Patented Medicine Prices Review Board
Conseil d'examen du prix des médicaments brevetés

Canada

Drug Shortages in Canada and their Impact on Public Drug Plans

2017/18 to 2019/20

National Prescription Drug Utilization Information System
NPDUIS

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About the PMPRB

The Patented Medicine Prices Review Board (PMPRB) is an independent quasi-judicial body established by Parliament in 1987. The PMPRB has a dual regulatory and reporting mandate: to ensure that prices at which patentees sell their patented medicines in Canada are not excessive; and to report on pharmaceutical trends of all medicines and on research and development spending by patentees.

The NPDUIS Initiative

The National Prescription Drug Utilization Information System (NPDUIS) is a research initiative established by federal, provincial, and territorial Ministers of Health in September 2001. It is a partnership between the PMPRB and the Canadian Institute for Health Information (CIHI).

Pursuant to section 90 of the *Patent Act*, the PMPRB has the mandate to conduct analysis that provides decision makers with critical information and intelligence on price, utilization, and cost trends so that Canada's healthcare system has more comprehensive and accurate information on how medicines are being used and on sources of cost pressures.

The specific research priorities and methodologies for NPDUIS are established with the guidance of the NPDUIS Advisory Committee and reflect the priorities of the participating jurisdictions, as identified in the NPDUIS Research Agenda. The Advisory Committee is composed of representatives from public drug plans in British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Yukon, the Non-Insured Health Benefits (NIHB) Program, and Health Canada. It also includes observers from CIHI, the Canadian Agency for Drugs and Technologies in Health (CADTH), the Canadian Drug Agency Transition Office, the Ministère de la Santé et des Services sociaux du Québec (MSSS), and the pan-Canadian Pharmaceutical Alliance (pCPA) Office.

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Executive Summary

This study provides insight into the impact of drug shortages in Canada, focusing on the effects on Canadian public drug plans and their beneficiaries. Drawing on data from fiscal years 2017/18 to 2019/20, the analysis examines trends in the number, market segment, therapeutic area, and duration of drug shortages in Canada and explores their impact on public drug plan beneficiaries as well as on public plan spending.

Disruptions in the availability of medications are an international issue with wide-ranging impacts across global and domestic health-care systems. Canada's *Food and Drug Regulations* define a drug shortage as a situation in which a market authorization holder (manufacturer) is unable to meet the demand for the drug in its entirety and on time. This may arise under several different circumstances, including production issues, sole source contracting, unexpected surges in demand for a drug, and difficulties accessing raw supplies.[1]

The *Food and Drug Regulations* require manufacturers of certain drugs to report when they are not able to meet demand for a product or when they stop selling a product.[2] These shortages or discontinuations are published on the Drug Shortages Canada website, the primary data source used by the report. Compliance and enforcement activities related to these reporting requirements are overseen by the Regulatory Operations and Enforcement Branch, Health Canada. The public drug plan information used in the report comes from the Canadian Institute for Health Information's (CIHI) National Prescription Drug Utilization Information System (NPDUIS) database, which includes data for the following jurisdictions: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Yukon, and the Non-Insured Health Benefits Program.

This report provides a broad overview of the issue of drug shortages in Canada using the Drug Shortages Canada website. Its study period, which precedes the COVID-19 pandemic and its associated complexities, will provide useful reference information to understand the effects of the pandemic and the multiple efforts to prevent and mitigate shortages since its onset. Although the report uses a wide perspective, the negative impact

1 https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-shortages.html
2 https://www.drugshortagescanada.ca/

of drug shortages on individual patients and the health care system should not be overlooked, particularly when substitutions are not possible or when variations in strength and formulation are not interchangeable.

The information provided in this report is of value to all those affected by shortages, including Canadian patients, healthcare providers, and public and private payers.

Key Findings

- **Between April 1, 2017, and March 31, 2020, a total of 8,558 shortage reports were filed by Canadian manufacturers**, for an average of 238 new reports per month.
- **In 2019/20, shortages were reported for 29% of the medicines sold in Canada**. Generic drugs and drugs with a low treatment cost (<$10,000/year) had higher rates of drug shortages. No association was found between the relative international price of drugs and shortage rates in Canada.
- **The vast majority (91%) of shortage reports concerned multi-source non-patented medicines**, for which substitutions to the same pharmaceutical ingredients from another manufacturer were possible in most cases. Patented medicines and single-source non-patented medicines accounted for 7% and 2% of reports, respectively.
- **Over half (55%) of the drug shortages reported were resolved within three months of their onset**. About three quarters of shortages (74%) were updated to "resolved" within six months. Shortages of patented and single-source non-patented medicines were resolved faster than those of multi-source non-patented medicines.
- **Of the drugs with a shortage reported, 70% had fewer than 1,000 monthly NPDUIS public drug plan beneficiaries before the shortage**, while just 5% had over 10,000 monthly beneficiaries.
- **At the drug level, 40% of shortages were followed by a steep decline (>20%) in public plan beneficiaries**. However, when considering chemical subgroups of drugs (groups of similar chemicals that can be used as substitutes for drugs in shortage), only 8% of shortages were associated with a steep beneficiary decline.
- **Shortages associated with a steep decline in beneficiaries primarily occurred in chemical subgroups of drugs with small market sizes**, characterized by low spending, small numbers of public plan beneficiaries, and few generic drugs available for substitution. On average, these shortages lasted three months longer than those with a modest decline in beneficiaries.
- **Most shortages did not significantly disrupt spending patterns for public plans**. When accounting for substitutions to other drugs, less than a quarter of shortages (19%) resulted in a shift in spending greater than 20%. Shortages were associated with significant spending decreases as often as increases (9% and 10% of shortages, respectively).

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Introduction

Shortages in the supply of medications have become an issue of great importance to Canadian patients, healthcare providers, manufacturers, distributors, group purchasing organizations, and insurers. A 2020 study estimated that shortages affected nearly 25% of drugs marketed in Canada between 2017 and 2018 (Zhang et al. 2020). In cases where substitutions are unavailable or ineffective, these disruptions can pose a significant health risk to patients.

