The wider impact of the promise of the patent doctrine in Canada

Final report

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Table of contents

Executive summary.................................................................................................................................................. 3

1. Introduction.......................................................................................................................................................... 8
   1.1. Background on the promise of the patent doctrine and the project......................................................... 8

2. The effect of promise doctrine on international pharmaceutical revenues due to External Reference Pricing ........................................................................................................................................ 11
   2.1. Background on external reference pricing................................................................................................. 11
   2.2. The spillover effect of prices: establishing the ERP links ......................................................................... 12
       2.2.1. The direct impact of lower Canadian prices......................................................................................... 14
       2.2.2. The indirect impact.................................................................................................................................. 17
   2.3. Quantifying the spillover impact.................................................................................................................. 19
       2.3.1. The hypothetical model approach....................................................................................................... 20
       2.3.2. The actual model approach .................................................................................................................. 24
   2.4. Conclusion..................................................................................................................................................... 25
Table of Figures

Figure 1: Setting out the link between Canada and other markets .................................................. 4
Figure 2: The first year impact of the promise doctrine in international markets: a hypothetical effects approach .................................................................................................................. 5
Figure 3: The first year impact of the promise doctrine in international markets: an actual effects approach .................................................................................................................. 6
Figure 4: Setting out the link between Canada and other markets .................................................. 19
Figure 5: The first year impact of the promise doctrine in international markets: a hypothetical effects approach .................................................................................................................. 23
Figure 6: The first year impact of the promise doctrine in international markets: an actual effects approach .................................................................................................................. 25

Table of Tables

Table 1: Countries affected by prices in Canada through ERP links ............................................... 13
Executive summary

Pharmaceutical Research and Manufacturers of America (PhRMA) asked Charles River Associates (CRA) to identify and quantify the impact of the promise of the patent doctrine to the innovative pharmaceutical industry outside of Canada. In particular, the objective was to demonstrate and quantify the impact that lower prices of affected products in Canada has on prices in other markets due to external reference pricing (ERP).

Since the introduction of the promise doctrine in 2005, a series of legal cases have been brought and the Federal Court has decided to revoke the patent using the utility argument for 17 products. These decisions have allowed generic manufacturers to launch earlier than would otherwise be the case.\textsuperscript{1}

\textit{The effect of promise doctrine on international pharmaceutical revenues due to External Reference Pricing}

The first task was to set out the countries that reference Canada directly or indirectly (by referencing countries that reference Canada. We used a range of international databases to establish the countries that included Canada and the ERP rules. The results of this is shown in Figure 1 below.

\textsuperscript{1} Needham, (2014), “Pharmaceutical companies express concerns about Canada revoking drug patents over their usefulness”.
There are two approaches to estimating the impact that prices of medicines in Canada have on any of the countries discussed above.

First, we can use the ERP relationship and the distribution of prices to determine the impact if the rules are applied following the price reduction. We call this the hypothetical approach because

- We assume that the ERP rules are updated following the price reduction and calculate the impact on sales.
- This estimates the impact in the absence of any other changes in the market rather than using actual prices observed in the market.

The results of the model are presented in Figure 2 below. The international effects of Canada’s invalidation of patents through the “promise of patent doctrine” amount to a total estimated loss of USD $110.41 million in originator product sales outside of Canada in the first year after genericisation. This is composed of USD 105.36 million losses in first round markets (markets that directly reference Canada) and the remaining USD 5.05 million in second round countries. This represents the lost sales in the year following the generic entry
in Canada, so represent a significant underestimation of overall losses expected prior to loss of exclusivity for the 17 products.

**Figure 2: The first year impact of the promise doctrine in international markets: a hypothetical effects approach**

<table>
<thead>
<tr>
<th>Round I ($m)</th>
<th>Round II ($m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>44.66</td>
</tr>
<tr>
<td>Colombia</td>
<td>2.95</td>
</tr>
<tr>
<td>Egypt</td>
<td>1.73</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>2.14</td>
</tr>
<tr>
<td>South Africa</td>
<td>7.48</td>
</tr>
<tr>
<td>Taiwan</td>
<td>6.40</td>
</tr>
<tr>
<td>Australia</td>
<td>28.07</td>
</tr>
<tr>
<td>Mexico</td>
<td>8.17</td>
</tr>
<tr>
<td>New Zealand</td>
<td>3.13</td>
</tr>
<tr>
<td>Bahrain</td>
<td>0.09</td>
</tr>
<tr>
<td>Jordan</td>
<td>0.02</td>
</tr>
<tr>
<td>Lebanon</td>
<td>0.09</td>
</tr>
<tr>
<td>Morocco</td>
<td>0.06</td>
</tr>
<tr>
<td>Oman</td>
<td>0.13</td>
</tr>
<tr>
<td>South Korea</td>
<td>4.28</td>
</tr>
<tr>
<td>UAE</td>
<td>0.38</td>
</tr>
</tbody>
</table>

**Total round I losses: 105.36 Total round II losses: 5.05**

*Source: CRA analysis*

The estimated losses above are substantial but only represent the impact in the first year after genericisation of the products in Canada. Estimating the overall impact of the losses associated to these products over time is challenging. To carry out such an analysis, would require information on when market exclusivity is lost in each of the markets and whether this would have occurred before the loss of exclusivity in Canada (in the absence of the impact of the promise doctrine).

