Innovative Medicines Canada

An assessment of Canada's current and potential future attractiveness as a launch destination for innovative medicines

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Building a better working world

Disclaimer

Ernst & Young LLP ("EY") was engaged by Innovative Medicines Canada ("IMC") and Pharmaceutical Research and Manufacturers of America ("PhRMA") in July 2018 to assess Canada's comparative performance in launch sequencing of innovative drugs and the impact of the current policy environment and market conditions on launch sequencing ("the Project"). This project has been funded and sponsored by The Pharmaceutical Research and Manufacturers of America ("PhRMA").

In preparing this document ("Report"), EY relied upon data and information from a variety of sources verified and audited by PhRMA (collectively, the "Supporting Information"). EY reserves the right to revise any analyses, observations or comments referred to in this Report, if additional Supporting Information becomes available to us subsequent to the release of this Report.

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Executive Summary

The draft amendments to the *Patented Medicines Regulations* proposed in Canada Gazette Part I by Health Canada in December 2017[1] are the most significant potential changes to the jurisdiction of the Patented Medicines Prices Review Board (PMPRB) in more than twenty years.

In the wake of these potential regulatory changes as well as ongoing concerns regarding access, affordability, and the sustainability of expenditures on drugs, this study aims to assess Canada's timely availability of innovative therapies from global companies relative to comparable jurisdictions and explore the market and policy factors that impact launch sequencing of therapeutics to global markets. The analysis uses recent data and information to understand launch sequencing of therapeutic prescription drugs in Canada in terms of total launches, launch lags, and the cumulative probability of launches in Canada relative to other comparable international jurisdictions. The report also discusses how market and/or regulatory factors may influence launch decisions internationally and in Canada.

Of the 243 new active substances (NASs) in the dataset of drugs launched from January 2011 to June 2018, 119 were launched in Canada, ranking Canada 14th out of the 69 jurisdictions in terms of total launch count. The analysis of the launch sequence data suggests that on average, Canada's outcomes as it relates to both launch counts and launch lags, are currently similar to peer jurisdictions as a launch destination.

The analysis further suggests that the USA is the most attractive destination for drug launches, with the highest number of total launch counts and the smallest launch lags, with Germany and the UK also ranking highly as launch destinations. A third cluster of countries with fewer launches and longer launch lags consists of countries such as South Korea, Australia, and New Zealand, with more stringent price regulations.

The analysis also found that drugs launched in Canada are often previously launched in and/or only also launched in the USA, suggesting that the proximity of the USA market may influence the decision to launch in Canada. Finally, probabilities of drug launches over time vary by price and GDP/income levels and are positively correlated with total launch counts, also suggesting that drug prices and macro-economic factors may also be key factors for launch decisions.

These findings support the results from a number of existing academic research papers which find that price regulations leading to significantly lower transparent or visible drug prices are correlated with an increase in launch delays. Ultimately, if proposed cost containment measures are successful in significantly reducing drug prices in Canada, Canada's future attractiveness as a preferred launch destination market may erode over time.

[1] Government of Canada, Department of Health. 2017. *Regulations Amending the Patented Medicines Regulations*. December 2.

Context

Background

Similar to many jurisdictions, Canada has been taking steps in recent years to manage the overall sustainability of its healthcare system, including its drug costs, which is one of the top three health spending line items. According to the Canadian Institute for Health Information (CIHI), spending on all drugs in Canada was expected to account for 15.7% of total health care spending in 2018, whereas expenditures on hospitals and physicians were expected to account for 28.3% and 15.1%, respectively.[2] While the recently proposed changes to the Patented Medicines Prices Review Board's (PMPRB) *Patented Medicines Regulations*[3] have raised questions regarding the potential impact on the innovative pharmaceutical industry's decisions regarding its ongoing economic footprint[4], the impact of the proposed changes on the timing of the launch of new medicines in Canada has also been a subject of discussion.

The purpose of this research is to evaluate Canada's comparative performance, relative to similar jurisdictions in terms of GDP per capita and broad structure of their health care systems, with respect to its position in the launch sequencing of innovative medicines and to assess the potential impact of evolving market and regulatory conditions on launch decisions in Canada, including a lower-priced Canadian market. While a cross section of comparator international jurisdictions, generally comparable from a GDP/capita and health system structure perspective, has been included in the analyses, the focus of this study is the current pharmaceutical sector landscape in Canada in terms of product launches and the potential impact of changing market conditions on future launches and launch sequencing of innovative medicines.

Policy Environment

Decisions to launch new chemical or new active substances (collectively, "NASs") are typically made by Canadian affiliates of international pharmaceutical companies in consultation with their respective headquarters. Traditionally, Canada has been among the early launch jurisdictions, meaning that Canadians have been among the first in the world to obtain access to new innovative products.

The increased use of external reference pricing (ERP) by many jurisdictions is one potential source of concern for the industry, both at the local Canadian as well as global levels. ERP refers to the practice of a given jurisdiction to use prices in other jurisdictions to inform local drug prices. Since most comparable jurisdictions currently use some form of ERP to inform local pricing[5], the proposed PMPRB regulatory changes, if implemented, may result in a lower public ceiling price used as an external reference price by other countries. Since companies typically sequence launches to minimize successive reductions in ceiling prices over time, this may potentially result in Canadian launches being delayed in favour of more attractive jurisdictions, as it would avoid lower prices being externally referenced relatively early in a product's life cycle.

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[2] CIHI. 2018. *National Health Expenditure Trends, 1975 to 2018.*

[3] Patented Medicines Prices Review Board. 2018. *Guidance document on changes to the Guidelines.*

[4] EY. 2017. *Data Analytics and Member's Economic Footprint and Impact in Canada.*

[5] Kavanos, Panos, Anna-Maria Fontrier, Jennifer Gill, and Dionysis Kyriopoulos. 2017. *The Implementation of External Reference Pricing within and across Country Borders.*

Decision-making factors regarding regulatory filing or launch sequencing are generally not consistently documented or understood. However, market conditions, particularly drug prices and access conditions, appear to have a notable impact on the launch sequence for pharmaceutical companies.[6] From a policy perspective, objective information on the evidence and decision-making factors used to determine the launch sequence for the Canadian market would be helpful in determining the potential impact of lower Canadian ceiling prices on innovative medicine launch sequencing.

International Policy Perspectives

Many countries have made concerted efforts to reduce delays in drug launches as a commitment to health care access by accelerating access to innovative drugs. For example, between 2006 and 2016, the median approval time for New Active Substances by the European Medicines Agency (EMA), U.S. Food and Drug Administration (FDA), Japanese Pharmaceuticals and Medical Devices Agency (PMDA), Health Canada, Swissmedic, and Australian Therapeutic Goods Administration was reduced from 565 days to 374 days.[7] Several countries have also implemented accelerated pathways to expedite access for specific critical treatments that are in demand and/or have few to no alternative treatments. The United Kingdom (UK) government, for example, has proposed the establishment of the Accelerated Access Pathway to fast-track roughly five innovative medical products per year.[8] In certain circumstances, countries have also introduced early access schemes to provide patients access to treatments before final authorization. Policy makers and regulators have committed to speeding access to drugs and are continuously looking to implement initiatives to further improve access. While not yet implemented, Health Canada has indicated that its "Regulatory Review of Drugs and Devices" (R2D2) will spur changes that will ultimately reduce regulatory approval times for certain designated innovative medicines.[9]

As an example, the aligned reviews between Health Canada and health technology assessment organizations is expected to help minimize regulatory delays.[10] However, other policy measures have had the unintended consequence of increasing delays or reducing access. For example, in New Zealand, cost containment measures through its Pharmaceutical Management Agency (PHARMAC), introduced in the 1990s, appear to have slowed overall spending on pharmaceutical expenditure but also may have impacted availability of new medicines.[11] A 2007 report highlighted a number of drugs that were either unfunded, restricted access, or had longer delays in access relative to other jurisdictions.

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[6] Danzon, Patricia M, Y. Richard Wang, and Liang Wang. 2005. "The Impact of Price Regulation on the Launch Delay of New Drugs - Evidence from Twenty-Five Major Markets in the 1990s." *Health Economics* 14 (3): 269-292; Lanjouw, Jean Olson. 2005. *Patents, Price Controls and Access to New Drugs: How Policy Affects Global Market Entry*; Kyle, Margaret K. 2007. "Pharmaceutical Price Controls and Entry Strategies." *The Review of Economics and Statistics* (The MIT Press) 89 (1): 88-99; Danzon, Patricia M., and Andrew J. Epstein. 2012. "Effects of Regulation on Drug Launch and Pricing in Interdependent Markets." *Advances in health economics and health services research* 23: 35-71; Cockburn, Iain M., Jean O. Lanjouw, and Mark Schankerman. 2016. "Patents and the Global Diffusion of New Drugs." *American Economic Review* 106 (1): 136-164.

[7] OECD. 2017. *New Health Technologies: Managing Access, Value and Sustainability*. OECD Publishing.

[8] Department of Health and Department for Business, Energy & Industrial Strategy. 2017. *Making a reality of the Accelerated Access Review*.

[9] Health Canada. *Improving the Regulatory Review of Drugs and Devices*.

[10] Health Canada. *Notice to industry: Aligned reviews between Health Canada and health technology assessment organizations*.

[11] Jacqueline, Cumming, Mays Nicholas, and Daubé Jacob. 2010. "How New Zealand has contained expenditure on drugs."