In recent years, multiple efforts were made to prevent and mitigate drug shortages in Canada. Key among them were the creation of the Multi-Stakeholder Committee on Drug Shortages in 2012 to address shortages in a collaborative and coordinated manner (MSSC, 2017) and the requirement for market access holders to report to the Drug Shortages Canada website since March 2017 (Donelle et al., 2018). Measures were also implemented within the context of the early COVID-19 pandemic and have since remained in place, such as the public disclosure of "Tier 3" drug shortages, which have the greatest potential impact on Canada's drug supply and health care system (Health Canada, 2022a), and the framework for the exceptional importation of drugs not otherwise licensed in Canada in response to such shortages (Drug Shortages Division, 2022; Health Canada, 2022b).

To inform these efforts and provide further details on the implications of drug shortages for the healthcare system, this report presents an overview of drug shortages in Canada and their impact, with a focus on the effects on publicly insured Canadians and public drug plans. The analysis draws from data collected on the Drug Shortages Canada website, which is maintained by Health Canada, as well as sales and utilization information from the IQVIA MIDAS® database and the Canadian Institute for Health Information's (CIHI) National Prescription Drug Utilization Information System (NPDUIS) database. Findings are focused on the three-year period spanning from fiscal year 2017/18 to 2019/20, which precedes most of the disruptions of the COVID-19 pandemic.

The report consists of five sections: Section A presents high-level trends in drug shortages

reported by Canadian manufacturers; Section B documents the types of drugs most likely to be impacted by shortages; Section C analyzes the resolution rates and duration of shortages; Section D explores the impact of shortages for beneficiaries of Canadian public insurance plans; and Section E examines the impact of shortages on public plan spending. This report may be considered a starting point, or benchmark, in the monitoring of the issue of drug shortages and its impact for Canadians.

Methods

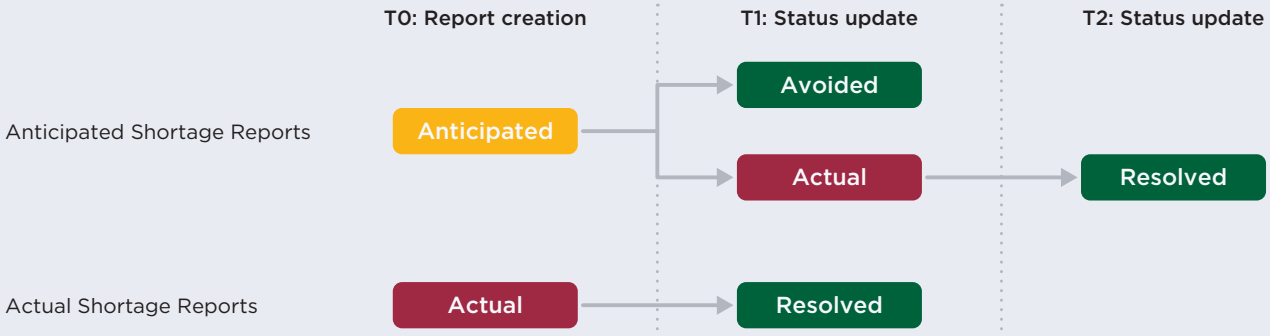
The key data source used for the report is the Drug Shortages Canada website, to which manufacturers to whom a drug market authorization was issued by Health Canada are required to report when they are not able to meet demand for a product and when they discontinue a product (Drug Shortages Canada, [n.d.]; Health Products Compliance Directorate, 2017). The requirement concerns prescription drugs for human use, drugs listed in Schedules D and C of the *Food and Drug Act*, drugs included in Schedules I to V of the *Controlled Drugs and Substances Act*, and certain non-prescription drugs administered under a practitioner's supervision (Health Products Compliance Directorate, 2017). These reports are made publicly available on the Drug Shortages Canada website database, which holds records dating back to March 10, 2017. For simplicity, this report will use the term "manufacturers" to refer to market authorization holders in the remainder of the text.

In-depth: Shortage reports

Shortage reports accessible on the Drug Shortages Canada website feature detailed drug information including the drug identification number (DIN), brand name, common name, company name, active ingredient(s), strength, dosage form, route, packaging size, and World Health Organization Anatomical Therapeutic Chemical classification system (ATC) code.

Information specific to shortages includes the reason for the shortage, shortage status as of the most recent report update, and start and end dates of the shortage. Because shortages are reported at the DIN and packaging-size levels, each distinct strength, form, brand name, and package size of a pharmaceutical ingredient in shortage are reported separately.

Shortage report status and transitions on the Drug Shortages Canada website



The status of a shortage report can change over time. When a report is first created, a shortage can be either "actual" or "anticipated". Companies can update the status of shortages at any time, and they can transition from their initial status to "actual", "avoided", or "resolved". In some cases, an "avoided" or "resolved" shortage status is accompanied by the creation of a discontinuation report, meaning that the drug is no longer sold by the manufacturer.

This report uses a May 2020 extract of the Drug Shortages Canada website data and contains information on the reports created from the website's launch until 30 April 2020. The majority of the analyses performed in this report use the 8,558 shortage reports created between April 1, 2017, and March 31, 2020, the study period. Shortages with a start date prior to the website creation in March 2017 were considered out of scope of the report.

Using these data, the report provides an analysis of pre-COVID-19 pandemic trends in Canadian shortages and their characteristics, including an analysis of the new shortage reports created monthly during the study period, the reasons most associated with shortages, and shortage duration.

To provide a sense of the scale of drug shortages within the Canadian pharmaceutical ecosystem, the report uses data from the IQVIA MIDAS® database (all rights reserved). MIDAS data reflects the national retail and hospital sectors in Canada and internationally, including payers in all market segments (public, private, and out-of-pocket). Sales and volume data encompass all versions of a drug available, produced by any manufacturer in any strength and form. Matching shortage reports with MIDAS data allows assessing the proportion of drugs available in Canada impacted by shortages and whether these are correlated with relative international prices.

Finally, to provide an assessment of the consequences of shortages for publicly insured Canadians and public payers, Sections D and E of the report conduct analyses using the Canadian Institute for Health Information's (CIHI) National Prescription Drug Utilization Information System (NPDUIS) database. The NPDUIS database houses pan-Canadian prescription claims-level data, focusing primarily on publicly financed drug benefit programs: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and Yukon, as well as Indigenous Services Canada's Non-Insured Health Benefits (NIHB) drug plan.