However, we can derive a ballpark estimate based on the calculated one year losses. On an average there is 6.75 years between when products lose exclusivity due to the promise doctrine and the loss of market exclusivity that would otherwise take place in Canada. Assuming the same loss would occur in each of these years, we can estimate the total loss over the period. The application of this methodology leads to overall losses of revenue due to
the promise of the patent doctrine and spillovers caused by ERP in international markets of $745 million.

The second approach uses actual prices to estimate the impact. This has the advantage of being based on actual data (so we don’t need to make assumption about the application of ERP rules) but in this case we cannot attribute the change in price to the promise doctrine with the same degree of certainty (as other changes will have occurred over the same period affecting prices). We apply the actual approach to a subset of countries, where we have IMS data and where they formally include Canada in their ERP rules. As Figure 3 shows, the loss attributed to this subset of countries in the actual and hypotheticals model are similar, USD 65.36 million versus USD 68.29 million. If we combine the estimated actual losses for the six markets with available IMS data with the estimated hypothetical losses for the remaining markets, the overall losses in first round countries are USD 108.29 million (compared to hypothetical estimation losses at USD 105.36 million) and overall first and second round losses are USD 113.34 million (compared to hypothetical estimation losses at USD 110.41 million).

Figure 3: The first year impact of the promise doctrine in international markets: an actual effects approach

<table>
<thead>
<tr>
<th>Hypothetical effects formal round I ($m)</th>
<th>Actual effects formal round I ($m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil 44.66</td>
<td>Saudi Arabia 2.14</td>
</tr>
<tr>
<td>Colombia 2.95</td>
<td>South Africa 7.48</td>
</tr>
<tr>
<td>Egypt 1.73</td>
<td>Taiwan 6.40</td>
</tr>
<tr>
<td>Total hypothetical losses 65.36</td>
<td>Total actual losses 68.29</td>
</tr>
</tbody>
</table>
Source: CRA analysis

Clearly in both approaches there are a large number of simplifying assumptions and caveats. The similarity between the estimates does not mean that there is not a significant degree of uncertainty regarding the actual damages due to ERP but provides significant reassurance regarding the order of magnitude.

Conclusion

The findings in this report shows that the promise doctrine has a negative international impact on markets that directly or indirectly (through referencing other markets) include Canada in their ERP baskets. We estimate a loss of over $110 million from ERP spillovers in the first year after genericisation alone due to the promise doctrine. Taking into account the sustained effect we estimate an overall loss of over $745 million. The losses calculated are subject to assumptions but given the two approaches are similar, they provide a robust estimation of the magnitude of impact. The two methodologies lead to very similar losses estimated but the price analysis based on actual sales data indicates that the real decrease in prices is even larger than the estimation. The analysis highlights that the application of the promise doctrine leads to substantial negative price spillovers in international markets.
1. **Introduction**

Pharmaceutical Research and Manufacturers of America (PhRMA) asked Charles River Associates (CRA) to identify and quantify the impact of the promise of the patent doctrine to the innovative pharmaceutical industry outside of Canada. In particular, the objective was to demonstrate and quantify the impact that lower prices of affected products in Canada has on prices in other markets due to external reference pricing (ERP).

1.1. **Background on the promise of the patent doctrine and the project**

Under the World Trade Organization’s Trade Related-Aspects of Intellectual Property Rights (TRIPS) agreement, in order to obtain a patent, an invention must be (1) new, (2) non-obvious and (3) useful (utility measure). Typically, the threshold of utility is easily met for inventions that have commercial applicability, such as a drug candidate. Unlike other countries, Canada has imposed an additional requirement that allows a patent to be challenged and claimed invalid on the grounds of promised utility. This is known as the ‘promise of the patent doctrine’.

The new doctrine, which was introduced in 2005 based on judicial interpretation of the Canadian Supreme Court’s 2002 decision in AZT, allows a patent to be challenged and declared invalid or void by the Federal Court in Canada under the Patent Act subsection 60(1). Under the promise doctrine, the patent application must demonstrate that the invention meets the promises deemed by the court to be made in the application, by:

- demonstrating use directly in working examples, or
- extrapolating from working examples via sound prediction by the filing date of the application.

Since its introduction in 2005, a series of legal cases have been brought on the ‘promise doctrine’ grounds and the Federal Court has decided to revoke the patent using the utility

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2 WTO, “TRIPS: Standard Concerning the availability, scope and use of Intellectual Property rights – Article 27”.

3 “The law surrounding the “promise of the patent” holds a patent claim invalid for lack of utility if the patented invention fails to achieve a promise made in the specification, even if the invention may otherwise possess a scintilla of usefulness”. Gold and Short (2014), “The promise of the patent in Canada and around the world”, Canadian Intellectual Property Review, 30:1.

4 The case of Eli Lilly v. Novopharm (olanzapine; 2010 FCA 197) is commonly quoted “Where the specification does not promise a specific result, no particular level of utility is required; a “mere scintilla” of utility will suffice. However, where the specification sets out an explicit “promise”, utility will be measured against that promise.”

