Marketing before patenting: implications for price controls in Canada

Joel Lexchin

Joel Lexchin, MD, is a professor of health policy in the School of Health Policy and Management at York University, Toronto, an associate professor in the Department of Family and Community Medicine at the University of Toronto, and works in the emergency department of the University Health Network, Toronto, Ontario, Canada.

Funding: There was no funding for this study.

Competing interests: In 2007 Joel Lexchin was retained by a law firm representing Apotex to provide expert testimony about the effects of promotion on the sales of medications. From 2007 to 2008 he was retained as an expert witness by the Canadian federal government in its defence of a lawsuit challenging the ban on direct-to-consumer advertising of prescription drugs in Canada.

Correspondence: Dr. Joel Lexchin, School of Health Policy and Management, York University, 4700 Keele St., Toronto ON M3J 1P3; 416 736-2100 x 22119, fax 416 736-5227; jlexchin@yorku.ca

Before 1987 Canada relied on the early appearance of generic drugs, via the compulsory licensing section of the Patent Act, to generate price competition and keep the prices of prescription medications affordable. The federal government began to abolish compulsory licensing with the signing of the Free Trade Agreement with the United States in 1987 and completed the task in 1993 following the adoption of the North American Free Trade Agreement and the Agreement on Trade Related Aspects of Intellectual Property Rights.

In place of compulsory licensing the government amended the Patent Act to establish the Patented Medicine Prices Review Board (PMPRB), which continues along the path of using a drug's patent status as a method of controlling prices. In the process Canada became the only country in the world to directly consider patent status as the basis for price regulation. Other countries have adopted a variety of other mechanisms for price control. At one extreme there is the United States, where Medicaid and the Veterans Administration require price discounts but otherwise prices are negotiated individually by pharmacy benefit managers and generic prices are determined by the discounts obtained through the buying power of pharmacy chains and pharmacy buying groups. The French system relies on an initial determination of the therapeutic value of the drug by the Haute Autorité de Santé. Then, depending on how beneficial the drug is, the Comité Economique des Produits de Santé allows companies to price it freely within reasonable boundaries (drugs with greater therapeutic value) or negotiates a price as well as a price-volume agreement (drugs with lesser therapeutic value). Generic drugs enter the market at a 40% discount or their prices are negotiated individually with the Comité.[1] The United Kingdom allows companies to set prices for their brand name drugs provided overall company profits are within 40% of a target that is negotiated between the Department of Health and individual companies. Companies do not set prices in isolation but adopt a pricing strategy for their entire range of products.[2] Similarly, companies marketing generic drugs are allowed to set their own prices provided they do not exceed the price of the brand name product.[3]

In Canada, once a medicine receives a patent the PMPRB has jurisdiction over its price, and that jurisdiction is lost only when the patent expires. Because generic drugs are not patented the PMPRB has no authority to regulate their prices. The PMPRB exercises its authority by subjecting each new patented medicine that is marketed to a series of pricing tests to determine whether the introductory price exceeds the price allowed under the board's regulations. In addition, while the product remains under patent the board also limits the rate at which the price can rise to roughly the rate of inflation.[4]

Companies do not always consider it necessary to obtain a patent before they market a drug, and each year a number of products are sold before they have received a patent; their prices, therefore, are by definition outside the authority of the PMPRB. As a consequence, companies have the freedom to set their own prices, although if prices are considered too high and less expensive equivalent products are available, the drugs may be rejected for listing on provincial drug formularies.

In Canada, authority to market a drug is termed a Notice of Compliance (NOC). Health Canada maintains a searchable online listing (http://205.193.93.51/NocWeb/nocqrye.jsp) of when drugs received their NOC. By drawing on the NOC database, annual PMPRB reports and a database listing when drug patents were applied for and granted (http://www.patentregister.ca/), it is possible to construct a list of drugs that were marketed before being patented over the period 2000–2008.

Over the 9 years a total of 192 new active substances (drug molecules that had never been sold before in Canada in any form) were introduced into the Canadian market, and 42 (22%) of these had no patent at the time they were first sold. Of these 42 drugs, 9 were excluded from further analysis because of inconsistencies between the 3 data sources. Table 1 lists all 33 drugs included in the analysis, along with the dates when they received an NOC and a first patent. Drugs were potentially being marketed between 54 and 2707 days before they came under PMPRB jurisdiction. (Table 1 gives the maximum period, as companies may choose to market a drug at some point after it receives an NOC.) One may have been on the market for over 7.4 years before being patented, and 12 may have been on the market for over 3 years before being patented. The time between patent application and receipt ranged from 1531 to 7096 days (data available on request).