Throughout, shortages are defined as a situation in which a drug or a drug within a chemical subgroup are reported as being in "actual" shortage. A drug is defined as a unique combination of a manufacturer, an ingredient or combination of ingredients, a strength, and a formulation (e.g., tablet). Chemical subgroups are defined based on the fourth level of the World Health Organization's Anatomical Therapeutic Chemical classification system, as detailed in In-depth box "Drug substitutions during shortages," in Section D. Ingredients in shortage are defined as distinct pharmaceutical ingredients for which drugs representing at least 90% of annual sales had a shortage report with an "actual" status. For analyses that use the IQVIA MIDAS® database, shortages are matched to drugs with sales in Canada using the ingredient, strength, form, and manufacturer listed on shortage reports. When the NPDUIS database is used, shortages are matched to claim using the DINs listed on shortage reports. Shortage rates are defined as the percent of drugs with sales in Canada that were matched with an "actual" shortage report, either at a specific date (Section A) or at any point during the 2019/20 fiscal year (Section B).

For market segment analyses, a medicine is classified as "patented" if the associated DIN was patent-protected in the year of the report's creation. A non-patented medicine is classified as "single-source non-patented" if its medicinal ingredient had a single manufacturer with sales in Canada during the year; "multi-source non-patented" indicates that the ingredient was available through multiple manufacturers.

Treatment costs are based on the IQVIA Private Drug Plan database and defined as the ratio between annual spending on a drug and the number of claimants. Oral solid medicines are drugs with a "tablet" or "capsule" formulation.

In sections D and E, the percent change in the number of active public drug plan beneficiaries and spending during shortages is calculated using the ratio of the average monthly number of beneficiaries and spending during the shortage and up to six months prior to the shortage. An active beneficiary is a public

plan enrollee who filed at least one claim in a given month. The period during the shortage excludes the onset month of the shortage. These calculations are restricted to the shortages for which NPDUIS claims were made both prior to the shortage and during the shortage.

Foreign-to-Canadian price ratios (FTCs) presented in this report are expressed as an index with the Canadian price set to a value of one and the international median reported relative to this value. Prices and sales in foreign currencies are converted into Canadian dollars using the average exchange rate for the year. International markets examined include Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, Spain, Sweden, and the United Kingdom (UK), which will comprise the PMPRB Schedule countries ("PMPRB11").

For more details on how Foreign-to-Canadian price ratios are calculated or for more information on the MIDAS Database, the NPDUIS database and other NPDUIS source materials, see the Resources Section of the Analytical Studies page on the PMPRB website.

Limitations

This study relies on reports featured in the Drug Shortages Canada database to represent the issue of shortages in Canada. However, while manufacturers are mandated to report shortages, the degree of compliance with the mandate has not been assessed and the true number of shortages could be greater than those reported on the website. In some cases, imperfect reporting could also mean that resolved shortages were not updated and continued to show as "actual" on the website after their resolution.

In addition, the self-reported nature of the data may suggest that reporting practices could differ from manufacturer to manufacturer and over time, for example regarding the reporting of "anticipated shortages" (which appeared to become less prominent during the study period) and selecting a reason for shortages.

Because shortages with a start date prior to March 10, 2017, were considered out of scope of the report, the number of drugs in shortage in Figures A2 and A3 is underestimated in the first half of 2017/18, during which time only the most recent shortages are included. Given the typical duration and resolution rates of shortages described in Section C, results from the second half of 2017/18 onward are more accurate in those figures.

Because the IQVIA MIDAS® database does not identify drugs using DINs, shortage reports were matched with this database using the ingredient, strength, form, and manufacturer listed on reports. For 10.2% of reports (N=878), drugs mentioned by reports could not be matched with MIDAS equivalents based on those fields, which suggests that shortage rates presented in Sections A and B underestimate true shortage rates.

Sections D and E document the change in the number of active beneficiaries and spending during shortages. These analyses are observational in nature and variations may be caused by other factors. For example, macroeconomic fluctuations and policy changes during the analysis may have impacted the population eligible for coverage and thus the number of active beneficiaries and spending.