Another report had found that, relative to Australia, New Zealand had funded 84 fewer innovative medicines.[12]

Research Objectives

Given the current global and domestic policy environment, this Report seeks to answer two fundamental research questions:

1. What is Canada's comparative performance relative to comparable jurisdictions in the launch sequencing of innovative drugs?

The analysis of Canada's competitive positioning in launch sequencing will primarily involve examining the following:

- Total launches;
- Launch lags; and
- The cumulative probability of launches in Canada relative to other jurisdictions.

An analytical understanding of launch data will help to evaluate whether Canada's performance in launch sequencing relative to other jurisdictions is among the top launch jurisdictions for global pharmaceutical companies.

2. What market and policy factors impact launches globally?

Building on the results from Canada's launch sequence performance, the analysis will further assess how certain market and policy factors impact global launch sequence. This analysis will focus on the factors most relevant to the environment in Canada today, how current market and policy conditions may impact launches and launch sequencing in Canada over time, and potential implications for investments in the life sciences sector over the long term.

[12] Ibid.

Introduction

Overview

Timely launches of innovative medicines are an important factor to ensure Canadians have access to the most advanced and effective drugs to raise living standards and increase positive health outcomes. With this in mind, it is valuable to consider the importance of launch sequence decisions of innovative drugs for pharmaceutical companies and the various factors that influence their decisions.

Global launch sequence strategies are integral to innovative pharmaceutical companies' overall business strategy. Initial launch pricing strategies are impacted by global price interdependencies, including ERP and parallel trade.[13] ERP is the mechanism through which drug prices from other countries are referenced to set or negotiate domestic prices, including maximum allowable prices. Conversely, parallel trade refers to the phenomenon of arbitrage where drugs are purchased in a country with a low-price environment and sold in a higher price country at a discount to domestic prices. To prevent any negative financial impacts from these linkages, firms place an emphasis on optimizing their pricing strategy. For example, given existing market conditions firms optimize their launch sequence strategy to allow them to maximally recoup their investments. When evaluating financially optimal price points and launch decisions, firms must consider the cost of developing new pharmaceutical products, competitive pressure in the market, country specific regulations, and revenue potential, among other considerations. These factors influence not only the prices that are set, but also the timing of launches in different jurisdictions and the decision on whether to launch in certain countries. Existing academic and industry research over the past 20 years have explored these relationships using historical variation in regulatory conditions and market access and suggest that a company's launch decisions are influenced by price regulations as well as price interdependency between countries.[14] Using updated data and information from more recent years, we performed an updated assessment in an attempt to validate the outcomes suggested from previous reports.

Global drug launch sequences reflect firm level decisions after accounting for relevant revenue and cost factors. This Report looks to analyze launch sequence data of NASs to further understand Canada's relative position as a market for launching innovative drugs, explore what factors are driving these results and provide context on the likely outcomes from the proposed PMPRB regulations and other future potential cost-containment measures. An analysis of the impact of the competitive and policy environment and changes to market conditions on launch sequencing behaviour is a potential area for future study.

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[13] Gregson, Nigel, Keiron Sparrowhawk, Josephine Mauskopf, and John Paul. 2005. "Pricing Medicines: theory and practice, challenges and opportunities." *Natural Reviews Drug Discovery*, 121-130.

[14] Danzon, Wang, and Wang. "Impact of Price Regulation." 269-292; Lanjouw. *Patents, Price Controls and Access to New Drugs*; Kyle. "Pharmaceutical Price Controls and Entry Strategies." 88-99; Danzon and Epstein. "Effects of Regulation." 35-71; Cockburn, Lanjouw, and Schankerman. "Patents and the Global Diffusion of New Drugs." 136-164.

Current Issues

Globally, the pipeline of new medicines and treatments in development is increasingly robust.[15] The number of new medicines approved for sale has been rising since 2010. New products are increasingly targeted towards small populations with specialized needs. In particular, there has been significant progress in rare disease treatments, oncology medicines, and gene and cell therapies. However, this growth in innovative offerings has also raised concerns regarding costs and affordability.[16]

These issues appear to be prevalent in the Canadian market, where Canada has among the highest per capita expenditure on health care, including hospital, physician and drugs when compared to OECD countries.[17] Similar to overall health care costs, expenditure on pharmaceuticals has increased and is projected to continue to grow as the population ages and more innovative therapies become available.[18]

Policy makers in Canada have identified access and affordability as related issues in the domestic pharmaceutical market. Health Canada has cited several challenges related to drug access and affordability in the preamble to its proposed regulatory amendments to *Patented Medicines Regulations* at the PMPRB level.[19] Concerns include low value-for-money on prescription drugs, increasing share of expenditure on medicines, and rising cost burdens for insurers and patients.

From the perspective of public payers in Canada, high costs for new drugs increase pressure on their budgets and often mean that some innovative drugs cannot be funded.[20] For private insurers who do not currently benefit from the same negotiation power as public plans, cost pressures from high-price drugs can impact their profitability. Manulife's recently established DrugWatch program is an example of a private insurer seeking to better manage its exposure to higher drug costs.[21]

These legitimate concerns regarding access and affordability of innovative drugs have led the innovative pharmaceutical industry to suggest that proposed measures to aggressively manage growth in drug spending could bring about greater uncertainty for their firms at a global level, and delay or even prevent new drugs from being introduced in Canada.

Based on the existing evidence, we hypothesize that individual country policy measures, such as those taken in Canada, will influence decisions at a global level. The purpose of this research is to test this hypothesis, based on historical data, and identify potential implications of measures currently being taken in the Canadian setting.

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[15] OECD. 2017. *New Health Technologies: Managing Access, Value and Sustainability*. OECD Publishing.

[16] Ibid.

[17] Canadian Institute for Health Information. 2018. *How does Canada's health spending compare internationally?*

[18] Public Policy Forum. 2018. *Pathways to Sustainable Access to Innovative Medicines for Canadians.*

[19] Government of Canada, Department of Health. 2017. *Regulations Amending the Patented Medicines Regulations*.

[20] Canadian Health Policy. 2015. *Pharmacare: what are the costs for patients and taxpayers?*

[21] Manulife. 2015. *Introducing Manulife DrugWatch: Applying rigorous oversight to help ensure value for money in a dramatically changing drug market*.

Data and Methodology

Data Review and Research

- Reviewed launch data and competitor pricing for consistency in definition
- Developed objective criteria to identify 15 jurisdictions that would be used to assess Canada's positioning

Literature Review

- Reviewed previous academic research on the factors of launch sequencing
- Gathered insights on how market conditions and regulatory policies impact launch decisions

Data Analysis

- Assessed Canada's competitive positioning as a preferred launch destination for innovative drugs
- Measured through total launch count and launch delays, and cumulative probability of launching

Secondary Market

- Conducted additional research to identify economic outcomes driven by policy reform in other jurisdictions

Analytical Methodology and Approach

This section details the methodological approach used for EY's analysis, with particular emphasis on the data used, definitions adopted, and additional research conducted for this report.

Two detailed datasets of global launch sequencing information were used to better understand how different countries compare as priority launch destinations for innovative drugs from the perspective of global pharmaceutical companies. Additionally, this Report draws on established academic and industry research to highlight key factors that drive launch sequencings. Lastly, other secondary market research is performed to identify the relationship between different policy reforms (in the form of average list prices of drugs for each country) on launch sequencing to directionally assess the likely impact of the proposed PMPRB regulations.

Together, these sources have been used to assess Canada's current positioning as a market for innovative drugs, and to consider how its status as a launch destination may evolve over time due to potential policy changes.

Launch Sequencing Data Analysis

Introduction

To conduct this analysis, EY used a dataset of launch dates for 243 NASs across 69 countries and jurisdictions that were approved by the U.S. FDA, EMA and/or Japan's PMDA between January 2011 and August 2018, and first launched anywhere globally during the same time period. PhRMA created this database of information based on information from regulatory agencies, IQVIA (MIDAS via the Analytics Link platform) and desktop research of publicly available sources.

The key variables of focus from this dataset in the competitive assessment of launch sequencing include:

1. **Launch Counts**: Defined as the number of NASs launched by country throughout the analysis period, whereby the launch date in a given country is reflected in MIDAS as the first date of audited sales (note that the first documented sale in Canada is generally in the private market soon after marketing authorization by Health Canada).
2. **Launch Lag**: Defined as the number of months between the first global launch date of a NAS and the launch date within a country.

