.	.	0.1148	.	.	0.747

Prices in Canadian Dollars in Different Countries										
Year	**Brand**	**DIN**	**Canada**	**Germany**	**France**	**Italy**	**Sweden**	**Switzerland**	**U.K**	**U.S.A**
2000	Warfarin	2240205	0.4186	.	.	.	.	.	0.144	0.7694
2000	Warfarin	2007959	0.3709	.	.	.	.	.	.	0.826
2000	Warfarin	1918354	0.24	0.3582	.	0.1112	.	.	0.2337	0.758
2000	Warfarin	1918362	0.4306	.	0.1682	.	.	.	.	1.1911

Endnotes

[1] The Task Force has representatives from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Nova Scotia, Health Canada and the Patented Medicine Prices Review Board (PMPRB). It was established to examine one of six pharmaceutical issues identified at the April 1996 meeting of federal/provincial/territorial Ministers of Health. The other issues included utilization, marketing, wastage, consumer education and research and development. The work is overseen by the Pharmaceutical Issues Committee (PIC) of the Advisory Committee on Health Services (ACHS), which reports to the Conference of Deputy Ministers of Health.

[2] For more detail on the current mandate and work of the Working Group on Drug Prices refer to Appendix I.

[3] Patricia M. Danzon, et al, "Cross-national price differences for pharmaceuticals: how large and why?", Journal of Health Economics 19 (2000) 159-195.

[4] Only tablets and capsules were included in the analysis in order to minimize any differences in reporting unit prices between countries. See Methodology for more info.

[5] A significant change from the previous study is the incorporation of the U.S. Federal Supply Schedule (FSS) price into the U.S. price. This is consistent with changes in PMPRB policy. The U.S. Department of Veteran Affairs (DVA) began publishing the FSS formulary prices in November 1997 and patentees are now required to submit the FSS price. As of January 1st, 2000 the PMPRB has incorporated the FSS price in conducting international comparisons for patented drugs.

[6] As of Jan 30th 1995, drug products with prematurely dedicated patents still fall under PMPRB jurisdiction. This does not describe any of the products used for this study.

[7] The ODB database/formulary was used to determine the number of competing manufacturers in the market place.

[8] PMPRB and IMS Health data, in the 1999 PMPRB Annual Report.

[9] The packaging or form of drug products that are not in tablet or capsule form could have a great deal of influence on the price. For example, a multi-use vial of one injectable drug product can be reasonably expected to have a different price from the single use ampoule of another product. This is also a problem for dosage forms such as sprays, foams and lotions. There may be particularly insufficient information on generic products listed to insure some forms and applicators are compatible.

[10] As of Jan 30th 1995, drug products with prematurely dedicated patents still fall under PMPRB jurisdiction. Drugs whose patent(s) were dedicated after Jan 30th, 1995 were excluded from this analysis. Dedicated patents are those that have not expired, but the patent holder has voluntarily surrendered the rights and entitlements of the patent.

[11] The ODB database/formulary was used to determine the number of competing manufacturers in the market place.

[12] Effective as of March 7th, 2001.

[13] Interprovincial price comparisons support the conclusion that no significant price differences exist between provinces at the ex-factory gate level and thus it is assumed that the ODP price is a good estimate of the Canadian price.

[14] For example, there may be two packages of 100 tablets. There would be a typical bottle or box of tables for a given price and then there would be a box of 100 individually packaged tablets in unit doses for as much as twice the price. These unit dose packages were excluded from the analysis.

[15] Bioequivalent drug products, for the purposes of this study, are products for which the combination of active ingredient(s), strengths(s), dosage form, and route of administration are the same.

[16] The discussion in section 2.1about using the median package size could be used as an analogy for the logic behind using the median product. This is an attempt to get a representative price.

[17] If there was more than one bioequivalent product found in a given country, either the manufactureror the product name, or both, were used to identify the brand name product most comparable to the Canadian product. In the rare case when neither of those criteria could be used, only products produced by manufacturers typically producing brand name products were considered. In the even rarer instances when there was still more than one comparable product found in that country, the prices were equal or extremely close. In these instances, the unit prices were averaged.

[18] Using the median price limits the possible bias that may be created by a correlation between country and package size. For example, the Italian government often only lists a single moderate package size for a drug product that is reimbursable. The U.S. Red Book often lists numerous package sizes including extremely large, relatively cheaper package sizes and expensive small packages. One concern is that some of these extreme package sizes listed by

numerous generic distributors may have unrepresentative unit prices and may be rarely purchased by special customers such as large hospitals. Using the median unit price is an attempt to capture a moderate unit price for each product and reduce the influence of such outliers.