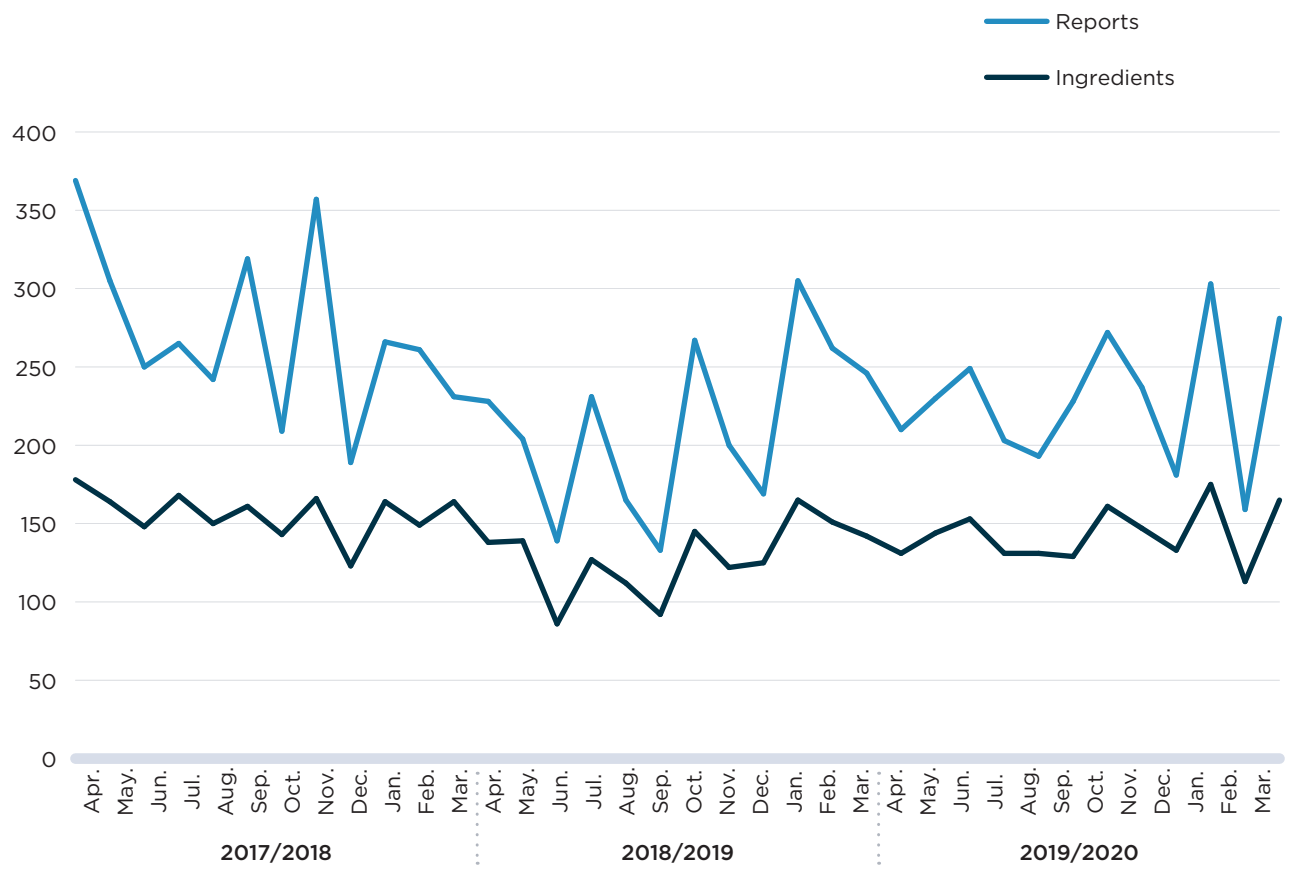
The chemical subgroup analyses capture substitutions within the chemical subgroup and do not capture potential valid alternatives from other subgroups. The analyses may also underestimate the impact of shortages in cases where the drugs in shortage represent a small portion of the chemical subgroup and the remainder of the subgroup does not provide valid substitutes. Additionally, although analyses conducted at the chemical subgroup level aim to account for substitutions during shortages, these substitutions may be underestimated as they do not capture all cases where drugs are compounded to fill the need created by the shortage. This limitation is explored in further detail in Appendix 1.

A. Trends in Canadian drug shortage reports, 2017/18 to 2019/20

This section provides an overview of the drug shortages reported in Canada between 2017/18 and 2019/20, finding a sizeable number of shortage reports from manufacturers during this period. In addition to the number of total drug shortages reported, this section also examines trends in the monthly number of reports created, as well as the number of ingredients mentioned, the number of "actual" shortages, and the reasons cited by manufacturers.

Between April 1, 2017, and March 31, 2020, a total of 8,558 shortage reports were created by manufacturers, for an average of 238 new reports per month. As manufacturers are mandated to report all formulations and pack sizes in shortage separately, these 238 new reports correspond to an average of 143 distinct pharmaceutical ingredients mentioned in reports each month (Figure A1). This indicates that an average of 40% of reports were for ingredients mentioned by other reports.

FIGURE A1. Shortage reports created monthly on the Drug Shortages Canada website and distinct ingredients mentioned by reports, 2017/18 to 2019/20

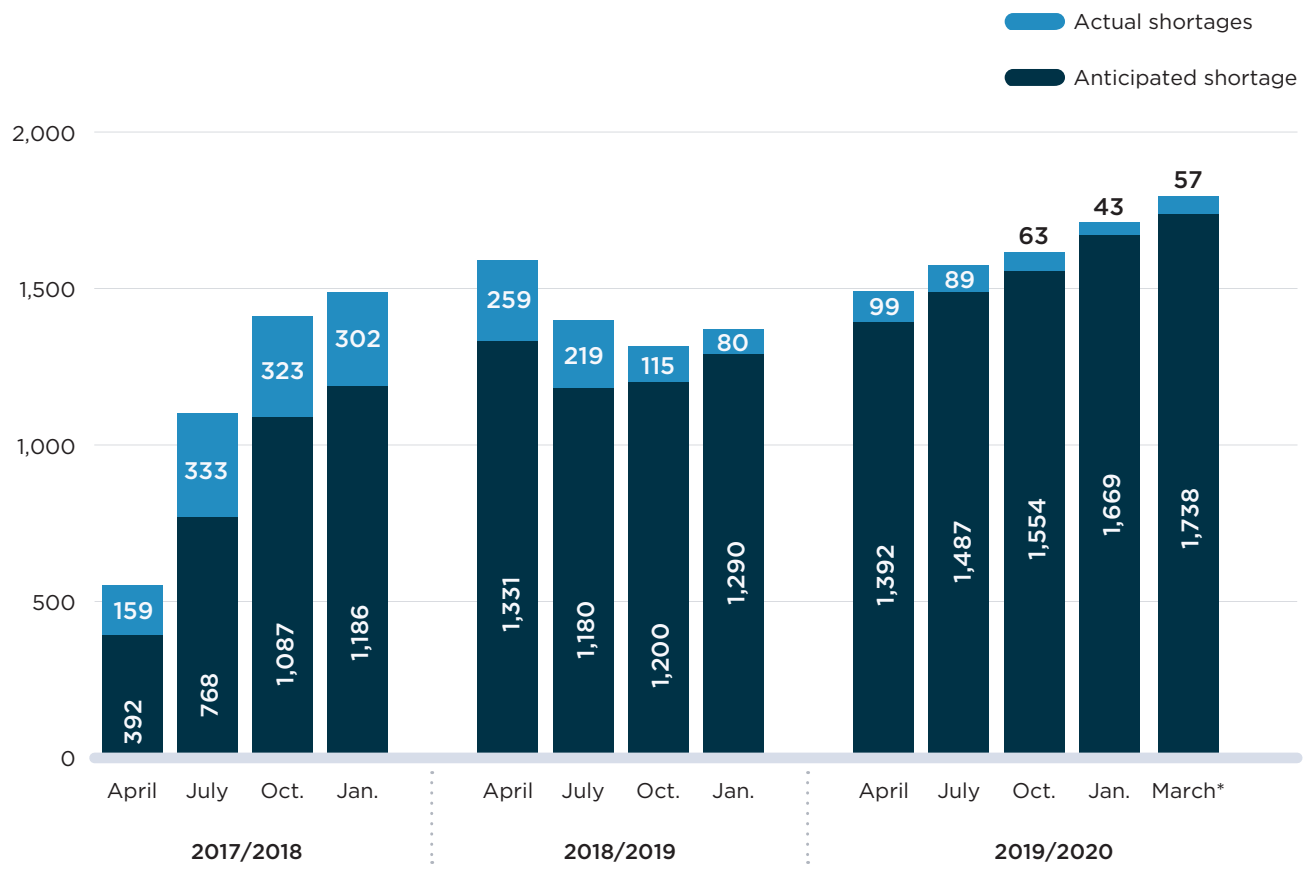


Data source: www.drugshortagescanada.ca.