5 Please note that during the analysis the notions of the ‘promise of the patent doctrine’ and ‘the promise doctrine’ will be used interchangeably.


argument on 17 products. These decisions have allowed generic manufacturers to launch earlier than would otherwise be the case.⁸

For a long time, other countries such as the US have voiced continuous concerns about the level of intellectual property rights (IPR) protection in Canada. In the past 25 years, Canada has been mentioned in every United States Trade Representative’s (USTR) Special 301 Report, which identifies countries with IPR deficiencies. Despite recognizing that progress has been made in several areas during recent years, both the 2014 and 2015 report emphasise a concern regarding the promised utility doctrine.⁹ The main arguments against this promise doctrine that countries or the industry have advanced, include its inconsistency with Canada’s international obligations and the significant uncertainty and burdens generated by the doctrine:

- This is regarded unfair and burdensome for innovators as the promise doctrine involves three aspects: (1) a subjective interpretation of the ‘patent application’ from a judge, (2) the additional requirement that the promised utility either be demonstrated or be based on a “sound prediction” of utility at the time of the patent application; and (3) the evidence for the predicted utility be disclosed in the original patent application. These involve a degree of subjectivity and additional burden to innovators.¹⁰ In particular, it is argued it “puts at risk many useful patents, because any stray phrase professing a benefit of the invention could be construed as a promise by the courts”.¹¹

- The promise doctrine poses significant uncertainty to patent holders or future patent applicants leading to reduced incentives to invest in innovation in pharmaceuticals. This is caused by the requirement to have a ‘sound prediction’ of the future use of the invention, which in order to be accurate can be costly, time consuming and risk the novelty of the invention.¹² Indeed, the World Economic Forum has reported that Canada’s innovative power has decreased in recent years in terms of patents and pharmaceutical industry export share.¹³

- International companies and their significant investments and trade arrangements are also negatively impacted. The promise doctrine is damaging for trade and conflicts with provisions included in international trade agreements such as the North America

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⁸ Needham, (2014), “Pharmaceutical companies express concerns about Canada revoking drug patents over their usefulness”.


¹¹ Szweras and Rana July 2014, “Promise of the patent: Post Plavix”, Biotechnology Focus

¹² Ibid.

Free Trade Agreement (NAFTA) and the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights.¹⁴

The most obvious impact of the promise doctrine is generic entry in Canada. This clearly has an impact on the revenues of the effected patent holder. However, there are other potential impacts outside of Canada. The aim of this research is this by quantifying the impact of the ‘promise doctrine’ due to External Reference Pricing (ERP) channel, i.e. the impact of lower prices of medicines in Canada on prices in other pharmaceutical markets.

2. **The effect of promise doctrine on international pharmaceutical revenues due to External Reference Pricing**

In this chapter, we look at the impact of the ‘promise doctrine’ on international pharmaceutical markets due to ERP. This uses a number of different approaches to quantify the impact of price reduction observed in Canada (due to entry of generics) for the set of 17 molecules in other markets that directly or indirectly reference the country.

2.1. **Background on external reference pricing**

Countries use a range of policies and mechanisms in order to determine prices of pharmaceutical products, including statutory pricing, ERP, negotiations and price-volume agreements. The focus of this analysis is on the impact arising due to ERP, which is a commonly implemented pricing mechanism that has been used for a long time and is being applied by an increasing number of countries. ERP is commonly associated with European countries, however, it is increasingly used globally by high and middle income countries. By definition, ERP is the practice that involves using the prices from a basket of other countries to set national pharmaceutical prices, which creates pricing relationships and links between pharmaceutical markets. There are a range of different ways that ERP can be applied:

- **The pricing rule**: the method of calculating the ERP varies dramatically across countries. The most common methods include the use of the average price, the lowest price and the median price of all the countries in the reference basket and may allow for an additional adjustment (for example, an arbitrary difference of 10%).

- **Formal versus informal**: where a formal ERP system is defined as a set of rules by which the prices in a basket of countries are used in a formula to determine prices. In contrast, an informal system is one in which the use of these prices and the inclusion of particular countries are determined on an ad-hoc basis.

- **At launch versus updated over time**: many systems implement ERP to set the price of a product when it is launched onto the market but some of these prices are subsequently updated over time. Over recent years we have seen more systems frequently update their prices. This can occur at regular intervals or at the discretion of the payer. With the benefit of modern computer data systems, it is relatively easy to update the international price comparisons and apply a succession of price cuts country-by-country for established products.

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15 We use the term external reference pricing through this report. It also known as international reference pricing; in both cases this refers to the practice by which a country sets pharmaceutical prices based on a comparison with prices in other countries.

At regulatory approval or during the reimbursement negotiation: in some countries ERP is applied when the product receives regulatory approval as opposed to during the negotiation for reimbursement.

Primary method versus part of a system of price determination: In some systems ERP is the primary determinant of prices whereas in other it contributes in the process but other mechanisms are given priority. For example, following reforms in 2011, Germany uses ERP but this is only used if other methods of determining prices are not possible (internal reference pricing or a negotiation with the manufacturer).

The impact of ERP occurs both directly and indirectly. A direct effect arises when country X references the prices in country Y. However, country Y can also have an indirect effect on country Z, as it references country X (which was affected by the prices in country Y). The countries that reference Canada directly and indirectly will be discussed in the sections below. The countries that directly reference Canada are also referred to as ‘first round countries’, whereas the countries that indirectly reference Canada are also referred to as ‘second round countries’.