[19] The previous study referenced in the introduction used only the most comparable brand-to-brand comparison, and thus does not encounter this problem in the same way. Appendix A5 reproduced the analysis done with the exact methodology as the previous study, but with the new price levels. This included taking the mean and not the median package price. There was no significant change comparable results.

[20] Ex-factory prices were calculated after adjusting for retail and wholesale mark ups, as well as, value added taxes, when applicable. These mark ups are legislated in most countries. See the PMPRB's (1998) "Verification of Foreign Patented Drug Prices" for a description of how ex-factory prices were derived in six of the seven countries (excluding the United States).

[21]The 36 month average was taken over the months proceeding Dec 1998. This methodology is consistent with the way the PMPRB determines exchange rates for the International Price Comparison on patented products.

[22] The Red Book price is an average wholesale price, but was converted to a manufacture's list price before being averaged with the FSS price - see Appendix C. The Patented Medicines Regulations requires that patentees file all publicly available prices for their products in the seven comparitor countries, including the US. In November of 1997 the Department of Veterans Affairs started publishing the Federal Supply Schedule (FSS) prices that it negotiated for it's self and some other federal agencies. In 1998 the PMPRB started requiring patentees to file the FSS price. As of January 1st, 2000 the FSS price is incorporated into the International Price Comparison test used in implementing the Board's guidelines.

[23] For the purpose of this analysis, availability in a country is equated with the presence/absence of the product from the public source used in that country.

[24] The geometric mean is a more appropriate measure of the mean of ratios. Due to the distribution of the ratio values, the arithmetic mean tended to bias the average towards high valued outliers. The Geometric mean is the equivalent to the arithmetic mean of the log-transformed data.

[25] The number three was chosen because it made the MIP the least susceptible to outliers. In this way, the price recognized as the international price must have foreign prices both above and below it.

[26] For example, for each product found in Italy, the Italian product was compared to a MIP that included Canada, but did not include the Italian price. The geometric mean of the Italian to this MIP was then presented.

[27] Just as the ODB price was used as a proxy for the 'Canadian' price, expenditures and quantities found in the ODB database for 1998-1999 were used as a proxy for the Canadian expenditure and utilization levels.

[28] Since the geometric mean was used for the analysis, the pairwise t-tests were done on the log-transformed data.

[29] Again the cost is expressed in Canadian dollars using an exchange rate averaged over 36 months.

[30] For example, thirty-two of the products in this study are also found in Italy. Figure 3.10 compares the Canadian costs on these thirty-five products with what expenditure on these products would have been had consumers paid Italian price levels, (holding utilization constant).

[31] The inclusion of a value in the 95% confidence interval means that there is insufficient evidence (at significance level 0.05), to reject the hypothesis that this value is the actual mean for the population of which the sample is meant to represent. Conversely, the exclusion of the value "1.00" suggests there is sufficient evidence to reject this hypothesis.

[32] This was the equivalent of setting up the price comparison of each DIN as a Bernoulli experiment and testing the null hypothesis that there is no significant difference between the Canadian and foreign price. The likelihood value calculated then acts like a p-value. If the likelihood calculated was below the significance value used for this report, 0.05, that there was sufficient evidence to reject the hypothesis that Canadian prices are equally likely to be priced below or above the foreign country in question.

[33] As described in the methodology section, the publicly available lists were used as a proxy for the selection of products available in that country.

[34] The UK does have an active generics market, but only the prices of brand product are controlled through profit controlling policies. The Drug Tariff list provides price information on generic products, however, over the period of analysis, supply shortages had made determining an accurate generic price problematic and thus only brand name prices – ie. the regulated prices, were included for this analysis. See Appendix C for more details.

[35] This is the result of the reimbursement system and price setting scheme in this country. For more information see Appendix C.

[36] For details on the reimbursement and pricing scheme in Germany see Appendix C.

[37] Generally the generic products listed in the FSS product list were a subset of those offered in the Red Book list, but both lists contained the brand name products.

[38] This is the percent share of market sales for out-of-hospital pharmaceuticals at the retail prices. This share is taken from the total out-of-hospital retail market sales for the seven countries. The U.S. market is taken as a whole.) Last, Elaine and Neil Turner. Pharmaceutical Pricing and Reimbursement 2000, A Concise Guide, PPR Communication Ltd, Cambridge, UK. 2000.