As shown in Figure A1, the number of new shortage reports decreased during 2017/18, stabilizing through 2018/19 and 2019/20. The number of ingredients mentioned by reports remained stable throughout this period.

Although the number of new reports filed every month was relatively stable between 2018/19 and 2019/20, a breakdown of reports with "actual" and "anticipated" status shows a steady increase in the number of actual shortages since October 2018 (Figure A2). This indicates that there were more new shortages added to the website during this period than shortages reported as "resolved". By the end of the study period, there were 1,738 reports with an "actual" status. Meanwhile, the number of reports with an "anticipated shortage" status has declined over time and accounted for only 3% of unresolved reports as of the end of 2019/20.

FIGURE A2. "Actual" and "anticipated" shortages listed on the Drug Shortages Canada website, 2017/18 to 2019/2020



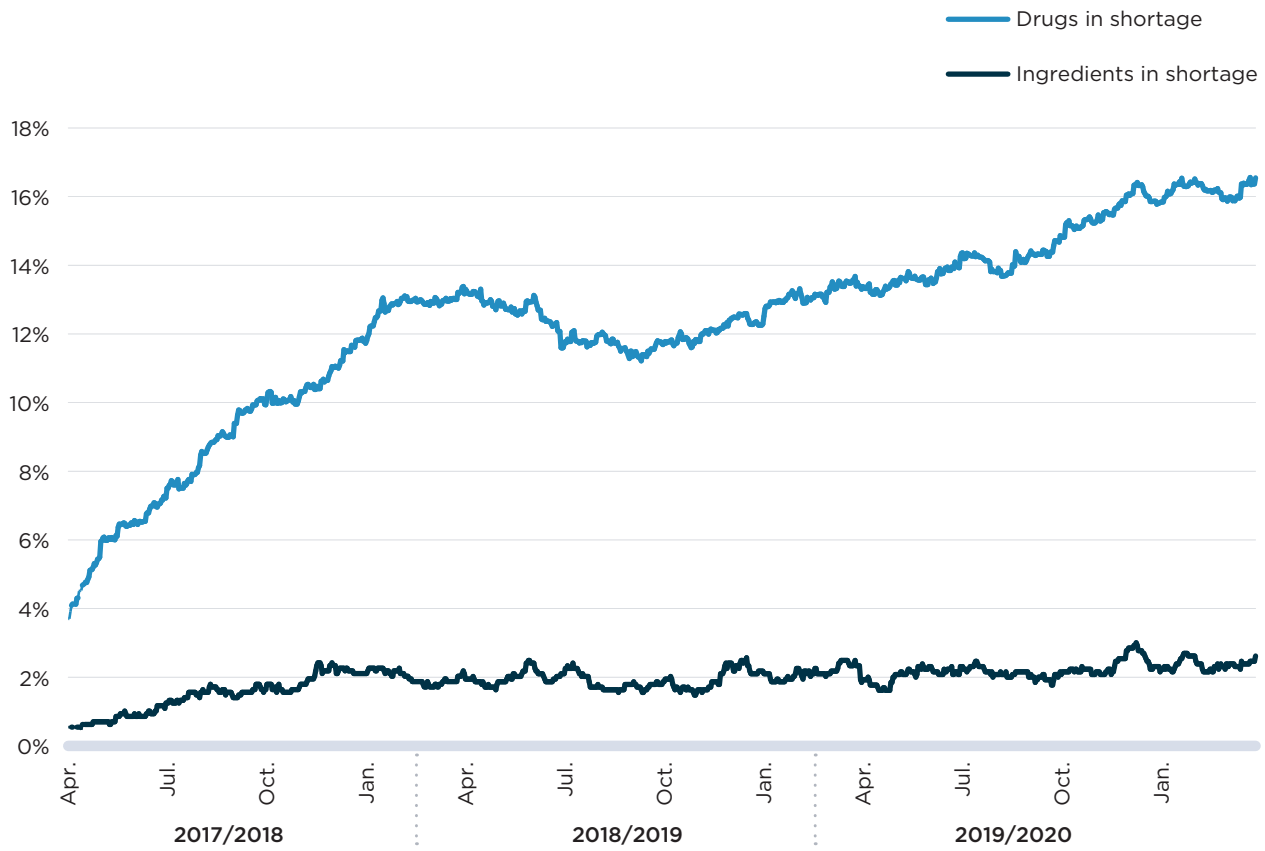
Note: Actual/anticipated shortages are the number of shortage reports with an "actual"/"anticipated" status on the first day of the month. These are determined using the report creation date, shortage start date, and shortage avoided/end date listed in the reports.
* The March 2020 values correspond to the shortages on March 31, 2020, which was the last day of the study period.
Data source: www.drugshortagescanada.ca.

To put these reports into perspective, Figure A3 gives the proportion of distinct drugs on the market in Canada that were impacted by an "actual" shortage. The results mirror the trend in the number of shortages observed in Figure A2, showing a steady increase in shortage rates since October 2018. By the end of the study period, 17% of drugs sold in Canada were reported as being in "actual" shortage.

In many cases, the same ingredient can remain available for sale during a shortage because the ingredient is offered in the same formulation and strength from a different manufacturer. Also, the same ingredient can be available to patients in a different strength or formulation, although such variations are not always interchangeable. As such, the proportion of drugs in shortage is not necessarily representative of pharmaceutical ingredients with limited access.