Once the drug receives a patent of any sort, the PMPRB gains control over the pricing of the drug and reviews its price from the time it was initially marketed. If the price during the period between marketing and patenting is found to be excessive, the PMPRB calculates the excess revenue the company earned on the drug until the patent was granted and can order the company to repay the excess revenue to the federal government. Of the 33 products, 3 were eventually determined by the PMPRB to have exceeded the maximum introductory price, and the total excess revenue for these, as recorded in the PMPRB annual reports, was $9,289,688. The PMPRB is still investigating the price of one product to determine if it is excessive.

It is unclear why these drugs were marketed before they had a patent. One possibility is undue delay between when the patent was applied for and when it was granted. The mean time for all 33 drugs between the 2 dates was almost 10 years. Companies may have filed for patents later in the life cycle of these drugs than is commonly the case, but this would be an internal company decision without any public record. Whether the delay between applying for a patent and receiving one is different for drugs marketed before being patented and those marketed after being patented is not known.

Although only 3 of the 33 (9%) drugs were found to be overpriced, the fact that prices can go unregulated for up to 7.4 years is troublesome. If companies are charging excessive prices, then the additional revenue paid to the company may limit the ability of provincial formularies to list additional drugs. Only 1 of the 3 drugs with an excessive price was put on the Ontario Drug Benefit Formulary, which may not seem to represent a significant problem, but this loophole in the way drug prices are regulated needs to be recognized and monitored since more instances may occur in the future.

Although the excess revenue is eventually recovered, it is paid to the federal government, not the provincial governments, which funded the drug through their drug benefit schemes. If drugs are not covered by provincial plans, then private insurers and people paying out-of-pocket are still disadvantaged, and, like the provincial plans, they do not recover the excess money they paid out. Companies may not ultimately benefit by taking advantage of this loophole in the PMPRB regulations, but all payers suffer negative economic consequences.

Drugs marketed after being patented may also be initially priced excessively, but in these cases the board's authority starts as soon as the drug is being sold and therefore excessive prices will be recognized and reduced much earlier.

This commentary highlights a hitherto undocumented problem and presents an additional argument for moving towards a different method of controlling drug prices. Regulating drug prices based on patent status leaves significant gaps in the federal government's ability to control overall spending on medications. Brand name products whose patents have expired and generic drugs are not under federal price controls. Off-patent brand name products and generic drugs represented just over 35% of total ex-factory sales of $20 billion in 2008.[4] Although provinces may establish rules regarding prices for generic drugs, these rules are not uniform from province to province, and some provinces may be paying more for generic drugs than others. Thalidomide, now used for the treatment of multiple myeloma, is neither approved nor patented in Canada but is available under Health Canada's Special Access Program. The drug costs $44,000 for a standard course of treatment as a result of the United States distributor raising the price five-fold. Since the drug is not patented here the PMPRB is powerless to prevent such increases.[5]

After the PMPRB was created companies attempted to evade price controls by dedicating patents. (Patent dedication is essentially a voluntary surrender of the patent for public use.) Until the PMPRB changed its regulations and stopped this practice in early 1995, companies dedicated 449 patents on 136 drug products. At least 43 of these products were priced above the level allowed by the PMPRB, costing Canadian consumers an excess of almost $40 million.[6] The fact that few drugs have been overpriced to date is no indication of what may happen in the future. Patent dedication indicates that companies do not regard patent status as necessary in all cases in