[39] In a previous study conducted by the F/P/T Task Force, Canadian prices on NPSS drugs were found to be, on average, 30% higher than the international median price.

[40] The implication of this is as follows: Having the Canadian price above the MIP 32 times of 56 provides insufficient evidence, at significance level 0.05, to reject the hypothesis that the Canadian price is equally likely to be above or below the MIP.

[41] Using only brand name products in the analysis, if it was equally likely to be above or below the international price, the probability of observing 30 instance of the Canadian price above the international median price would be 9%.

[42] If the Canadian price was equally likely to be above or below the international price for the 39 products sampled, the probability of the Canadian price being above for 25 products is 3%.

[43] The foreign to international median ratio was generated for all those products found in that country. The median prices were composed of the remaining countries and Canada.

[44] Canadian expenditure and utilization weights are used for weighting the average ratios for all countries.

[45] Statistical significance was tested at 0.05.

[46] At first glance this result suggests that the products with highest Canadian to MIP ratios have the highest expenditure. This is, however, not necessarily supported by the data when this question is further analyzed in Appendix A6. This is only actually true for the single top-selling product with over 14% of the baskets expenditure and by far the highest Canadian to MIP ratio (3.23).Most of the products with the top Canadian to MIP ratios are not amongst the ones with the highest expenditure.

[47] Similar results using a brand-to-brand price comparison are presented in Appendix A. The average Canadian to MIP ratio changed if only the most comparable brand foreign products were used in the analysis. Canadian prices were 7% above the MIP. The U.S. premium over the MIP under these circumstances is increased to 93%, and the Germany premium increases to 15%, (Appendix, Figure A.1). Changes in other countries are relatively insignificant. A series of Figures showing the average Canadian and foreign to MIP ratios with changes in the interpretation of the U.S. price are in Appendix, Section A.2. (i.e., the FSS or the Red Book price was used, but not both.)

[48] The U.S. price being the average of the FSS and Red Book price. Drug product prices at the ex-factory (manufacturers) level.

[49] This may be problematic if there is a correlation between the availability of prices in two or more countries. For example, a Swedish price is generally only available if a price is also found in the other five European countries. In this way, the Swedish price, unlike the Canadian, is only compared to MIP ratios composed of a significant number of European prices.

[50] Canada was predominantly being compared to the U.S. price which was a much higher price, thus Canada looked relatively cheaper. The U.S. was predominantly being compared to Canada, which was generally priced higher than Europe, thus the U.S. looked relatively cheaper than it would have presumably if prices were available for a larger variety of countries.

[51] Appendix A2 contains figures analogous to Figure 3.2, but with the FSS or Red Book prices as the U.S. price, (i.e., not the average of the two prices). This analysis is shown using both foreign brand products and all available foreign products

[52] The U.S. price is the FSS and Red Book prices..

[53] Statistical significance was tested at alpha equal to 0.05.

[54] If the Canadian products were equally likely to be above or below German prices, the probability of observing a higher Canadian price 22 times out of 35 would rise to 4.3%. This is higher than the value calculated using all German products including generics, but this is still lower than 0.05;

[55] Drug product prices at the ex-factory (manufacturers) level.

[56] The only exception was the FSS were prices were on average higher for the products in the smaller basket.

[57] Both averages, i.e. patented and non-patented Canadian to MIP ratio averages, were weighted by expenditure.

[58]The U.S. price was the FSS Prices and Red Book Price.

[59] ODB Plan utilization is used to represent Canada for the purpose of this analysis.

[60] Utilization was based on ODB database.

[61] These results most comparable to the Last Non-Patented Single Source Study

[62] Although the Canadian price was very high, it was not the highest. The U.S. price was 68% higher.

[63]There are four main sources used as references for the heavily summarized and integrated information in this background section : i) Kanavos, Dr. Panos. Scrip Reports: Pharmaceutical Pricking and Reimbursement in Europe, PJB Publication Ltd, London, UK. 1999. ii) Last, Elaine and Neil Turner. Pharmaceutical Pricing and Reimbursement 2000, A Concise Guide, PPR Communication Ltd, Cambridge, UK. 2000. iii) Report To the President: Prescription Drug Coverage, Spending, Utilization and Prices. Prepared By the U.S. Department of Health and Human Services. Iv) PMPRB, Verification of Foreign Patented Drug Prices.1998. Other Sources are referenced further.