2.2. The spillover effect of prices: establishing the ERP links

This part of the analysis focuses on identifying the impact that lower prices in Canada as a result of generic entry following the application of the promise doctrine have on prices of medicines in other markets due to ERP links. In order to quantify this effect, we need to set out the links between countries that may be impacted. In Table 1 below, we present a list of countries that reference Canadian prices, both directly and indirectly, in the ERP application. The table includes the size of the ERP basket, the pricing rule adopted and whether the ERP process is formal or informal.
Table 1: Countries affected by prices in Canada through ERP links

<table>
<thead>
<tr>
<th>Country</th>
<th>ERP basket size</th>
<th>Price rule</th>
<th>Formal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First round</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>9 countries</td>
<td>Minimum ex-factory price</td>
<td>Yes</td>
</tr>
<tr>
<td>Colombia</td>
<td>17 countries</td>
<td>25% percentile of list/transaction price</td>
<td>Yes</td>
</tr>
<tr>
<td>Egypt</td>
<td>36 countries</td>
<td>Minimum price in the basket discounted at 10%</td>
<td>Yes</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>30 countries</td>
<td>Minimum ex-factory and wholesaler price</td>
<td>Yes</td>
</tr>
<tr>
<td>South Africa</td>
<td>4 countries</td>
<td>International benchmarking</td>
<td>Yes</td>
</tr>
<tr>
<td>Taiwan</td>
<td>10 countries</td>
<td>85% of median wholesaler price</td>
<td>Yes</td>
</tr>
<tr>
<td>Australia</td>
<td>3 countries</td>
<td>Not exceed referenced prices</td>
<td>No</td>
</tr>
<tr>
<td>Mexico</td>
<td>14 countries</td>
<td>Average of 7 countries + not exceed the other 7</td>
<td>No</td>
</tr>
<tr>
<td>New Zealand</td>
<td>3 countries</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>Bahrain</td>
<td>5 (GCC) countries</td>
<td>Minimum price in EU and export price in SA</td>
<td>Yes</td>
</tr>
<tr>
<td>Jordan</td>
<td>8 countries</td>
<td>Median ex-factory</td>
<td>Yes</td>
</tr>
<tr>
<td>Lebanon</td>
<td>14 countries</td>
<td>Minimum ex-factory, wholesaler &amp; retail prices</td>
<td>Yes</td>
</tr>
<tr>
<td>Morocco</td>
<td>7 countries</td>
<td>Minimum ex-factory, wholesaler &amp; retail prices</td>
<td>Yes</td>
</tr>
<tr>
<td>Oman</td>
<td>5 (GCC) countries</td>
<td>Minimum CIF import price</td>
<td>Yes</td>
</tr>
<tr>
<td>South Korea</td>
<td>8 countries</td>
<td>No formula – price negotiation</td>
<td>No</td>
</tr>
<tr>
<td>UAE</td>
<td>5 (GCC) countries</td>
<td>Minimum ex-factory and import prices</td>
<td>Yes</td>
</tr>
</tbody>
</table>


Table 1 above represent the ERP rules at the time of writing this report. In reality the products affected by the promise doctrine observed generic entry over different periods of time, such that different ERP rules may have applied. This is therefore a simplifying assumption.
2.2.1. The direct impact of lower Canadian prices

The prices of medicines in Canada directly impact the prices of medicines in countries that include Canada as one of the reference countries in their ERP system. Canada is included directly in the basket of nine countries, namely: Brazil, Colombia, Egypt, Saudi Arabia, South Africa, Taiwan, Australia, Mexico and New Zealand. These are countries of disparate levels of economic development and are located across different geographic regions.

**Brazil**

Price regulation in Brazil is primarily defined by the Pharmaceutical Price Council (CMED), which is an inter-ministerial body linked to the Ministry of Health (MoH). After a dossier for a new medicine is submitted by the manufacturer, the National Health Surveillance Agency, Anvisa, performs a clinical and economic assessment against a chosen comparator and the Office of Economic Evaluation of New Technologies and the Office of Economic Regulation make a recommendation to CMED on the ceiling price. The Executive Secretariat of CMED then makes the decision on the ceiling price (within a deadline of 3 months after submission). These prices, which are set at launch, are maximum commercialisation prices (price caps) in the Brazilian market and are set based on ERP and other P&R mechanisms.\(^{22}\)

**Colombia**

The National Price Commission of Pharmaceutical and Medical Devices (NCPM) is the authority with responsibility for price setting in Colombia. In theory, there should be two prices in Colombia, separately in the private (no price controls) and public sectors (price controls). However, prices set in the public sector are often used in both markets. The ERP system in Colombia was first established in 2006 but it was focused on setting the prices of a number of selected molecules at the average of the three lowest prices in the basket of neighbouring countries. The basket of countries has since been updated to exclude Uruguay and Venezuela and include Organisation for Economic Co-operation and Development (OECD) countries. Maximum prices are set at the 25\(^{th}\) percentile of a basket of 17 to 18 countries, selected from the two groups above-mentioned.\(^{23}\)

**Egypt**

Historically, despite Egypt being the largest pharmaceutical market in the Middle East/North Africa Region, pharmaceutical prices have been set at very low levels. In 2009, Egypt switched from a cost plus to an ERP system in an attempt to reduce corruption and modernise the industry, bringing it more in line with international best practice. Under the new framework, which was reinstated by a Ministerial Decree (No. 499) in 2012, prices of medicines were to be set to retail medicine costs in other countries. Price is set referring to price data from 36 countries and applying 10% discount to lowest price in the basket.\(^{24}\)

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reference price used in the basket countries is the public price - not the Net Wholesale Price (NWP) - and local mark-ups are deducted to derive local NWP (reducing the reference price further still).