Methodological Notes and Limitations

There are a number of important considerations and limitations when interpreting the outcomes of the analysis:

- The analysis considers a domestic launch date to be the date that a NAS is first sold in the country. This definition allows for comparisons of market entry on a consistent basis, whereas alternative definitions such as the date of marketing authorization would not reflect additional delays to patient access associated with pricing and reimbursement. This definition also aligns with how launches are defined in many academic papers studying the impact of price regulations on launch timing and market entry.[22]
- To avoid double counting, combination products that share individual NASs are counted only when the product represents the first time that an individual NAS launches in a given country. The analysis does not distinguish between hospital sector and retail sector NASs.
- NAS launch data does not include Sri Lanka and Algeria, which had no recorded NAS launches.
- Therapeutic categorization for this project was assigned based on the Anatomical Therapeutic Chemical (ATC) Classification System whereby the World Health Organization Collaborating Centre for Drug Statistics Methodology (WHOCC) classifies active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Our source for a product's ATC code was IQVIA MIDAS (2018) and in most cases therapeutic category assignment was straightforward. However, in cases where a product has multiple ATC codes, the product's indication at launch in the first country of launch was primarily used to determine therapeutic assignment, however in certain cases where dual indications were present in the launch year, the indication with a majority of volume utilization was used to assign a category.
- This project does not assess the additional delay from launch to public reimbursement. This is an important distinction as countries vary in their mix of public and private reimbursement, as well as in their public reimbursement policies and timeline. Work on public plan drug listing timelines is already done by IMC and two manuscripts have been submitted for publication that will address this question.
- The main analysis focused on 15 countries that were considered similar to Canada in terms of broad health care system structure, general standard of care, and level of economic development (i.e. GPD/capita) to provide a better understanding of Canada's relative position: the United States

[22] Danzon, Wang, and Wang. "Impact of Price Regulation." 269-292; Lanjouw. *Patents, Price Controls and Access to New Drugs*; Kyle. "Pharmaceutical Price Controls and Entry Strategies." 88-99; Danzon and Epstein. "Effects of Regulation." 35-71; Cockburn, Lanjouw, and Schankerman. "Patents and the Global Diffusion of New Drugs." 136-164.

of America (USA), Germany, the UK, Sweden, Norway, Italy, Switzerland, Spain, France, Japan, Belgium, South Korea, Netherlands, Australia and New Zealand.

- Launch lags are only calculated for NASs launched during the regulatory and launch parameters described above. Product- and country-specified launch lags cannot be calculated for NASs that have not yet launched in a given country, which is more likely to impact NASs that were first launched globally more recently. This limitation was addressed by complementing the analysis with additional statistical methods that can account for these limitations.
- Launch lag calculations cannot isolate for different factors that may impact launch delays due to data availability. For example, factors that contribute to total lags can include delays in the submission of market authorization, obtaining authorization, submission of price or reimbursement approval, finalizing reimbursement or prices, or listing drugs, depending on the process in the respective jurisdiction.[23]
- The median lag is the lag of the NAS product that lies at the midpoint or the middle of the distribution when the products launched in a country are ordered by value of lags. If the number of products launched are even, the median lag is the average of the two product lags in the middle of the distribution.
- Sales and unit data from IQVIA MIDAS were also analyzed. Average prices were calculated using the total sales based on invoiced prices and the standard units sold for each country. Although invoiced prices do not reflect final effective prices, as they do not account for any additional discounts and rebates, EY believes they are a reasonable proxy for the impact of regulations on prices. A number of empirical research papers have used lagged average list prices to assess the impact of price regulation on launch sequencing including: Danzon, Wang, and Wang (2005); Danzon and Epstein (2012).

[23] Danzon, Patricia M, Y. Richard Wang, and Liang Wang. 2005. "The Impact of Price Regulation on the Launch Delay of New Drugs - Evidence from Twenty-Five Major Markets in the 1990s." *Health Economics* 14 (3): 269-292.

Analytical Results

Total Launch Counts

The IQVIA data are used to assess how Canada compares relative to other jurisdictions in terms of total NAS launches over the period analyzed. Total NAS launch counts are used as a proxy for the relative ranking of different jurisdictions as launch destinations.

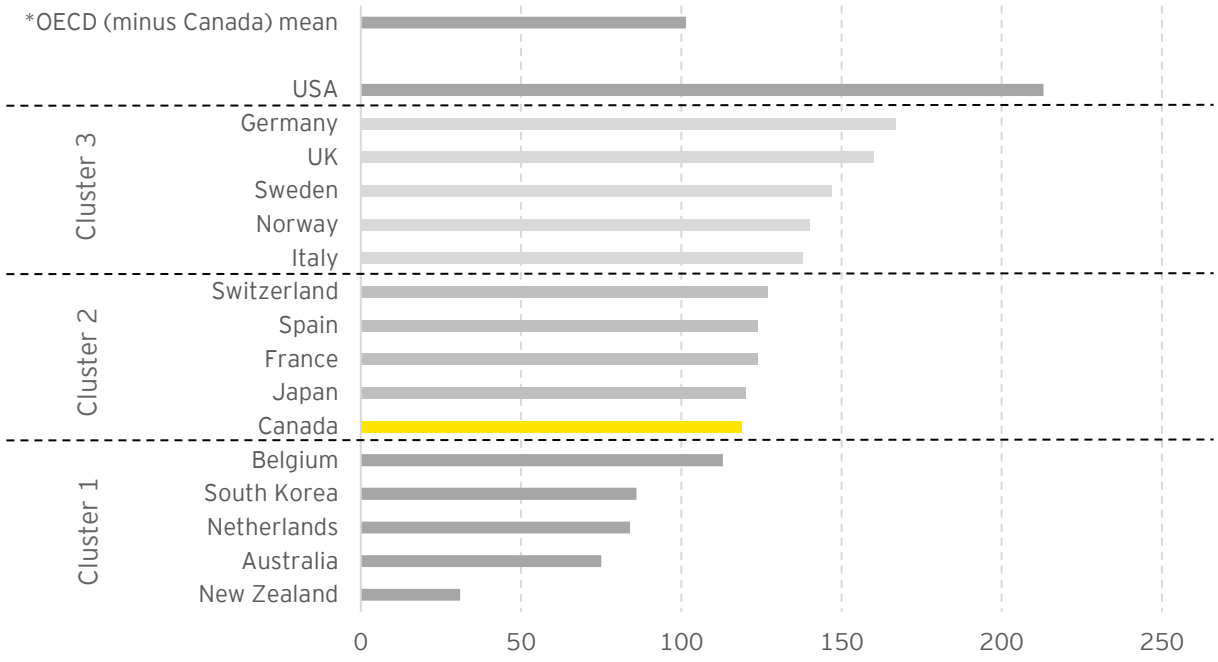
Between January 2011 and June 2018, 119 NASs were launched in Canada out of the 243 NASs launched globally. While this represents the total number of launches within the given timeframe analyzed, many of the NASs currently not available for sale in Canada may launch in the future. Additionally, of the NASs not launched in Canada, approximately 50 percent have only been launched in one or two other jurisdictions. From the 69 jurisdictions included in this study, Canada ranks 14th in terms of total launch counts. A complete ranking of jurisdictions by total launch count can be found in Appendix A.1.

The USA is ranked 1st with 213 drugs launched over the same period, while Germany has the second highest total at 167 launches. Canada's performance based on this metric is marginally higher than the OECD country average launch count of 101.5 (The OECD comparison is defined as the subset of OECD countries included in the data other than Canada, Denmark, Iceland, and Israel).

Although all 69 jurisdictions were analyzed, additional emphasis was placed on understanding Canada's relative performance to 15 other "peer" countries. These countries were chosen based on comparability of income levels, standard of care, and health system factors among other factors. The comparator jurisdictions also include the new suggested basket of countries for international price comparisons set out the in the draft PMPRB regulations, in addition to USA and Switzerland, which are part of the current PMPRB basket.

Figure 1 illustrates how Canada compares relative to the 15 peer jurisdictions with respect to launch counts. A cluster of jurisdictions ahead of Canada in total launches includes several Western European countries (Germany, UK, Sweden, Norway, Italy, Switzerland, Spain, and France) and Japan. Another cluster of five countries ranked below Canada consists of jurisdictions with more stringent price regulations, such as South Korea, Netherlands, Australia, and New Zealand. The USA ranks notably higher than any other jurisdiction – it is by far the first launch destination for firms, influenced by, among other factors, it's more favorable drug pricing environment as compared to other nations.

Figure 1. Launch Count Overview for Select Countries



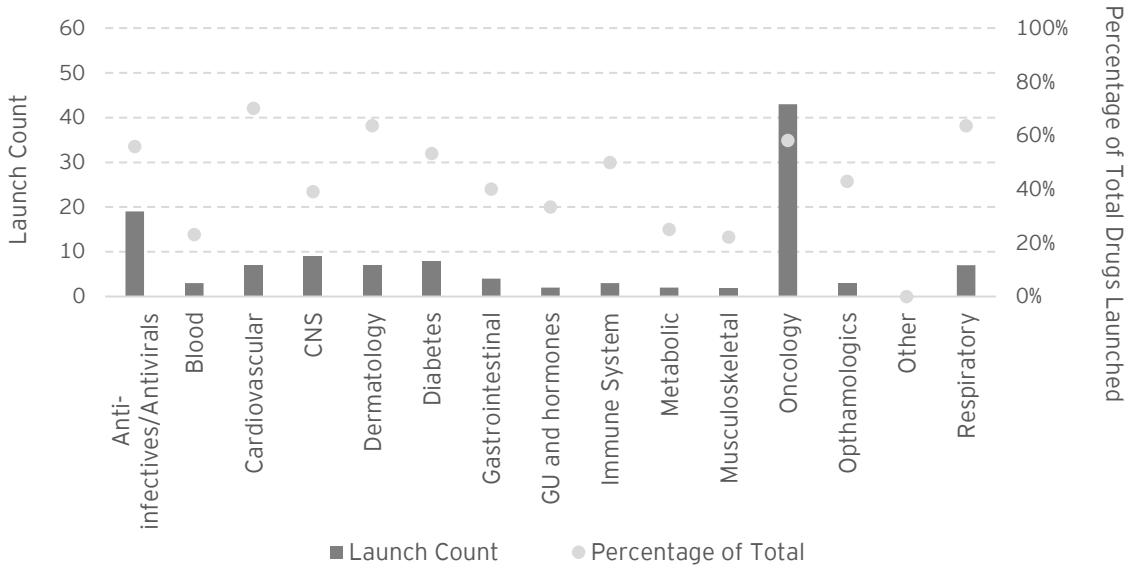
Note: The OECD comparison is defined as the OECD countries included in the dataset other than Canada, which excludes Denmark, Iceland, and Israel.