To better reflect the proportion of ingredients with possible access issues, Figure A3 shows the proportion of ingredients for which drugs impacted by shortages represented over 90% of sales for the given ingredient. These situations are significantly rarer and have remained stable since August 2017, at levels between 1.7% and 2.5% of ingredients sold in Canada.

FIGURE A3. Rates of drugs and ingredients in shortage, 2017/18 to 2019/20

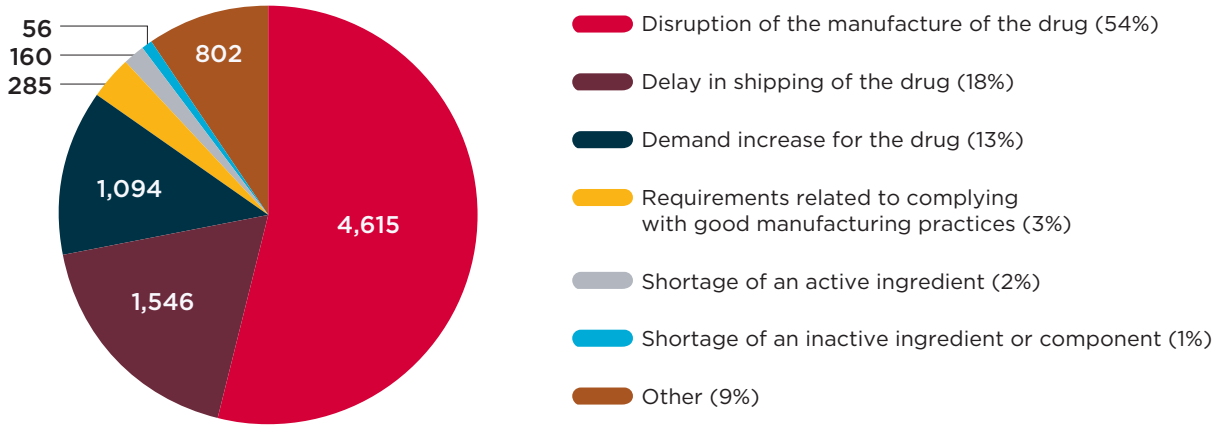


Note: Rates of drugs in shortage correspond to the percent of drugs with sales in Canada for which a shortage report had an "actual" status on a given day. Rates of ingredients in shortage correspond to the percent of distinct pharmaceutical ingredients or combination of ingredients for which drugs representing at least 90% of annual sales had a shortage report with an "actual" status on a given day.

Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; PMPRB.

Figure A4 breaks down the distribution of shortages by the reasons cited in the manufacturer's report. Most reports identified supply-side causes, with "disruption in the manufacture of the drugs" being cited by over half (54%) of reports. In 13% of reports, the reason for shortage was cited as "demand increase for the drug," the only demand-side cause available in the reporting template.

FIGURE A4. Distribution of drug shortage reports by reason, 2017/18 to 2019/20



Data source: www.drugshortagescanada.ca.

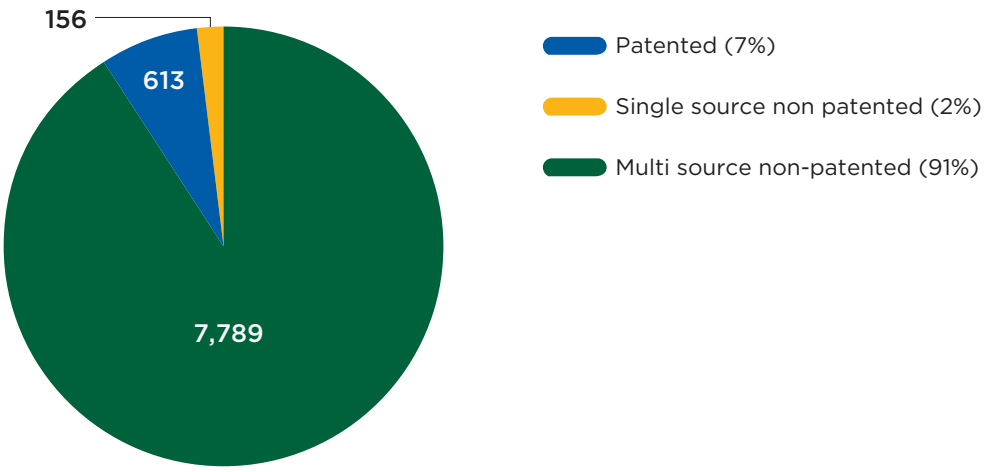
B. The drugs with the highest shortage rates

This section details the drugs that were most impacted by shortages between 2017/18 and 2019/20. It reports on trends in the annual shortage rate, defined as the proportion of drugs with sales in Canada for which at least one "actual" shortage was reported during the year. Shortage rates are further broken down by market segment, drug characteristic, therapeutic class, and international price levels. The findings show that while no group of drugs is shortage-free, certain types of drugs are more likely to be in shortage than others.

Exploring the market segments affected by drug shortages can provide important insight into the potential implications for patients. When shortages affect patented or single-source non-patented medicines—that is, non-patented medicines sold by a single manufacturer—there is a greater risk that patient access to the pharmaceutical ingredient will be compromised because no direct substitute is available. In contrast, when shortages concern multi-source non-patented medicines—that is, non-patented medicines offered by multiple competing manufacturers—there is a greater likelihood that patients will be able to access the same ingredient in another product with the same formulation and strength.