Saudi Arabia

Saudi Arabia is characterized by a complex and non-transparent ERP system. In 2011, a new pricing regime was established. ERP is determined by considering the lowest medicine prices in a basket of 30 countries, including markets that have a significantly different level of economic development, therapeutic focus and demography.25

The Saudi Drug and Food Authority (SFDA) approves the price of innovative products prior to their launch in the market. SFDA fixes the lowest price through the use of ERP, and bases the pricing of products on:26-27

- The manufacturer’s ex-factory, wholesale, and retail prices in the country of origin.
- Proposed export Cost, Insurance and Freight (CIF) prices to Saudi Arabia.
- CIF prices in thirty other countries where the product is marketed (including other markets in the region where prices are relatively low, such as Algeria and Egypt).

Amongst the criteria, the SFDA also considers therapeutic significance, pharmacoeconomic results and prices of similar therapeutic alternatives.

The SFDA revises prices every five years, which is the timeframe for renewal of product registration. The revised price is again based on the ERP. Prices can also be revised earlier than five years when the product’s price in the country of origin changes or there are significant changes in the exchange rate and the company requests re-pricing to the SFDA.28

South Africa

In South Africa, the price of medicines is highly regulated and since 1997 the medicines law29 requires a “single exit price” (SEP) for all medicines sold in the private market. SEP is set for all prescription medicines by government (at ex-factory level) regardless of the channel of purchase. Pharmaceutical manufacturers must inform the pricing committee of the price they intend to market the product. SEP is reviewed and adjusted if necessary using therapeutic reference pricing using a basket of similar drugs. For innovative drugs, multinational companies must benchmark their products directly against equivalent products in a basket of

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28 Products that are priced at less than 20 SR are exempted from price revision.
countries. The countries selected in the basket are Australia, Canada, New Zealand, Spain and South Africa. Medicines are sold into retail pharmacies in South Africa at the SEP, which is printed onto the packaging of the medicine and is regarded as the fixed maximum selling price of medicine, excluding the dispensing fee issued by a pharmacy.

**Taiwan**

In Taiwan, the manufacturer submits a dossier for review to the National Health Insurance Administration (NHIA) and the latter requests the National Institute of Health Technology Assessment (NIHTA) to conduct an independent assessment and send a report with recommendations back. These form the basis of the Pharmaceutical Benefit and Price Schedule (PBPS) decision of reimbursement and price. Prices of medicines are initially recommended by the expert consultation group and further approved by the PBPS stakeholder meeting which delivers the final decision to the NHIA. ERP is one of the options used by the NHIA in setting prices of all branded, both on- and off-patent medicines and the price level represents the reimbursement price for all medicine providers within the NHI system. In addition, price incentives in the form of premiums are offered for the use of local data and pharmacoeconomic analysis included in the dossier. The NHIA carries out biennial price reviews to reflect market conditions.

**Australia**

In Australia, the prices of medicines listed under the Pharmaceutical Benefits Scheme (PBS) are set by the Pharmaceutical Benefits Pricing Authority (PBPA or Pricing Authority). When setting prices, ERP is used as a supportive criterion, among several other pricing methods. The countries that Australia references are Canada, the UK and New Zealand, as reported in PBPA Policies, Procedures and Methods.

**Mexico**

In the private sector in Mexico, prices are regulated by the Ministry of Economy. Manufacturers voluntarily submit the maximum retail price for patented medicines and information about ex-manufacturers’ prices in the six markets where the medicine has the highest sales. Prices are then set at the weighted average of ex-factory in these six markets.

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31 Kennedy-Martin et al., (2014), “The Health Technology Assessment environment in Mainland China, Japan, South Korea and Taiwan”, Value in Health Regional 3C.


New Zealand

In New Zealand, the body with responsibility for controlling pharmaceutical products is the Pharmaceutical Management Agency (PHARMAC). The agency makes decisions to assist the government with pharmaceutical spending, including negotiation of prices subsidy levels and subsidised lists. In the price setting process, PHARMAC involves an informal comparison and benchmarking of prices of medicines to those in Australia, Canada and the UK.

2.2.2. The indirect impact

There is an additional impact of prices of pharmaceutical products in Canada on countries that reference countries that include Canada in the basket of countries in their ERP system. Canada is included indirectly in the basket of seven countries, namely: Bahrain, Jordan, Lebanon, Morocco, Oman, South Korea and the UAE. Based on these relationships there is potential for a considerable impact on the Middle East countries and particularly in the GCC countries.

Bahrain

The National Health Regulatory Authority (NHRA) in Bahrain is the body with responsibility for price setting. The Pharmaceutical Products Regulation Department set the price as the minimum of prices in the other GCC countries.