Source: IQVIA, PhRMA, and EY analysis

Total Launch Counts by Therapeutic Area

Pharmaceutical products can be further divided into different groups of drugs, or therapeutic areas, depending on their targeted organ or system and unique properties. Beyond the general trend in launch counts, launch sequencing of drugs can be assessed across different drug groups. In this analysis, NASs are divided into the following categories: Anti-infectives or Antivirals, Blood, Cardiovascular, Central Nervous System (CNS), Dermatology, Diabetes, Gastrointestinal, Genitourinary (GU) and Hormones, Immune System, Metabolic, Musculoskeletal, Oncology, Opthamologics, Respiratory, and 'Other' drugs. Oncology, Anti-infectives or Antivirals, and CNS drugs, accounted for the majority of drugs launched over this period, with 74, 34, and 23 drugs launched respectively.

Figure 2. Drug Launches in Canada by Therapeutic Area



Source: IQVIA, PhRMA, and EY analysis

Figure 2 above showcases launch counts in Canada and the proportion of total global launches represented across different drug classifications. A detailed table on Canada's total launches and ranking can be found in the Appendix A.2. Canada's launch count is favorable relative to other jurisdictions for Cardiovascular, Dermatology, Diabetes, Gastrointestinal and Opthamologics drugs. Within these drug groups, Canada ranks amongst the top 5 highest ranking jurisdictions in terms of total launches. The relative ranking of countries by category is often reflective of the total drugs launched globally within that category. Within the Opthamologics drugs category, Canada's relative ranking is partly driven by the low total number of drugs launched in this category globally (only 7). Conversely, Canada is ranked 12th in total launch counts for Oncology drugs despite having a total of 43 launched since 2011. Still, within Oncology, 58 percent of total drugs launched globally have also been launched in Canada.

One common factor among the four countries with the lowest launch count within the 16 peer group countries (New Zealand, Australia, Netherlands, and South Korea) analyzed was a low number of launches in Oncology. Between these countries, South Korea had the most drugs launched in this category with 35 out of 74 total drug launches, ranking 23rd out of the 69 jurisdictions examined. Low launch outcomes in the Oncology category impacted overall rankings as Oncology drug launches accounted for the greatest share of launches (roughly 30 percent of total). New Zealand, in particular, had low launch counts in every category.

Launch Counts in other Jurisdictions

To place the findings on drug launches for Canada in perspective, it is instructive to highlight findings from several comparator countries, including Australia, New Zealand, and Germany, which represent contrasting approaches to price regulation among the peer group of countries.

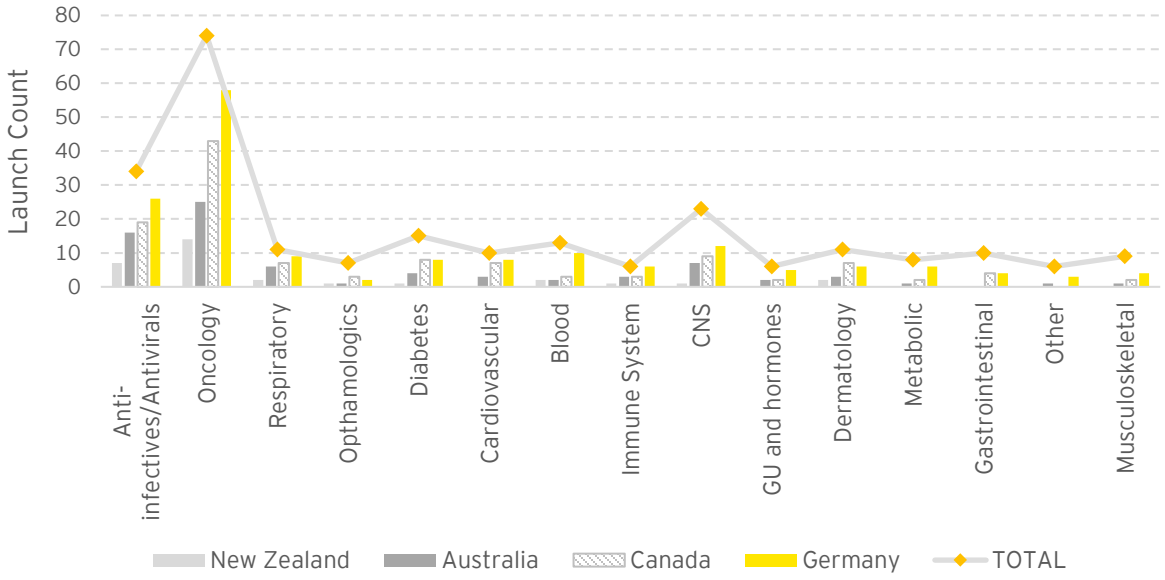
In general, based on the analysis, Australia ranks below the top 10 jurisdictions by launch count across

drug categories. Its relative ranking for launches is especially low for Diabetes, Oncology, and Gastrointestinal drugs. Similarly, New Zealand has 2 or fewer drugs launched in every drug category outside of anti-infectives or antivirals and oncology, where it was still ranked in the bottom half of jurisdictions by total launch count. From a policy perspective, both Australia and New Zealand have public insurance schemes with caps on pharmaceutical expenditures as a proportion of the health budget.

In contrast, Germany is demonstrably a preferred jurisdiction for drug launches, ranking within the top 5 jurisdictions for drug launches in each drug category. For most categories, at least 50 percent of globally launched drugs are launched in Germany. It should be noted, that unlike Australia and New Zealand, Germany has a system of public and private drug plans which allow for free pricing during the first year after launch and which in general do not place a cap on drug expenditures as a proportion of budget.

In summary, within this sub-group of countries, Germany almost always outperforms the other jurisdictions in total counts across all categories of drugs, with Canada close behind. Conversely, New Zealand is usually ranked at the bottom (Figure 3).

Figure 3. Select Group Launch Count by Therapeutic Area



Source: IQVIA, PhRMA, and EY analysis

US Launches of Drugs Launched in Canada

The close proximity between Canada and the USA, in addition to similarities between the two markets and populations, may influence a firm's decision to launch in either country. For Canada in particular, drug launch decisions are likely to be impacted by the USA market. This section assesses the link between the Canadian and USA market by analyzing launch sequencing in the USA and Canada versus other key markets. This additional level of empirical analysis complements the previous dataset by providing data that allows for a closer examination of the link between the USA and Canadian pharmaceutical market, in particular the influence of the USA market on innovative products sold in

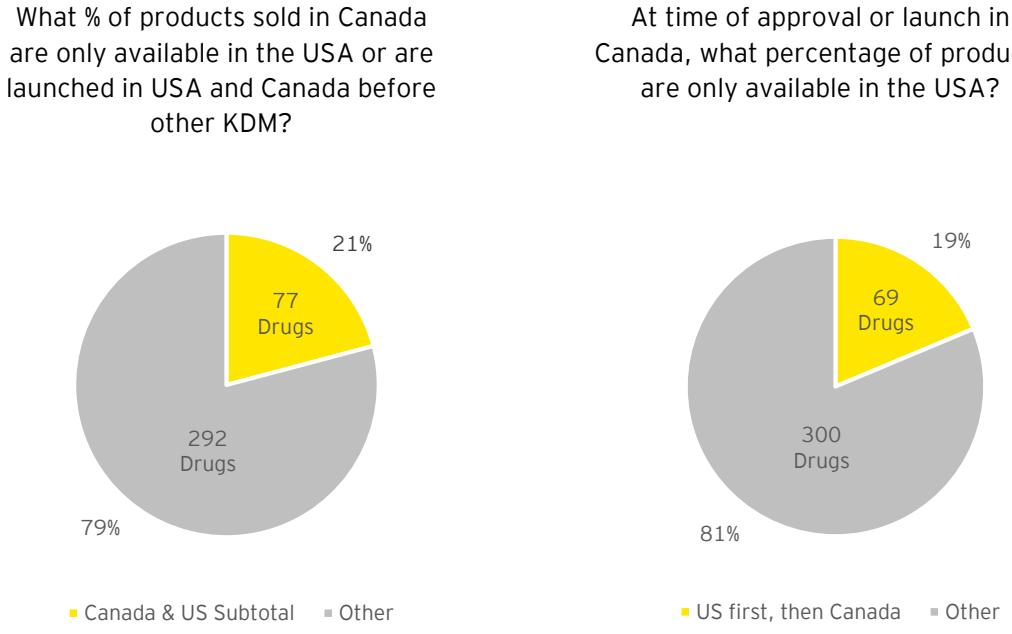
Canada.

The information on product launches is derived from New Product Intelligence (NPI), and has been consolidated, synthesized and analyzed by IQVIA and PhRMA. The data provided includes products launch dates for brands with active sales in Canada since 2008 and where product launch dates in Canada and other jurisdictions were on or after January 1st 2000. The other markets examined in this section are five major European countries (France, Germany, Spain, Italy, and the UK) and Japan, who are collectively referred to as 'Key Developed Markets' (KDM). A total of 369 drugs are covered in this dataset, where the earliest Canadian launch date for a product is August 2000, and the latest is March 2018.