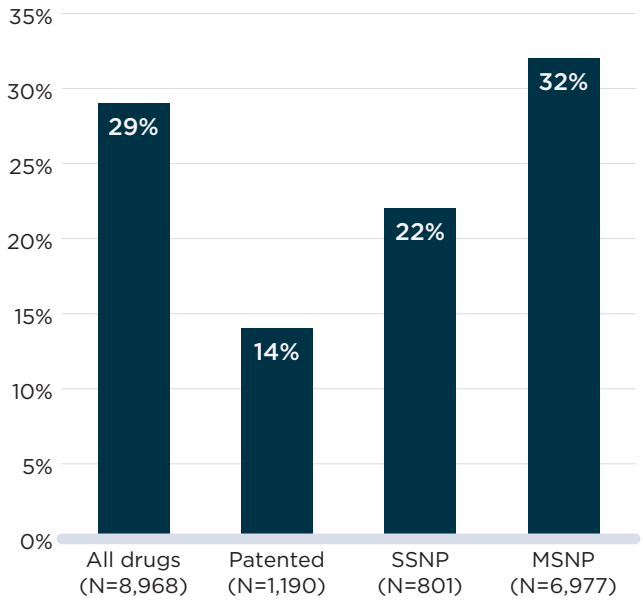
As shown in Figure B1, a vast majority (91%) of the shortage reports created from 2017/18 to 2019/20 concerned multi-source non-patented medicines. Patented medicines and single-source non-patented medicines accounted for 7% and 2% of reports, respectively. This suggests that direct substitutions were available to patients in most cases when a drug was reported as being in shortage. Figure B2 complements these results with an analysis of the annual shortage rates by market segment in 2019/20. It shows that patented medicines and single-source non-patented medicines had a markedly lower likelihood of being in shortage during the 2019/20 fiscal year than their multi-source counterparts.

FIGURE B1. Number of drug shortage reports by market segment, 2017/18 to 2019/20



Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; PMPRB.

FIGURE B2. Rates of drug shortages by market segment, 2019/20



Note: SSNP: Single-source non-patented. MSNP: Multi-source non-patented.
Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; PMPRB.

In Table B1, 2019/20 shortage rates are presented for multiple groups of drugs. In addition to market segment, several other characteristics are associated with higher shortage rates:

- Generic drugs were twice as likely as brand drugs to be in shortage (34% vs. 16%);
- Drugs with an annual treatment cost below $10,000 had shortage rates three times higher than that of those with a treatment cost over $10,000 (30% vs. 11%);
- Oral solid drugs had higher shortage rates (32% for tablets and 29% for capsules) than solutions (20%); and
- Drugs that were primarily provided by community pharmacies were more likely to be in shortage than those mainly provided in a hospital setting (30% vs. 18%).

The table also gives results for shortage rates by market size and by whether the medicinal ingredients were listed on the WHO list of essential medicines,[3] though no notable variations were found for either measure.

3 This aimed to measure the proportion of drugs with ingredients identified as "essential" by a recognized international institution in shortage in Canada. As of the writing of this report, Canada does not use an essential medicine list to guide its policy.

TABLE B1. Drug shortage rates by drug characteristics, 2019/20

Group	Drugs	Drugs with a shortage report	Share of drugs in shortage
All drugs	8,968	2,571	29%
Segment			
Patented	1,190	169	14%
Single-source non-patented	801	178	22%
Multi-source non-patented	6,977	2,224	32%
Generic status			
Generic	6,180	2,099	34%
Brand	2,254	362	16%
Non-categorized	534	110	21%
Treatment cost			
Treatment cost < 10,000$	8,508	2,520	30%
Treatment cost ≥ 10,000	460	51	11%
Setting for majority of revenues			
Community	7,763	2,350	30%
Hospital	1,205	221	18%
WHO essential medicine list			
Listed	2,762	819	30%
Not listed	6,206	1,752	28%
Formulation			
Tablet	4,929	1,562	32%
Solution	1,440	294	20%
Capsule	1,180	343	29%
Other	1,419	372	26%
Market size for the molecule			
Less than $1M	2,553	609	24%
$1M to $5M	3,124	938	30%
$5M to $10M	1,240	404	33%
$More than $10M	2,051	620	30%
Number of manufacturers for the molecule			
1 manufacturer	1,458	245	17%
2	669	153	23%
3	770	213	28%
4	579	176	30%
5	519	162	31%
6+ manufacturers	4,973	1,622	33%

Note: WHO: World Health Organization. The World Health Organization essential medicine list status was assigned based on whether the drug's pharmaceutical ingredients were listed in the 21st model list of essential medicines (World Health Organization 2019).
Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; IQVIA Private Drug Plan database; PMPRB.

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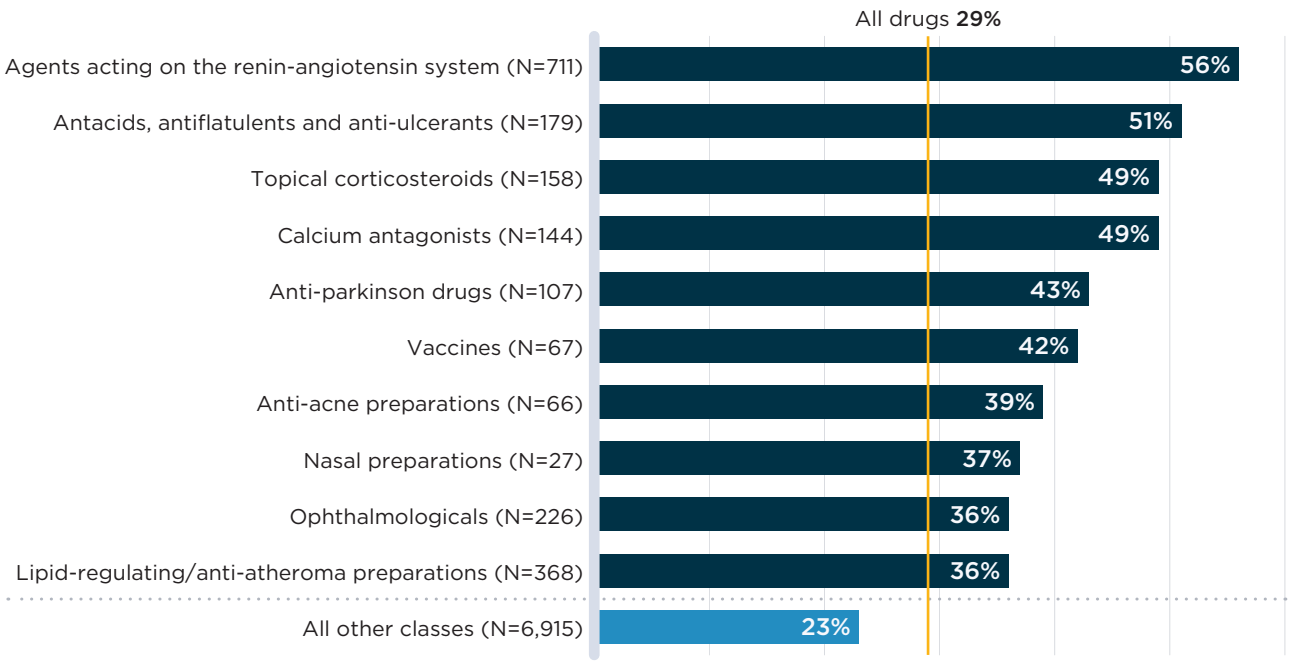
Some therapeutic classes are also more frequently in shortage than others. Figure B3 shows the 10 classes with the highest annual shortage rate in 2019/20. Seven of these classes had over 100 drugs with sales in Canada during the year, suggesting that substitution within the therapeutic class was possible in many cases. Six classes displayed shortage rates higher than 40%, meaning that at least 4 in 10 drugs within these classes were in shortage at some time during the year.