Jordan

In Jordan, pharmaceutical prices are set by the Pricing Committee of the Jordan Food and Drug Administration (JFDA). It determines price of all on- and off-patent innovative medicines at the median ex-factory reimbursed price in selected European markets including: UK, France, Spain, Italy, Belgium, Greece and the Netherlands, the export price to Saudi Arabia and the price in the country of origin.

Lebanon

In Lebanon, the price of innovative medicines is set by the Pricing Committee, which is part of the Ministry of Health. The price is determined as the minimum of ex-factory, wholesaler and retail prices in 14 countries, including Saudi Arabia. In 2004, following a survey on medicine


37 NHRA (2013), “Resolution No (4) of 2013 with respect to the pricing of medicines and pharmaceutical products and setting the profit margin”, Available at: http://www.nhra.bh/SitePages/View.aspx?PageId=42.


39 Ibid.
prices in Lebanon, the government reviewed the price comparing these to Jordan and Saudi Arabian markets. This resulted in the lowering of prices for a large number of medicines. The Government also implemented regressive margins for importers, wholesalers and retailers, and published "patient prices" on a website and in the Lebanon National Drug Index.40

**Morocco**

The Ministry of Health in Morocco determines prices of innovative medicines by referring to wholesale prices (excluding taxes) in seven countries. The Moroccan price is set at the lowest price in the basket of countries, including: France, Belgium, Spain, Portugal, Greece, Turkey and Saudi Arabia.

**Oman**

In the Sultanate of Oman, pharmaceutical prices are set by the Directorate General of Pharmaceutical Affairs and Drugs Control. ERP is applied to all the products in the market and medicine prices are set as the minimum CIF import price in the GCC countries.41

**South Korea**

Since 2006, South Korean reimbursement and pricing authority and decision making is split between two separate agencies, HIRA and NHIC, respectively. First, HIRA carries out an HTA evaluation and then prices are decided though negotiations between the manufacturer and NHIC. During the price setting, the body considers a medicine’s clinical usefulness and cost effectiveness, which includes an element of ERP to set a price ceiling as a starting point for negotiations. ERP has previously been the main price-setting mechanism but has now a more informal and ad-hoc application.42

**United Arab Emirates**

The responsible body for medicine price setting in the UAE is a Ministry of Health Committee. The prices of all innovative products with minor exceptions are determined as the minimum ex-factory and import prices in the Gulf Cooperation Countries (GCC) and the country of origin.43 In addition, they are regular updates, for example in 2006, following a survey the prices of many innovative products were reviewed and subsequently reduced.

The direct (as indicated by a solid line) and indirect effects (as indicated by a dotted line) are summarised in Figure 4.

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40 Cameron et al. (2011), "The world medicines situation 2011", WHO.
41 Ibid.
43 Ibid.
2.3. Quantifying the spillover impact

There are two approaches to estimating the impact that prices of medicines in Canada have on any of the countries discussed above. First, we can use the ERP relationship and the distribution of prices to determine the impact if the rules are applied following the price reduction in Canada. We call this the hypothetical approach because

- We assume that the ERP rules are updated following the price reduction in Canada and calculate the impact on sales in the ERP markets.
- This estimates the impact in the absence of any other changes in the market rather than using actual prices observed in the market.

The second approach uses actual prices to estimate the impact. This has the advantage of being based on actual data (so we don’t need to make assumptions about the application of ERP rules) but in this case we cannot attribute the change in price to the promise doctrine with the same degree of certainty. We discuss this approach in the next section.
2.3.1. The hypothetical model approach

The first approach uses a simulation model that is based on the size of the market for the 17 products across all impacted countries, the pricing rule they apply and the price drop that is observed in Canada.

First, using IMS quarterly data from Q1 in 2005 to Q4 2014, the price drop in Canada is calculated for the 17 products whose patent has been revoked as a result of the promise of the promise doctrine application. The price drop, estimated at 28.4%, is calculated from the weighted average prices of all branded forms of the 17 molecules in each Canada, for a period before and after the entry of generic.44

We use this price drop and the ERP rules to determine the impact on prices in the other countries. This hypothetical effects model requires a number of assumptions:

- **One-year effects**: The model accounts for a single year impact, occurring in the year following generic entry in Canada. This provides a more accurate estimation and avoids the potential future impact of a patent expiring at the time initially projected.

- **Frequency of price updates**: The different ERP systems encountered in the analysis have diverging rules for price update frequency, from biennial to once in a few years or even driven by a particular market event. However, for simplicity it is assumed that all the markets included in the analysis update the prices in the year following generic entry in Canada.

The first task is to determine the impact of the price reduction. We have created price indices for all the countries included in the model.45 We adjust the Canada price index to reflect the price after genericisation. We then use this to determine if the price reduction in Canada would have had an impact on the prices in other countries (given the ERP basket and the distribution of prices). For example, if the system uses a minimum price but the Canadian prices is not the lowest, we would not expect any impact on that market. We describe this as

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44 The molecule-by-molecule difference in branded product prices between Time Period 1 (the quarter of patent protection loss and the three quarters prior) and Time Period 3 (the fifth through eighth quarters after patent protection loss) were calculated. All price differences (Time Period 3 minus Time Period 1) that were negative were summed in order to find a weighted average price drop. Then the summed weighted average price drop was divided by the sum of all of the weighted average brand prices for Time Period 1. This results in the price drop figure of 28.4% for the 17 products in Canada where the patent was revoked as a result of the “promise of patent doctrine.”