[64] The consensus view, based on prior studies, has been that countries with strict price regulation have lower medicine prices than countries with less restrictive regulation, such as the UK, or no regulation, as in the US. A study by Patricia M. Danzon had recently challenged this view in a study published by The Office of Health Economics. In that study, Danzon, et al concluded that the average price differences are smaller than previously suggested. These conclusions are based on indexes of manufacturer-level drug prices for seven major markets – UK, US, Canada, France, Germany, Italy, and Japan – using comprehensive data of all molecule sales in 1992 outside of hospitals.

[65] Approximately half of the population is exempt from paying their own dispensing fees, including persons over 60, unemployed persons, low income groups, children under 16, full-time students under 19, pregnant woman, mothers with a child under the age of one, inpatients and the chronically ill. Contraceptives dispensed are also exempt. From April 1998 to April 1999, the dispensing fee was £5.75. In 1999, 85% of prescriptions dispensed were exempt from co-payments.

[66] Generally, drug products are distributed to the pharmacies through a wholesaler. This mark-up may be shared with the pharmacies, and on average the pharmacies themselves are charged only a 5% wholesale mark-up.

[67] Pharmacies are reimbursed at the listed price. Generally the listed price does not take into account supply discounts available to the pharmacy which they are encouraged to pursue. Direct revenue received by pharmacies is deducted directly from the listed reimbursement price, but other discounts are only partly recovered by the government. The Clawback rates imposed may vary between 2% and 10% depending on the pharmacies turnover rates, but an average rate of 7.74% is the targeted.

[68] Price levels are set differently for products with different numbers of competing manufacturers, but generally reimbursement levels are based on a weighted average price of the main suppliers of the generic drug product.

[69] Bioequivalent drug products for this study are products for which the combination of active ingredient(s), strengths(s), dosage form, and route of administration are the same

[70] Patients must pay Lit3,000 on a single prescription, Lit6,000 on two or more prescriptions and Lit1,000 on long-term care medications. There is a maximum per prescription of Lit70,000. In addition, patients must pay 50% of products listed as having high cost-benefit ratios or 100% of products without proven efficacy or with proven efficacy for minor diseases. Low income households, children up to 7, people over 65 with a family income below Lit70 million, pregnant woman, the unemployed, or some handicapped and/or chronically ill patients are exempt from co-payments.

[71] The four countries used are France, Germany, Spain and the UK, of which France and Spain have price control policies.

[72] In 1997 the CIPE cut the wholesale and pharmacy mark-ups on many products whose price exceeded Lit300,000. A regressive system was introduced such that mark-up percentages decreased as absolute prices increase. None of the products identified for analysis in this study were priced above Lit300,000.

[73] This is lower then the standard 20% VAT added to most products in Italy.

[74]This committee was formally known as the Economic Drug Committee, Comité Économique des Médicaments, (CEM). The committee was renamed in 1999 because of the added responsibility of pricing medical devices.

[75] Wholesalers are required to pay levy 1.2% of pre-tax sales to social security, effectively reducing the profit value of the mark-up from 9.70% to 8.50%.

[76] This change was implemented after the time period examined in this study. Had this change been relevant, it would have affected 10 of the 114 products identified as top-selling non-patented single source drug products in this study, 8 of which are tablets and capsules used in the analysis.

[77] For an example, if the manufacture's price of a product were FFr200, the total pharmacy mark-up allowed would be FFr39.15 + FFr5.0 = FFr44.15. (26.1% of 150 = 39.15 and 10.0% of the remaining 50 = 5.0)

[78] The standard tax charged in France is 18.6%. France has been officially reprimanded repeatedly by the European

Union who consider the reduced tax rates on reimbursable pharmaceutical products to be too low.

[79] For example, the mark-up used in this study for reimbursable pharmaceuticals priced below SKr34.25 was (WPx1.30) + 18.00.

[80] Families with children under the age of 18 may have the total cost of the prescriptions for the children lumped together.

[81] If a patients 12 month accumulated spending is SKr2,000 then they are reimbursed SKr0 for the first SKr900 (0% of 900=0), they are reimbursed 50% from SKr901 - SKr1700 (50% of 800 = 400), and finally 75% of the remainder (75% of 300=225). This means for a total accumulation of SKr2,000, the patient is reimbursed a total of SKr625 and pays the remaining SKr1375.

[82] This excludes non-prescription products suitable for sale at all outlets or obtainable from specialized outlets.

[83] Criteria for determining that a product is superior and therefore deserving or higher prices/reimbursement levels include: reduced treatment times, reduced overall treatment costs, significant improvement in the combination of active ingredients, innovation of a new chemical entity, improvement in dosage form.