According to the data, only about 2 percent or 6 of the 369 drugs launched in the Canadian market were not launched in any other country. These numbers represent all launches over the period covered by the dataset. The data further demonstrates that approximately 5 percent of drugs sold in Canada have also only been launched in the USA but not in other KDM. An additional 16 percent of drugs were launched in Canada and the USA first before other KDM. Altogether, a subtotal of 21 percent of total drugs sold in Canada are either only launched in Canada and the USA or are launched there before other KDM.

These results suggest that the USA is an important influence on the market for innovative drugs sold in Canada. This is further supported by the fact that 19 percent of NASs sold in Canada were previously only available in the USA when they were first launched in Canada (Figure 4). Conversely, 8 percent of global products launched in Canada were previously only available in other KDM before being launched in Canada.

Figure 4. Canada and USA launch comparison



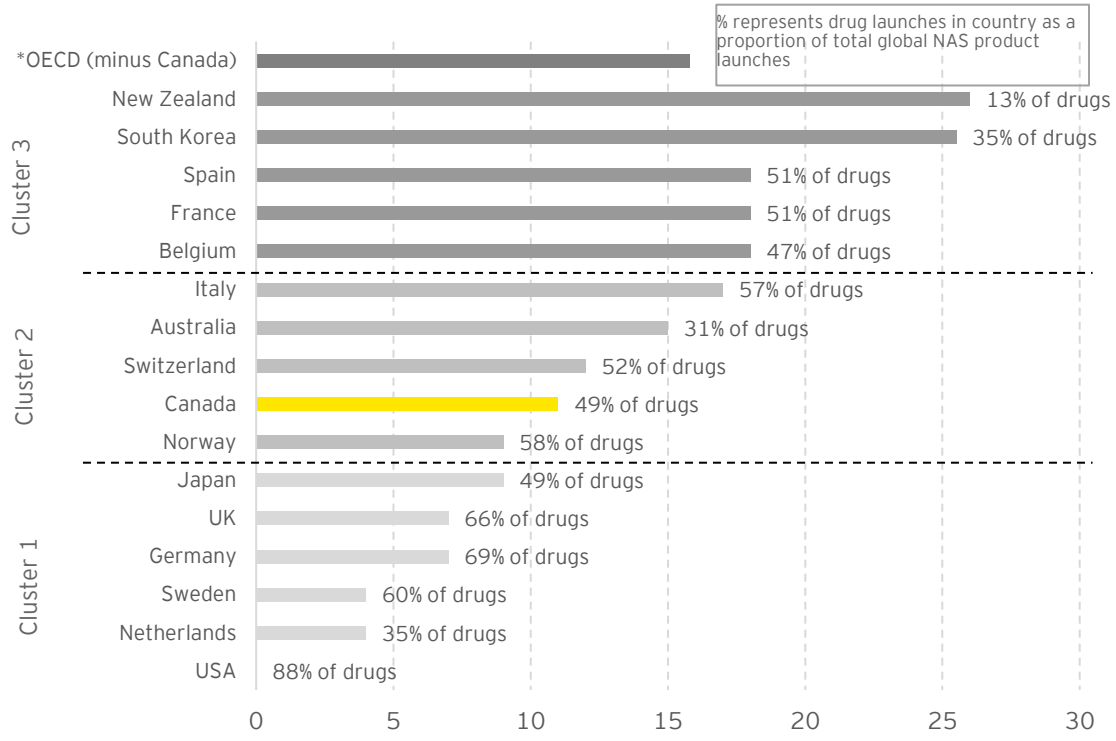
Note: Key Developed Markets are defined as BIG5 EU countries and Japan. Products are counted even if available 1 month earlier in 'Canada & US first' group (typically considered 'concurrent').

Source: NPI, PhRMA, and EY analysis

Launch Lags

Launch lag, defined as the number of months between the global first launch date (defined by first documented sale) and the domestic launch date, is another useful metric to assess the relative speed of access to innovative drugs in Canada relative to other jurisdictions. While related to total launch counts, lags are particularly useful in understanding if there are substantial delays associated with drug launches. Even if drugs are launched eventually, lengthy delays may mean that patients have to wait long periods for access to newer more effective drugs. This is particularly relevant from a health outcome perspective for diseases that can negatively impact the life of patients over a short period of time.

Figure 5. Median Lag (Months) in Select Countries

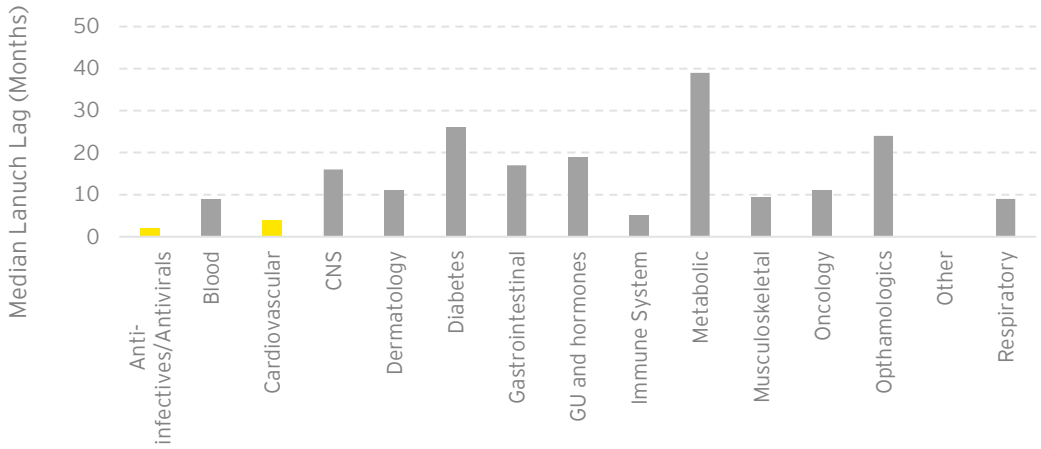


Note: OECD comparison is defined as OECD countries included in the data set other than Canada, which excludes Denmark, Iceland, and Israel. The median lag is the lag of the NAS product that lies at the midpoint or the middle of the distribution when the products launched in a country are ordered by value of lags (in months). If the number of products launched are even, the median lag is the average of the two product lags in the middle of the distribution.

Source: IQVIA, PhRMA, and EY analysis

Median lags are used in this analysis to illustrate differences across jurisdictions. The median lag value is used instead of the average lag as averages are impacted by outliers. The average may not be representative of where most of the data points lie if the data is skewed. Figure 5 above presents launch lags for 3 clusters of relevant comparators to Canada. Canada has a median launch lag of 11 months after a launch has taken place in any one country and ranks 10th overall between all 69 jurisdictions included in this study. Among its 15 peer countries, Canada is approximately in the middle of the range. The USA is the only country with a median launch lag of 0 months, as more than 60 percent of the 243 NASs studied were either launched in the USA first or within the same month of a global launch elsewhere. However, launch lag data must be interpreted cautiously as lags are only calculated based on observed launches in a given country and would not include launch data for NASs that were launched in countries outside of the time frame covered in the sample period. As an example, Netherlands only has a median launch lag of 4 months but 65 percent of globally launched NASs have not been introduced in the Netherlands within the same period examined. The median lag of innovative drugs launched in Canada is at least 2 months higher than that of the other top 10 jurisdictions. Moreover, except for Netherlands, all of these jurisdictions also launched at least as many drugs as Canada. The Netherlands stands out as jurisdiction that ranks considerably higher in terms of launch lags than in total launch counts.

Figure 6. Median Lag (Months) in Canada by Therapeutic Area



Source: IQVIA, PhRMA, and EY analysis

When assessed by therapeutic areas, Canada performs well in terms of launch lags in Anti-infectives or Antivirals and Cardiovascular drugs, ranking 2nd and 4th respectively (Figure 6). Cardiovascular drugs appear to stand out as Canada's best performing drug group, ranking within the top 5 jurisdictions for both launch count and lag time.

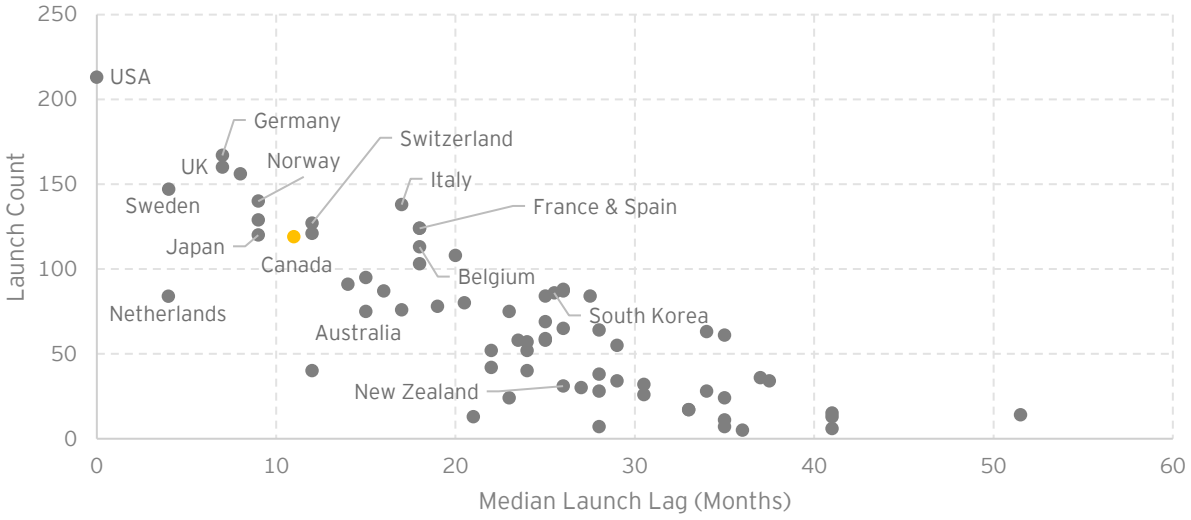
Relationship between Total Launches and Launch Lags

The data suggests that launch lag outcomes are also closely linked with total launch counts. As illustrated in Figure 7, the total launch and launch lags are inversely related as countries that often take longer to launch drugs on average are more likely to have fewer drugs that have launched within a given time period. The same reasons that influence firms to delay launches may also apply to decisions

to not launch at all. This graph shows that most of the countries with more launches than Canada also launch drugs at a faster rate. For example, Sweden has more favourable outcomes in both total launches and launch lags than Canada, Australia, France, Spain, Belgium and Netherlands.