45 Where price indices don’t exist we have estimated the price level rankings relative Canada, these are indexed as per 2013 GDP per capita at PPP used as the proxy for pharmaceutical price levels in those countries. GDP per capita PPP (international USD) are retrieved from the World Bank database.
a situation where the Canadian prices is not “binding”. To determine prices we assume the following:

- **For first round country price reduction with minimum price rule:** A scaled price reduction occurs in countries where a minimum price formula is applied and there is an estimable probability that Canada is sometimes the country with the lowest price levels in the ERP basket. In these cases, we take into account the number of countries in each ERP basket that might have the lowest prices (as defined by a given percentage from the lowest price). This method is applied in: Brazil, Egypt, Saudi Arabia, and New Zealand.

- **For first round country price reduction using 25th percentile price rule:** A scaled price reduction occurs where a 25th percentile formula is applied and there is a probability that Canada falls in this category. This method is applied in Colombia.

- **For first round country price reduction with an average/median price rule:** Here, the model accounts for the percentage change in average or median normalized price levels before (t) and after (t+1) the price drop in Canada. This percentage change in the median or average price level of the reference basket is applied as a scaled reduction to the 28.4% price drop seen in Canada allowing for the number of product in the basket. This method is applied (with appropriate variations) in: Taiwan, South Africa, Australia, and Mexico.

An adjustment is also made depending on whether the system is formal or informal ERP. In countries where an informal ERP system is used, an additional scaled reduction is applied to account for the likelihood that ERP will not be used systematically in some cases. An informal reference system is used in Australia, Mexico, and New Zealand.

The same rules are then applied to second round countries – using the price reduction in the first round country. Indirectly affected markets that apply minimum price formula, namely South Korea, UAE, Oman, Bahrain, Lebanon, Morocco, and Jordan are bound by a scaled price reduction relative to the price drop in the 1st round country that they reference in their ERP basket (Saudi Arabia or Taiwan). The scaled adjustments are based on the normalized post-price drop price level in the applicable reference country, and their magnitude is dependent on the number of countries in addition to the target 1st round reference country in a given reference basket that might have the lowest prices.

The price reduction is then applied to the market size of the 17 products in the first and second round countries. In those countries where IMS data is available (Brazil, Colombia, Egypt, Saudi Arabia, South Africa, and Taiwan), the market size is calculated from product revenues for the 17 molecules in the year prior to generic entry. In the remaining set of

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46 The middle income countries impacted by Canadian price through ERP, are significantly less wealthy countries than Canada and have lower price levels. As a result, a price decrease in Canada would not normally have an impact on these markets. (We describe this a situation where the price in Canada is not binding). However, given the size of the price reduction due to loss of patent protection, Canadian prices are likely to have an impact on these markets in some cases.
countries where IMS is not available, a proxy is used. This is calculated by the portion of the prescription pharmaceutical market ($ value) that the 17 molecules in T1 in each country would represent, then averaged across the six non-Canada countries for which IMS data is available. This average is then applied to the prescription pharmaceutical market in each of the 1st round countries for which there is no readily available IMS data (Australia, Mexico, and New Zealand). The resulting value of the 17 molecule market-proportion average applied to the drug market size in each country is used as a proxy for the total USD value of the 17 products in each of those markets. Similarly, for second round countries the portion of the prescription pharmaceutical market ($ value) that is represented by the 17 molecules in T1 in their specific reference country (in this case either Saudi Arabia or Taiwan) is applied to the prescription pharmaceutical market size in each second round country.

The results of the model are presented in Figure 5 below. We note that the international effects of Canada’s invalidation of patents through the promise doctrine amount to a total estimated loss of USD $110.41 million in originator product sales losses outside of Canada in the first year after genericisation. In line with the size of the markets and expected magnitude of impact, it is estimated that USD 105.36 million losses are caused in first round markets and the remaining USD 5.05 million in second round countries. However, as mentioned in the assumptions above, these estimations are restricted to a one year impact and present a significant underestimation of real overall losses expected prior to loss of exclusivity for the 17 products.
Figure 5: The first year impact of the promise doctrine in international markets: a hypothetical effects approach

<table>
<thead>
<tr>
<th>Round I ($m)</th>
<th>Round II ($m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>44.66</td>
</tr>
<tr>
<td>Colombia</td>
<td>2.95</td>
</tr>
<tr>
<td>Egypt</td>
<td>1.73</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>2.14</td>
</tr>
<tr>
<td>South Africa</td>
<td>7.48</td>
</tr>
<tr>
<td>Taiwan</td>
<td>6.40</td>
</tr>
<tr>
<td>Australia</td>
<td>28.07</td>
</tr>
<tr>
<td>Mexico</td>
<td>8.17</td>
</tr>
<tr>
<td>New Zealand</td>
<td>3.13</td>
</tr>
<tr>
<td>Bahrain</td>
<td>0.09</td>
</tr>
<tr>
<td>Jordan</td>
<td>0.02</td>
</tr>
<tr>
<td>Lebanon</td>
<td>0.09</td>
</tr>
<tr>
<td>Morocco</td>
<td>0.06</td>
</tr>
<tr>
<td>Oman</td>
<td>0.13</td>
</tr>
<tr>
<td>South Korea</td>
<td>4.28</td>
</tr>
<tr>
<td>UAE</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Source: CRA analysis

The estimated losses are substantial but only represent the impact in the first year after genericisation of the products in Canada. Estimating the overall impact of the losses associated to these products over time is challenging. To carry out such an analysis, would require information on when market exclusivity is lost in each of the markets and whether this would have occurred before the loss of exclusivity in Canada (in the absence of the impact of the promise doctrine).