[84] These are appropriate mark-ups used for the data collected for study. Generic products are subject to a different wholesale mark-up scheme. It is similar but with a simpler scale system and with mark-ups ranging from 11% to 15% of the ex-factory price.

[85] The government did intervene in price setting in 1993, when they imposed price cuts and/or freezes to all products until 1995.

[86] The negative list frequently included combinations of drugs with more than three active ingredients or drugs with disputed therapeutic efficacy. Exceptions were made for special treatments or to individually named patients.

[87] Products may now be excluded from reimbursement if: the drugs are not necessary for treatment of condition, the drug is not proven effective, or other treatments, non-pharmaceutical treatments or monotreatments (in the case of combinations therapies) are shown to be more effective or cost effective.

[88] Most companies do lower their prices when a product is generised and grouped at a level one grouping (See below for meaning of level one grouping.) But there are many companies who choose to keep their prices, on average, above the reference price.

[89] This includes imports, generics and parallel imports. Greatest market share is used to break a tie.

[90] This formula is used unilaterally despite any differences in recommended dosage for different indications, differences in acute or maintenance regimes, or if a range as oppose to a single dose is recommended.

[91] The reference price is often set specifically to meet this target, but this is not always the case. At the other extreme, the price for monosubstance ACE inhibitors was set so high that all of the brand prices were below the maximum reimbursable price and the generics were even lower.

[92] Children below the age of 18 and pregnant woman are exempt from co-payments and there are thresholds and exceptions for the elderly, the poor and the chronically ill.

[93] Extending Medicare to include pharmaceuticals had been considered by the previous U.S. administration.

[94] Both prices , cash customer and third party purchaser at point of sale, include both the patient and insurers portion. In 1998, 25% of all prescriptions filled at retail pharmacies were paid for by cash customers.

The results on the gap between cash and third party purchasers was confirmed with analysis repeated with the median price for cash customers and the median third party customers in an attempt to discount extreme values. The median percent difference of this distribution was 17.3%.

[95] The cash customer vs. third party price ratio was distributed throughout a large range for generic products. The analysis showed a small peak in the distribution of the price difference between 0% and 10%, but the range included non-negligible numbers of observation with negative price differences and differences between positive 40% and almost 100%. Brand name products had a concentrated peek in cash customer vs. third party prices between 10% and 20%. The analysis done showed no instances where cash customers paid less than third party customers for brand products.

[96] The 25% most common drugs used in the analysis were used to derive this figure.

[97] In establishing upper payment limits for the state Medicaid programs it is assumed the AWP overstates the actual acquisition cost to pharmacies by 10%-20%. (State Medicaid Manual, sec.6305.1)

[98] Literature suggests that pharmacy margins have been dropping and PBM' becoming more common. There may be incentives for a retail pharmacy to sell to a PBM to spite the low price, for example these may attract customers who would than frequent the establishment and presumably purchase other products. In order to cover costs pharmacies must raise prices for cash customers or lower operating margins.

[99] Some states allow for generic substitution but all require a prescriber's permission to switch one brand for another. Pharmacies may call prescribers and suggest a brand substitution.

[100] The Veterans Health Administration in the U.S. is responsible for providing hospital care, nursing home and domiciliary care, outpatient medical coverage and dental care for any person in the U.S. who served on active, uniformed duty for a specific time period.

[101] For brand name drugs with out competition or for some innovator drugs with competition, the manufacturermust actually charge the lesser of the FSS price or the "Federal Ceiling Price" to some customers. The customers are the VA, the Department of Defense, the Public Health Service and the Coast Guard. These lower prices are not available to other agencies that use the FSS price list.

[102] Special allowances are made if the prescriber specifies a higher priced brand product with no substitutions allowed.

[103] Generic products are reimbursed at the price specified in the Drug Tariff list.

[104] The actual wholesale mark-up is usually closer to 5%, and the remainder is often passed on to pharmacies. This does not effect how to estimate the best possible ex-factory price based on the NHS price, as it is still a 12.5% mark-up assumed to establish the list price.

[105] The wholesale mark-up is still 10.74% for product priced below FFr150, but the mark-up is only 6% for products priced above that. These new mark-ups were not implemented until September 1999 and where therefore not considered in the backing out process for products in this study

[106] The VAT was increased to 16% from 15% in April of 1998 and is therefore appropriate for the Rote Liste publication used and the pharmaceutical prices in this study.