The inverse relationship between the launch counts and launch lag is weakened partly because launch lags are only calculated based on observed launch data. Launch lags are calculated based on launches that have already occurred, and therefore do not reflect products that have not yet launched or may never launch. Australia, for example, has a lower median launch lag compared to Italy, France, Spain, and Belgium, but only 31 percent of total drugs launched globally are accounted for in its median launch lag estimate.

Figure 7. Relationship between Launch Counts and Launch Lags



Source: IQVIA, PhRMA, and EY analysis

Probability of Drug Launches and other Analyses

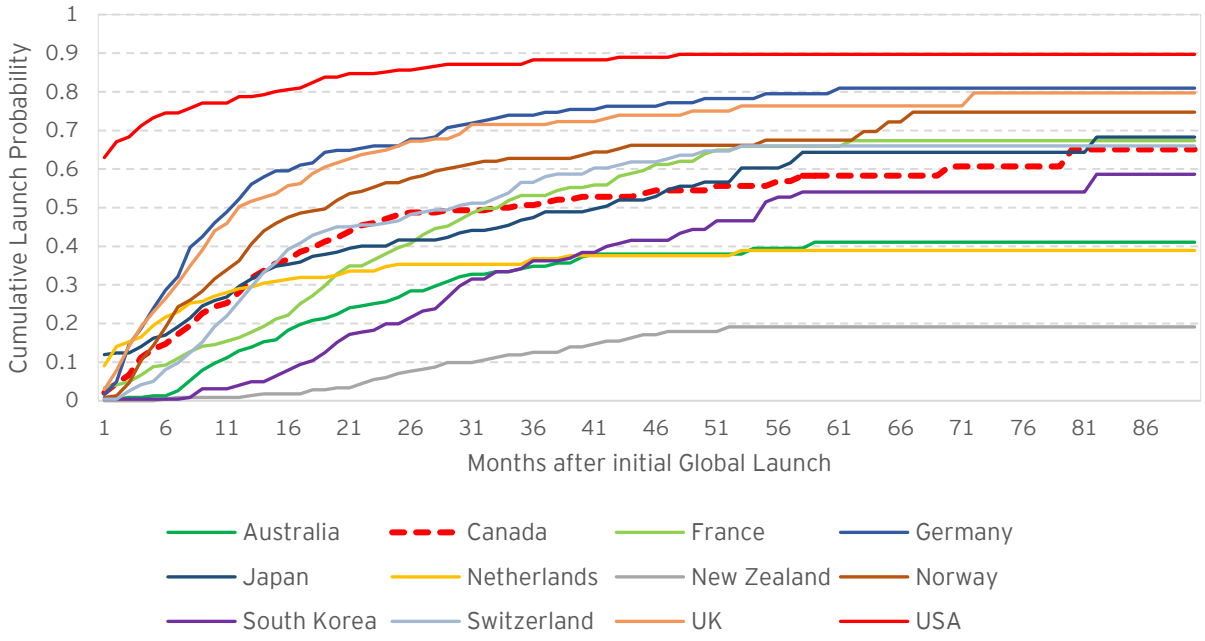
Launch delay calculations do not account for the possibility that drugs might be launched outside of the observed sample period or for drugs that will never launch in a country. However, using statistical methods, we can account for missing data on drugs that have not launched. For example, the Kaplan-Meier methodology[24] allows for comparisons of launch sequencing across countries over time that accounts for limitations in the source data. The function estimates what proportion of total drugs launched globally are launched in a given country after initial global launch. The Kaplan-Meier method also illustrates how time to launch for drugs varies across jurisdictions. Figure 8 below graphs the proportion of total potential drugs that have been launched in a given country from the time of global launch.

As illustrated in Figure 8, most drug launches occur within 5 years of first global launches. The cumulative launch probability of NASs in the USA exceeds all other countries at any given point in time

[24] Rich, Jason T., J. Gail Neely, Randal C. Paniello, Courtney Christine Joan Voelker, Brian Nussenbaum, and Eric W. Wang. 2010. "A practical guide to understanding Kaplan-Meier curves." *Otolaryngology - Head and Neck Surgery* 143 (3): 331-336.

after a global launch. Within about 4 years after a global launch, approximately 90 percent of global drugs are launched in the USA. Among the set of countries analyzed, Canada's cumulative launch probability is initially positioned in the middle. Despite surpassing Netherlands, Japan, and Switzerland in the short term, Canada is overtaken by a number of countries over the long-run. Canada has a cumulative proportion of 65 percent of total drugs launched by the end of the time period examined. The cumulative launch probability of a drug launch in Canada is always lower than countries like the USA, UK, and Germany, but higher than New Zealand, South Korea and Netherlands. In New Zealand, the cumulative launch probability never exceeds 20 percent.

Figure 8. Kaplan-Meier Estimates of Cumulative Launch Probability by Select Countries



Source: IQVIA, PhRMA, and EY analysis

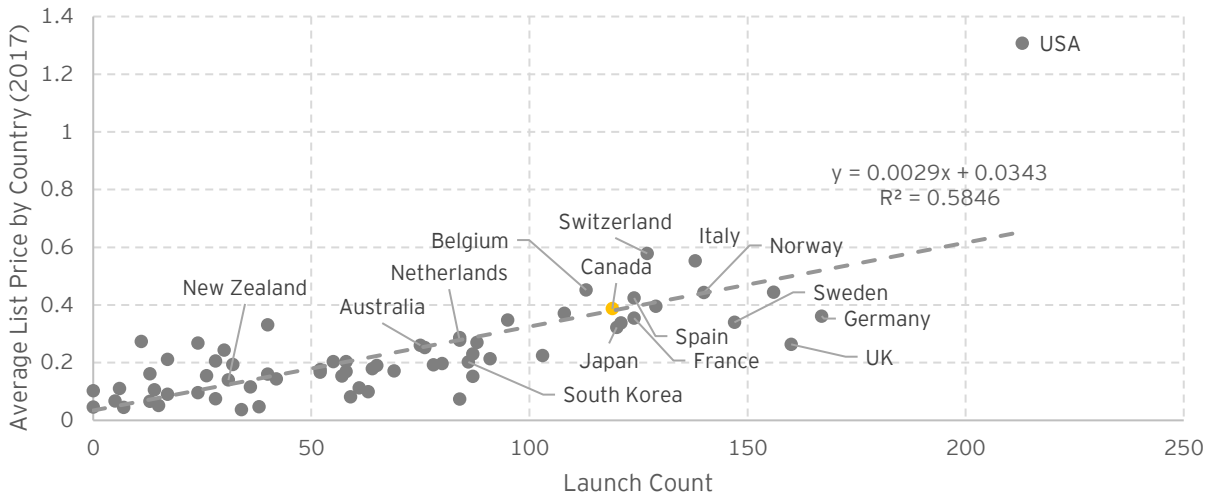
Relationship between Price and Launches

The proposed implementation of the amendments to the *Patented Medicines Regulations* will, according to the PMPRB, significantly reduce the maximum prices for many innovative drugs in Canada.[25] As such, it is important to consider how changes in price ceilings could impact the launch sequencing of new drugs. The existing academic and industry research suggests that price is among the key factors for launch decisions and launch sequencing. In other words, stringent price control regimes are associated with increased delays in drug launches, after controlling for other factors that

[25] Patented Medicines Prices Review Board. 2018. *Guidance document on changes to the Guidelines*.

impact launch sequencing.[26] These results should be interpreted with some caution as most research papers on this topic cover a study period that is more than a decade old and the global pharmaceutical market has changed markedly in the past decade. Nevertheless, recent data on list prices supports the hypothesis that drug prices are positively correlated with drug launches. For example, Figure 9 shows that 2017 average list prices are positively related to total launch counts, and in fact, may explain up to 58 percent of the variation of launch counts for 2017. This positive relationship does not, however, imply causation. There are other factors that impact launch sequences, such as market size and demand, regulatory conditions, local and global market competitors, and more generally, economic, social, and financial factors. The estimated coefficient for list prices may be biased upwards for a number of reasons; For instance, higher list prices may represent more favourable market conditions for pharmaceutical companies, which in turn may proxy for strong institutional quality, which is correlated with more developed, richer economies. As such linear model merely reflects the positive relationship between launch counts and list prices.

Figure 9. Launch Counts and Average List Prices



Note: Average prices are computed by using the weighted average of list prices per standard unit for each country, using the data available through IQVIA for 2017.