However, we can derive a ballpark estimate based on the calculated one year losses. On an average there is 6.75 years between when products lose exclusivity due to the promise doctrine and the loss of market exclusivity that would otherwise take place in Canada. Assuming the same loss would occur in each of these years, we can estimate the total loss over the period. The application of this methodology leads to overall losses of...

"...overall losses of revenue due to the promise doctrine and spillovers caused by ERP in international markets are estimated at $745 million."
revenue due to the promise of the patent doctrine and spillovers caused by ERP in international markets of $745 million.

2.3.2. The actual model approach

This second approach that has been implemented, presents a direct estimate of the impact of the “promise doctrine” price drop on Canada on direct (1st round) reference countries (Brazil, Colombia, Egypt, Saudi Arabia, South Africa, and Taiwan) using IMS price and volume data. This method involves taking a molecule-by-molecule average price, weighted by volume in Standard Units (SUs) in each country. The weighted average prices by country for each molecule are then normalized from the date of patent invalidation into quarters -3 through 8. These 12 quarters are then divided into three time periods (Time Period 1 (T1) to Time Period 3 (T3)) each consisting of four quarters. A simple average of the weighted average prices of each molecule by country is then taken across the four quarters in each of the three time periods to calculate the weighted average price in each time period.

The weighted average price of each molecule by country in T1 is then subtracted from the weighted averages of each molecule by country in T2 and T3 respectively to calculate a price reduction. An important assumption made in this model is that in all instances where a price drop between T1 and T2 or T3 has been recorded, the price difference is due to the promise of the promise doctrine, whereas in cases where the price has increased or remained the same, the price difference is zeroed out (and these molecules not included in the calculation). 47

Finally, in order to isolate the impact of price decreased through ERP relationships and not account for any dynamic market adjustments to volumes, the price difference for each molecule in each country for T2 and T3 separately is multiplied by total SUs for each molecule in each country over T1. The result is the weighted average price-based loss in originator sales revenues by molecule in each country. In order to remain in line with the previous method applied and for the two models to be comparable, the losses in T2 are set out. These amount to USD 68.29 million in the year following generic entry in Canada.

To compare this to the number from the hypothetical model we need to compare the same set of countries. As Figure 6 shows, the number in the actual and hypotheticals model are similar, USD 65.36 million versus USD 68.29 million. The results of this model highlight that:

- The two methods of estimation applied lead to similar losses and the degree of consistency provides evidence for the soundness of the approaches taken.
- In case we combine the estimated actual losses for the six markets with available IMS data with the estimated hypothetical losses for the remaining markets, the overall losses in first round countries are USD 108.29 million (compared to hypothetical estimation losses at USD 105.36 million) and overall first and second

47 The rationale for this is that the promise doctrine could not be responsible for price increases. However, price reductions could be due to factors other than the promise doctrine. This is the weakness of the actual effects approach.
round losses are USD 113.34 million (compared to hypothetical estimation losses at USD 110.41 million).

- It should be emphasized that both models provide an underestimation of real losses as they only account for a one year effect of the promise doctrine.

**Figure 6: The first year impact of the promise doctrine in international markets: an actual effects approach**

<table>
<thead>
<tr>
<th>Hypothetical effects formal round I ($m)</th>
<th>Actual effects formal round I ($m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil 44.66</td>
<td>Brazil 39.13 Saudia Arabia 1.29</td>
</tr>
<tr>
<td>Colombia 2.95 South Africa 7.48</td>
<td>Colombia 0.12 South Africa 3.53</td>
</tr>
<tr>
<td>Egypt 1.73 Taiwan 6.40</td>
<td>Egypt 1.42 Taiwan 22.80</td>
</tr>
<tr>
<td><strong>Total hypothetical losses</strong> 65.36</td>
<td><strong>Total actual losses</strong> 68.29</td>
</tr>
</tbody>
</table>

Source: CRA analysis

Clearly in both approaches there are a large number of simplifying assumptions and caveats. The similarity between the estimates does not mean that there is not a significant degree of uncertainty regarding the actual damages due to ERP but provides significant reassurance regarding the order of magnitude.

### 2.4. Conclusion

This analysis indicates that that the promise doctrine has a negative international impact on markets that directly or indirectly (through referencing other markets) include Canada in their ERP baskets. We estimate a loss of over $110 million from ERP spillovers in the first year after genericisation alone due to the promise doctrine. Taking into account the sustained effect we estimate an overall loss of over $745 million. The losses calculated are subject to
assumptions but given the two approaches are similar, they provide a robust estimation of the magnitude of impact. The two methodologies lead to very similar losses estimated but the price analysis based on actual sales data indicates that the real decrease in prices is even larger than the estimation. The analysis highlights that the application of the promise doctrine leads to substantial negative price spillovers in international markets.