Table 1: Drugs marketed in Canada before receiving a patent, 2000–2008

Year PMPRB* began price regulation	Brand name	Generic name	Manufacturer	Date of Notice of Compliance	Date first patent granted	Maximum possible days on market before PMPRB regulation	Excess revenue	Date of first listing on Ontario Drug Benefit Formulary
2000	Stemgen	Ancestim	Amgen	20 May 1999	28 Nov. 2000	558	None	
	Humalog & Humalog Mix	Insulin lispro	Eli Lilly	8 Oct. 1996	11 Apr. 2000	1281	$666,824	Sept. 15, 1999
	Alkeran	Melphalan	Glaxo Wellcome	27 Apr. 1994	10 Oct. 2000	2358	None	Dec. 1, 1994
	Renagel	Sevelamer	Genzyme	24 Feb. 2000	4 July 2000	131	None	
	Micardis	Telmisartan	Boehringer Ingelheim	26 Aug. 1999	21 Dec. 1999	117	None	Mar. 7, 2001
2001	Cerezyme	Imiglucerase	Genzyme	12 Feb. 1997	22 May 2001	1560	None	
	Coversyl	Perindopril	Servier	21 Sept. 1994	6 Mar. 2001	2358	None	Dec. 1, 1994
	Rescriptor	Delavirdine	Agouron	22 July 1998	20 Mar. 2001	972	None	Sept. 15, 1999
	Sustiva	Efavirenz	Bristol-Myers Squibb	19 Mar. 1999	28 Aug. 2001	893	None	Sept. 15, 1999
2002	Alphagan	Brimonidine	Allergan	24 Nov. 1997	3 Sept. 2002	1744	None	Sept. 15, 1999
	Cancidas	Caspofungin	Merck Frosst	19 July 2001	14 May 2002	299	None	Apr. 2, 2007
	Gleevec	Imatinib	Novartis	20 Sept. 2001	26 May 2002	432	None	
	Infergen	Interferon alfacon-1	InterMune	9 Mar. 1999	18 Sept. 2001	924	None	
	Integrilin	Eptifibatide	Schering	11 June 1999	20 Aug. 2002	1166	None	
	Lovenox	Enoxaparin	Aventis	26 Nov. 1997	30 July 2002	1707	None	Jan. 30, 2003
	Pulmozyme	Dornase alfa	Hoffmann-La Roche	8 Sept. 1994	5 Feb. 2002	2707	None	
	Travatan	Travoprost	Alcon	9 Nov. 2001	14 May 2002	186	None	July 29, 2002
	Zenapax	Daclizumab	Hoffman-La Roche	4 Jan. 2000	13 Aug. 2002	952	None	
2003	Agenerase	Amprenavir	GlaxoSmithKline	1 Mar. 2001	7 Jan 2003	677	None	Jan. 30, 2003
	Alertec	Modafinil	Shire	26 Feb. 1999	10 Dec. 2002	1383	None	June 27, 2008
	Evra	Norelgestromin / ethinyl estradiol	Janssen-Ortho	20 Aug. 2002	24 Dec. 2002	126	$3,000,000	
2004	Adderall XR	Mixed salts amphetamine	Shire	23 Jan. 2004	13 Apr. 2004	81	$5,622,864	
2005	Sensipar	Cinacalet	Amgen	Aug. 9, 2004	30 Aug. 2005	376	None	
	Zelnorm	Tegaserod	Novartis	Mar. 12, 2002	15 Mar. 2005	1099	None	
2006	Macugen	Pegaptanib	Pfizer	2 May 2005	14 Feb. 2006	288	None	
	Sativex	Delta-9-tetrahydrocannabinol/ cannabidiol	Bayer	15 Apr. 2005	25 Apr. 2006	375	None	
2007	Nexavar	Sorafenib	Bayer	28 July 2006	13 Feb. 2007	200	None	
	Orencia	Abatacept	Bristol-Myers Squibb	29 June 2006	22 May 2007	327	None	
	Replagal	Agalsidase alfa	Shire	26 Feb. 2004	26 June 2007	1216	None	
2008	Intelence	Etravirine	Janssen-Ortho	27 Mar. 2008	20 May 2008	54	None	
	Lucentis	Ranibizumab	Novartis	26 June 2007	10 June 2008	350	None	
	Myozyme	Alglucosidase alfa	Genzyme	14 Aug. 2006	29 Apr. 2008	624	None	
	Zevalin	Ibritumomab	Bayer	10 May 2005	15 July 2008	1162	Under investigation	

PMPRB = Patented Medicine Prices Review Board
Data sources: Date of Notice of Compliance: Notice of Compliance search at http://205.193.93.51/NocWeb/nocqrye.jsp; Date first patent granted: patent register search at http://www.patentregister.ca/; Excess revenue: *Annual report 2008.* Ottawa: PMPRB; 2009.

order to protect their products from generic competition. Marketing before patenting may become more common in the future.

The best remedy for the various problems associated with using patent status to regulate prices is simply to treat all drugs on the market equally and regulate all prices.

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Citation: Lexchin J. Marketing before patenting: implications for price controls in Canada. *Open Med* 2008;4(3):139-142.

Published: 27 July 2010