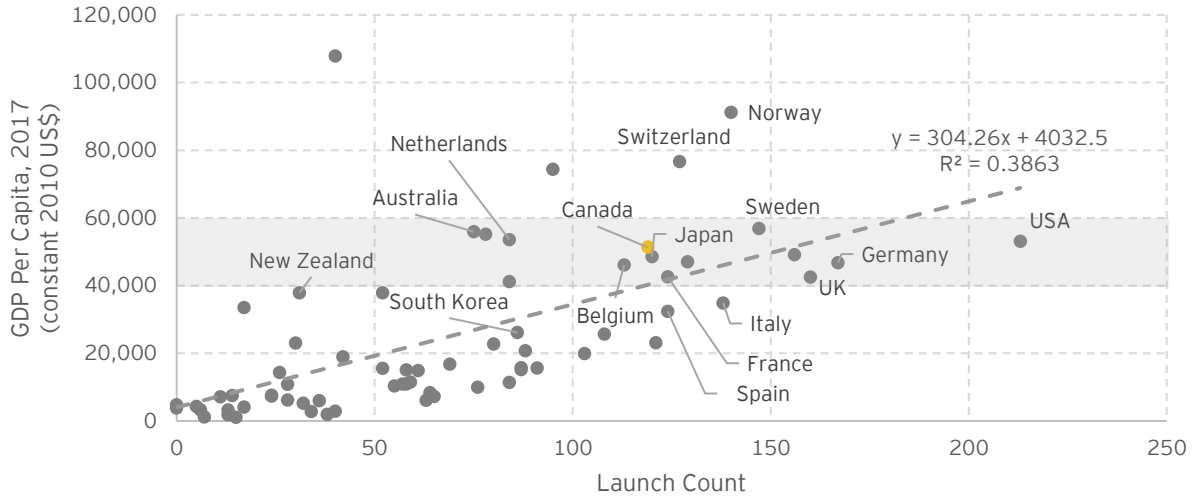
Source: IQVIA, PhRMA, and EY analysis

As an example, some of the differences in prices between countries may likely be driven by the variation in buying power for individuals across countries. As such, total launch count is likely positively correlated to per capita GDP, which would likely impact drug price levels as it determines the ability for local patients to pay for innovative medicines (Figure 10). However, the graph below suggests that there are considerable differences in launch counts across countries with similar levels of GDP per

[26] Danzon, Wang, and Wang. "Impact of Price Regulation." 269-292; Lanjouw. *Patents, Price Controls and Access to New Drugs*; Kyle. "Pharmaceutical Price Controls and Entry Strategies." 88-99; Danzon and Epstein. "Effects of Regulation." 35-71; Cockburn, Lanjouw, and Schankerman. "Patents and the Global Diffusion of New Drugs." 136-164.

capita, some of which can be attributed to price levels or other factors. For example, there is significant variation in total launch counts across countries with US$40,000 to US$60,000 in GDP per capita (shaded area). Germany had more than twice the number of total NAS launches as Australia, despite having a lower GDP per capita in 2017. Figure 10 illustrates a positive relationship between launch counts and GDP per capita, with GDP per capita capturing up to 38 percent in the variation of launch count. The low explanatory power is not surprising as there are a number of other contributing factors that influence launch decisions.

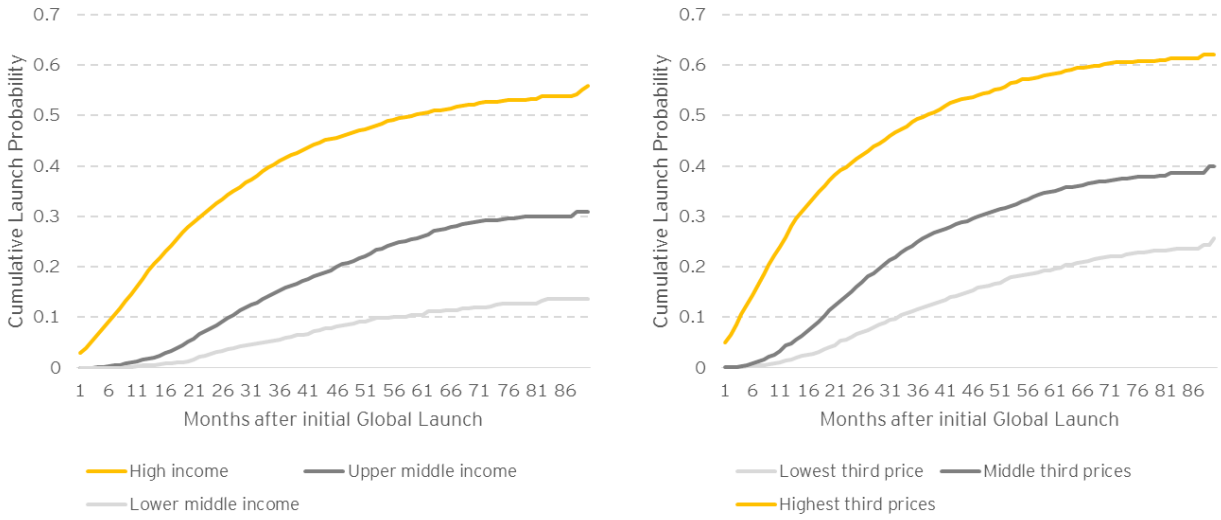
Figure 10. Launch Counts and GDP per capita



Source: The World Bank, IQVIA, PhRMA, and EY analysis

The Kaplan-Meier method can be used to further demonstrate how price and income levels are related to drug launches over time – Figure 11 below graphs the estimated cumulative probability of a NAS drug launch by price and income groups of countries. Details on country groupings can be found in Appendix A.4 and Appendix A.5. In particular, the Kaplan-Meier estimates across income groups reflect significant differences in launch probabilities between high income, upper middle income, and lower middle income countries. The gap between the bottom income group of countries and other countries noticeably increases over time. Similar differences in launch probabilities are seen between groups of countries by price levels. Countries with the highest third of average list prices outpace other countries in drug launches over time. For example, eight to nine months after initial global launch, they had a cumulative launch probability of 62.1 percent. For the middle and bottom third of countries, the cumulative probability was 39.9 and 25.7 percent respectively. While price levels are not the only factor for launch decisions, lower prices are associated with increased delays in innovative drug launches.

Figure 11. Launch Probabilities by Price and Income Levels



Note: "High income", "Upper middle income", and "Lower middle income" are income groupings for countries defined by the World Bank. Countries included in the launch dataset are grouped in three groups of price levels using the weighted average of list prices per standard unit from IQVIA for 2017.

Source: The World Bank, IQVIA, PhRMA, and EY analysis.

Discussion

Key Takeaways and Implications from our Analysis

- Current launch sequencing in Canada is relatively comparable to other similar jurisdictions in terms of total launch counts and launch lags: Canada ranks in the middle of the pack.
- Canada has more favourable drug launch outcomes than certain jurisdictions including Australia, New Zealand, and South Korea, but less favourable than USA, UK, and Germany.
- The USA is often the previous and/or the only other market for drugs launched in Canada, suggesting that the market conditions in the USA impact the launch sequencing of innovative drugs in Canada.
- Based on the launch sequencing data, launch counts have a significant positive correlation with invoiced prices and GDP per capita.

Based on recent data on global launch sequencing, relative to other comparator jurisdictions, Canada ranks in the middle or close to the average for global launches of innovative drugs. Further, the analysis from the current launch data suggests an inverse relationship between launch delays and drug prices, consistent with previous academic and industry reports suggesting that jurisdictions with more favourable pricing regimes are associated with more drug launches and faster launches.[27]

While it is difficult to predict specific outcomes of the proposed changes to the *Patented Medicines Regulations*, these findings suggest that the potential for a negative impact on launches of innovative drugs in Canada is not insignificant. There are legitimate concerns regarding the sustainability of drug expenditures; however cost-containment measures that significantly reduce the national price ceiling and the visible price may further delay the launch of innovative drugs in Canada, which may have negative consequences to patient access. The cost-benefit analysis conducted by Health Canada on the proposed amendments to the *Patented Medicines Regulations* did not explicitly consider costs or benefits as a result of potential changes in access to innovative medicines, such as longer delays or drugs that may never be launched as a result.[28]

Our analysis is focused on comparing Canada to 15 jurisdictions that are comparable in health care access, general standard of care, and standard of living to provide further insights on how changes to historical market conditions may have impacted launch decisions. For example, pricing policy changes in Australia and New Zealand and subsequent launch delays in these jurisdictions may demonstrate the potential consequences of adopting a stringent pricing regime for innovative medicines. Specifically, the price reforms undertaken by New Zealand's PHARMAC in the early 1990s appeared to have negatively impacted the availability of innovative medicines, as demonstrated in our analysis showing that New Zealand has long delays in drug launches and among the lowest total number of drugs launched. The results from our analysis are also consistent with the experience in Australia, where previous pricing policy changes significantly reduced the prices of innovative medicines, which may have in turn contributed to increased delays and reduced total launches.

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[27] Danzon, Wang, and Wang. "Impact of Price Regulation." 269-292; Lanjouw. *Patents, Price Controls and Access to New Drugs*; Kyle. "Pharmaceutical Price Controls and Entry Strategies." 88-99; Danzon and Epstein. "Effects of Regulation." 35-71; Cockburn, Lanjouw, and Schankerman. "Patents and the Global Diffusion of New Drugs." 136-164.

[28] Government of Canada, Department of Health. 2017. *Regulations Amending the Patented Medicines Regulations*.

In summary, based on our review of the data and our insights from previous research, significant drug price reductions in Canada due to the proposed amendments to the *Patented Medicines Regulations*, or other potential cost-containment measures, may reposition Canada as a lower priority destination for drug launches over the long term. More generally, this regulatory disruption may represent a risk for pharmaceutical companies, and ultimately adversely impact launches of innovative medicines in Canada over the long term.