[107] These mark-ups were effective as of July 1998 and are the most appropriate for the price source used. They differ from previous regulated mark-ups only by the inclusion of additional categories for extremely high priced drugs. This change is not applicable to any of the products in this study, as none of them are priced high enough to be effected.

[108] Analysis conducted by the F/P/T WGDP analysis is limited to those jurisdictions that had provided data to the PMPRB for the purpose of this analysis. It is expected that future analysis will include a wider range of territorial, provincial and federal drug benefit plans.

[109] The HDAP, as an advisory panel of the Board, will provide recommendations for the categorization of new patented drug products and the selection of comparable drug products. Its role is defined in the PMPRB's Compendium of Guidelines, Policies and Procedures.

[110] For more detailed information on PMPRB's price guidelines refer to the "Compendium of Guidelines, Policies and Procedures".

[111] Italy, France, Sweden, Germany, UK, Switzerland, and U.S.

[112] Italy, France, Sweden, Germany, UK, Switzerland, and U.S.

[113] Refer to PMPRB's Excessive Price Guidelines for more information on these price tests and their application to patented drugs.

[114] For products whose price was found to be in excess of the MNE, 1999/00 provincial utilization patterns were used to estimate the cost impact to provincial drug plans.

[115] 1996-97: 10 mg not listed in ODB, therefore, assumed price remained the same

[116] International = Exchange rates December 1995. Warfarin1mg passed based on 2 countries (UK , US {AWP}). Canada ranked second. Median simple average of UK and US. Warfarin 2mg passed based on 2 countries (France, US {AWP}). Canada ranked second. Median simple average of France and US. Warfarin 2.5mg passed based on 2 countries (Sweden, US {AWP}). Canada ranked second. Median simple average of Sweden and US. Warfarin 4mg passed based on one country US (AWP). No median. Warfarin 5mg failed based on 4 countries (Germany, Italy, UK, US {AWP}). Canada ranked 3rd highest above the median. Median average of 2 middle countries (Germany and Italy). Warfarin 10 mg passed based on 2 countries (France, US {AWP}). Canada ranked second. Median simple average of France and US

[117] No additional countries were added during these years

[118] This strength was not listed in ODB or Quebec formulary in 1999; listed in Quebec in 2000, therefore Quebec 2000 price used in 1999 and 2000.

[119] The application of the PMPRB Guidelines to the four drugs is based on publicly available price information. At the time of the analysis, the most current information available from a public source was for the year 2000.

[120] A notice of compliance for a generic coumadin was found in the Health Protection Branch database. Apotex is

listed as the manufacturer.

[121] The price information included in this table is based on the price information reimbursed by the drug plans. In the case of Saskatchewan and Ontario, this price represents a manufacturers' list price, for the other jurisdictions, the price may include a distribution margin. An WGDP study, conducted by the PMPRB, entitled "Inter-Provincial Price Comparison" estimated average distribution margins in 1999/00 to be 5.26% in British Columbia, 9.52% in Alberta, 10.01% in Manitoba, and 5.69% in Nova Scotia.

[122] In the ATC classification system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. The 4th level is a therapeutic/pharmacological/chemical subgroup.

[123] International = Exchange rates December 1995. The 10 mg strength passed based on 5 countries (Germany, France, Italy, Switzerland, US {AWP}). The 40mg passed based on one country (US {AWP}).

[124] References considered were The Canadian consensus conference on menopause and osteoporosis. Journal SOGC, Nov 1998. Gray J (ed. Therapeutic choices, 3rd edition. Canadian Pharmacist Association, 2000; Ottawa. AACE medical guidelines for clinical practice for management of menopause. Endocrine practice Vol. 5 No. 6; Nov/Dec 1999.

[125] International = Exchange rates December 1996 (did not go back 4 months);100 mg passed based on 2 countries (France, Switzerland). Median simple average of France and Switzerland. 1996-2000: PPS price of Prometrium 100mg remained the same. 1997-2000: Passed IPC (highest); 1998 Germany added and 2000 US (AWP) added 2000: IPC includes DVA

[126] The use of this product is relatively high in Manitoba's drug plan, represented 65% of the total estimated savings.

[127] The $6 million dollar figure assumes that the ODB price is not reflective of the manufacturers' list price in Ontario and assumes that the price increase experienced by the other provincial drug plans also exist in Ontario and will be submitted through the cost to operator mechanism.

[128] For the purpose of this calculation, the median Canadian ex-factory gate price was calculated based on the six provinces included in the analysis.