It is also important to note that increased launch lags and reduced access to innovative drugs for patients are but two potential impacts of cost containment measures for drugs. For policy makers, such an outcome may have longer-term implications for a life-sciences focused innovation agenda and for the overall life sciences innovation ecosystem, in the event that global pharmaceutical companies may re-prioritize discretionary investments in research, innovation and other areas.

For patients, reduced or delayed access to innovative medicines may narrow treatment options in an environment where patients and patient groups are increasingly aware of breakthrough innovations being developed at a global level, particularly for rare and orphan diseases. Moreover, the impact on patients on clinical trials in Canadian settings, may ultimately be significant if a manufacturer ultimately decides to delay or defer the launch of the product in Canada.

Next Steps

While the analysis in this report does not formally address these other potential impacts, the findings from this research should help facilitate future discussions and studies on the link between drug price containment measures and launch decisions on health outcomes over the long term. Moreover, impacts on the ability for pharmaceutical companies to recoup economic investments may also influence future investment plans. A review of responses from stakeholders, including patients, business advocacy groups, and industry, to the proposed changes to the Patented Medicines Regulations in Canada Gazette Part 1 reflects the variety of perspectives on potential impacts that may ensue.[29]

Ultimately, affordability, sustainability, patient access and outcomes, and investment in innovation are among the factors that must be balanced in determining the most effective policy in achieving the desired outcomes. To the extent that launch decisions impact any of these factors either positively or negatively, it is essential that all stakeholders consider the long-term consequences of short and mid-term decisions.

[29] Canada Gazette Part 1 Consultation Responses. February 2018. PDCI.

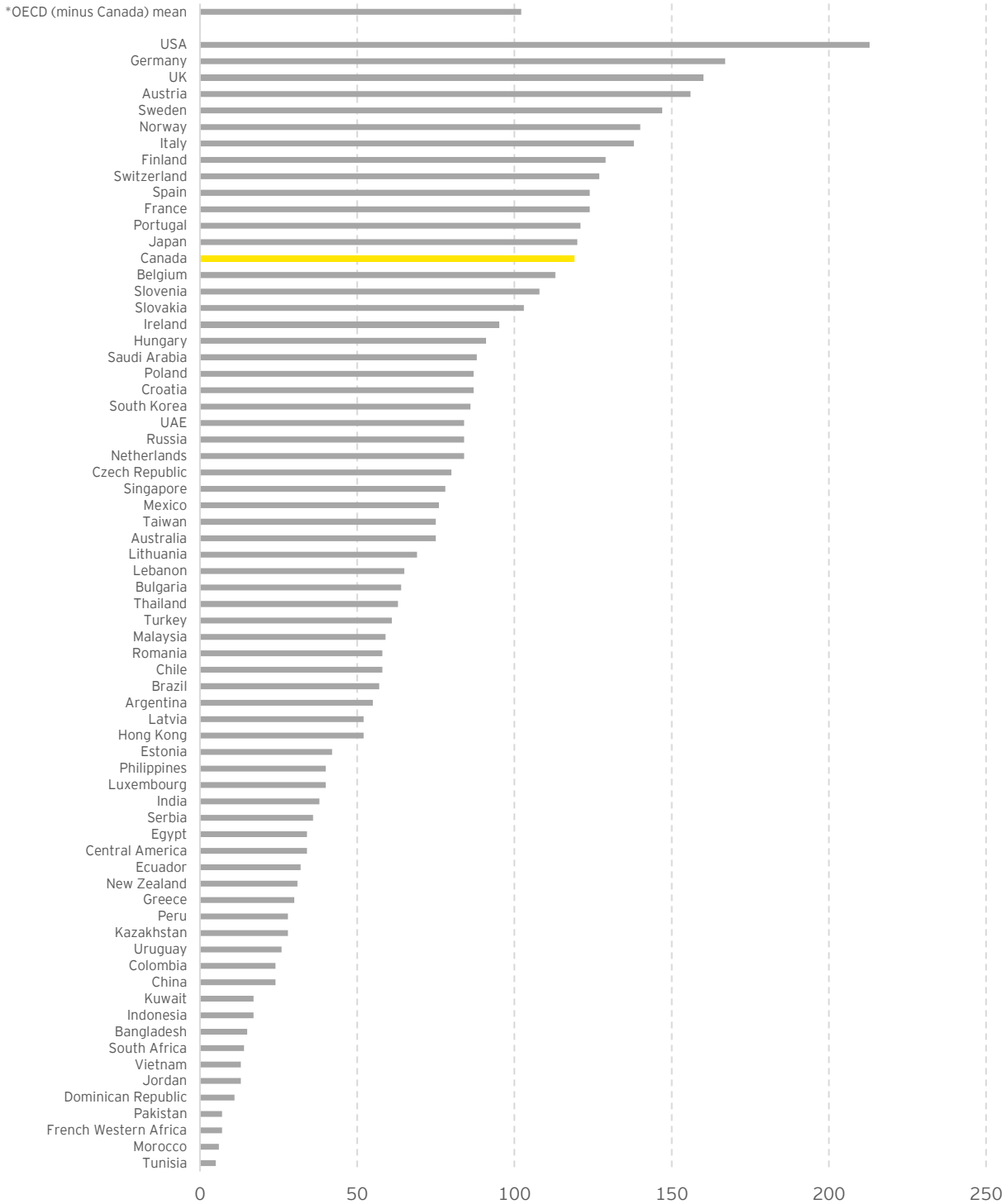
Appendix

Appendix A: Glossary

Terms	
PMPRB	Patented Medicines Prices Review Board
NAS	New Chemical or Active Substances
ERP	External Reference Pricing
EMA	European Medicines Agency
US FDA	US Food and Drug Administration
PMDA	Japanese Pharmaceuticals and Medical Devices Agency
R2D2	Regulatory Review of Drugs and Devices
PHARMAC	Pharmaceutical Management Agency
NPI	New Product Intelligence
KDM	Key Developed Markets

Appendix A.1

Launch Count Overview for all Jurisdictions



Source: IQVIA, PhRMA, and EY analysis

Appendix A.2

Drug Launches in Canada by Therapeutic Area

Therapeutic Area	Canada Count	Canada Rank	Total Count
Total Launch Count	119	14	243
Anti-infectives/Antivirals	19	16	34
Blood	3	22	13
Cardiovascular	7	5	10
CNS	9	10	23
Dermatology	7	2	11
Diabetes	8	3	15
Gastrointestinal	4	5	10
GU and hormones	2	20	6
Immune System	3	26	6
Metabolic	2	12	8
Musculoskeletal	2	14	9
Oncology	43	12	74
Opthamologics	3	2	7
Other	0	27	6
Respiratory	7	10	11

Source: IQVIA, PhRMA, and EY analysis

Appendix A.3

Launch Lags in Canada by Therapeutic Area

Therapeutic Area	Canada Median Lag	Canada Rank	Canada Count
Anti-infectives/Antivirals	2	2	19
Blood	9	12	3
Cardiovascular	4	4	7
CNS	16	18	9
Dermatology	11	11	7
Diabetes	26	45	8
Gastrointestinal	17	12	4
GU and hormones	19	7	2
Immune System	5	6	3
Metabolic	39	19	2
Musculoskeletal	9.5	9	2
Oncology	11	8	43
Opthamologics	24	31	3
Other			
Respiratory	9	10	7

Source: IQVIA, PhRMA, and EY analysis

Appendix A.4

Country Groupings by List Price

Lowest Third Prices	Middle Third Prices	Highest Third Prices
Algeria	Argentina	Austria
Bangladesh	Australia	Belgium
Brazil	Bulgaria	Canada
Colombia	Chile	China
Egypt	Croatia	Dominican Republic
Estonia	Czech Republic	Finland
India	Ecuador	France
Indonesia	Greece	Germany
Kazakhstan	Hong Kong	Ireland
Malaysia	Hungary	Italy
Morocco	Jordan	Japan
New Zealand	Kuwait	Luxembourg
Pakistan	Latvia	Netherlands
Poland	Lebanon	Norway
Russia	Lithuania	Portugal
Serbia	Mexico	Saudi Arabia
South Africa	Peru	Slovenia
Sri Lanka	Philippines	Spain
Thailand	Romania	Sweden
Tunisia	Singapore	Switzerland
Turkey	Slovakia	UAE
Uruguay	South Korea	UK
Vietnam		USA

Appendix A.5

Country Groupings by GDP per Capita

High Income		Upper Middle Income	Lower Middle Income
UAE	Italy	Bulgaria	Bangladesh
Argentina	Japan	Brazil	Egypt
Australia	South Korea	China	Indonesia
Austria	Kuwait	Colombia	India
Belgium	Lithuania	Dominican Republic	Sri Lanka
Canada	Luxembourg	Algeria	Morocco
Switzerland	Latvia	Ecuador	Pakistan
Chile	Netherlands	Jordan	Philippines
Czech Republic	Norway	Kazakhstan	Tunisia
Germany	New Zealand	Lebanon	Vietnam
Spain	Poland	Mexico	
Estonia	Portugal	Malaysia	
Finland	Saudi Arabia	Peru	
France	Singapore	Romania	
UK	Slovakia	Russia	
Greece	Slovenia	Serbia	
Hong Kong	Sweden	Thailand	
Croatia	Uruguay	Turkey	
Hungary	USA	South Africa	
Ireland			

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