FIGURE B3. Top 10 therapeutic classes with the highest rates of drug shortages, 2019/20



Note: Therapeutic classes are defined based on the second level of the European Pharmaceutical Market Research Association (EphMRA) Anatomical Classification of Pharmaceutical Products. Therapeutic classes with fewer than 20 drugs with sales in Canada are excluded from the figure. Detailed results are presented in Appendix 2.

Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database.

As shown in Figure A4, most reasons cited for Canadian shortages during the study period concerned supply disruptions, with disruptions in the manufacture of the drug and shipping delays cited as the reason for over 70% of shortages.

Because the supply chain of drugs where those disruptions and delays occur is global in nature (Multi-Stakeholder Committee on Drug Shortages 2017), it is worth investigating whether the relative international prices of drugs are correlated with shortages. If global supply chains prioritized countries with high prices when production disruptions occurred, we would observe higher shortage rates in Canada for drugs with low prices relative to other countries, and lower rates for drugs with high prices relative to other countries.

In-depth: International prices and drug shortages

To study relative prices, the PMPRB uses foreign-to-Canadian (FTC) price ratios, in which the prices of medicines in other countries are expressed as a ratio of the price in Canada. For example, the German FTC ratio for a given drug is:

$$\text{FTC} = \frac{\text{Unit price}_{\text{Germany}}}{\text{Unit price}_{\text{Canada}}}$$

Because the foreign price is the numerator of the ratio, an FTC ratio above 1 indicates a situation in which the Canadian price is lower than that of other countries; an FTC ratio below 1 indicates a situation in which the Canadian price is higher than that of other countries; and an FTC ratio of 1 indicates a situation in which the Canadian price is perfectly aligned with that of other countries.

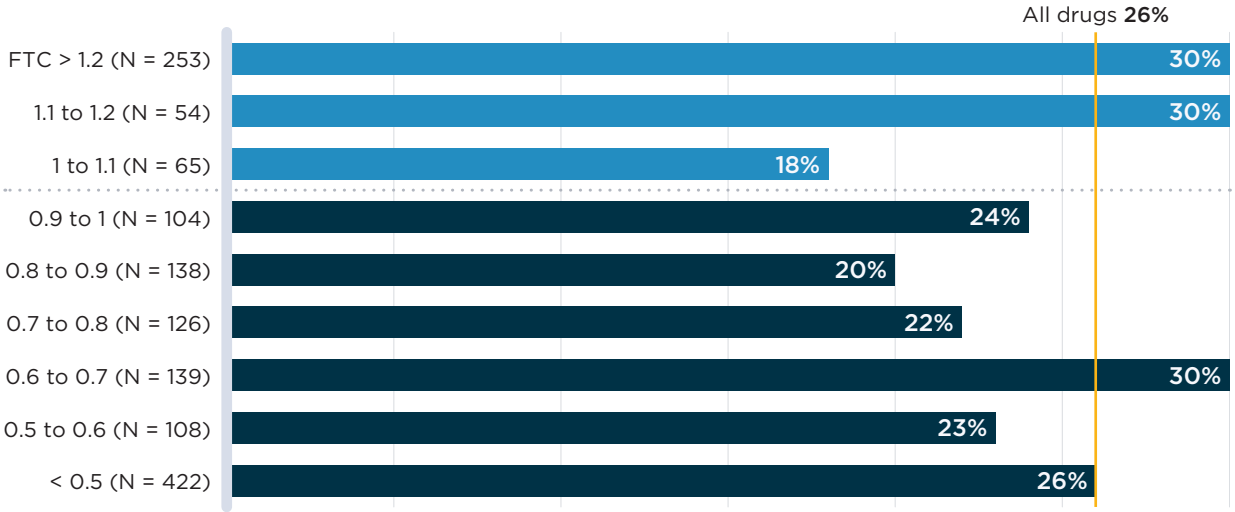
To investigate the association between international prices and drug shortages, the median FTC ratio across PMPRB11 comparator countries for all oral solid drugs with sales in Canada in 2019/20 was estimated using the IQVIA MIDAS® database. The shortage rates of drugs with three or more comparator countries were then compared by median FTC ratio level. A description of the sample used for this analysis is presented in Appendix 2 (Table 2.1).

These comparisons are used to test whether, on average, drugs with a relatively low Canadian price have higher shortage rates. Graphically, this would present as a strong positive association between FTC ratios and shortage rates.

In Figure B4, annual shortage rates of oral solid drugs with sales in Canada are plotted against the median list price FTC ratio across the PMPRB11 comparator countries. No clear association is found between higher foreign prices and shortage rates. To explore whether results differ between market segments, Appendix 1 presents the same analysis separately for patented and non-patented medicines.

In both cases, no association is apparent between relative prices and shortage rates. However, it is worth noting that these figures show average shortage rates over aggregated groups of drugs; lower relative prices may still contribute to shortages in specific cases.

FIGURE B4. Rates of drug shortages for oral solid drugs by median foreign-to-Canadian (FTC) price ratio, PMPRB11, 2019/20



Note: PMPRB11: Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, Spain, Sweden, and the United Kingdom. FTCs are the median foreign-to-Canadian price ratios calculated across PMPRB11 comparator countries (see *In-depth: International prices and drug shortages box* for details).

Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database.

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C. Resolution rates and duration of shortages

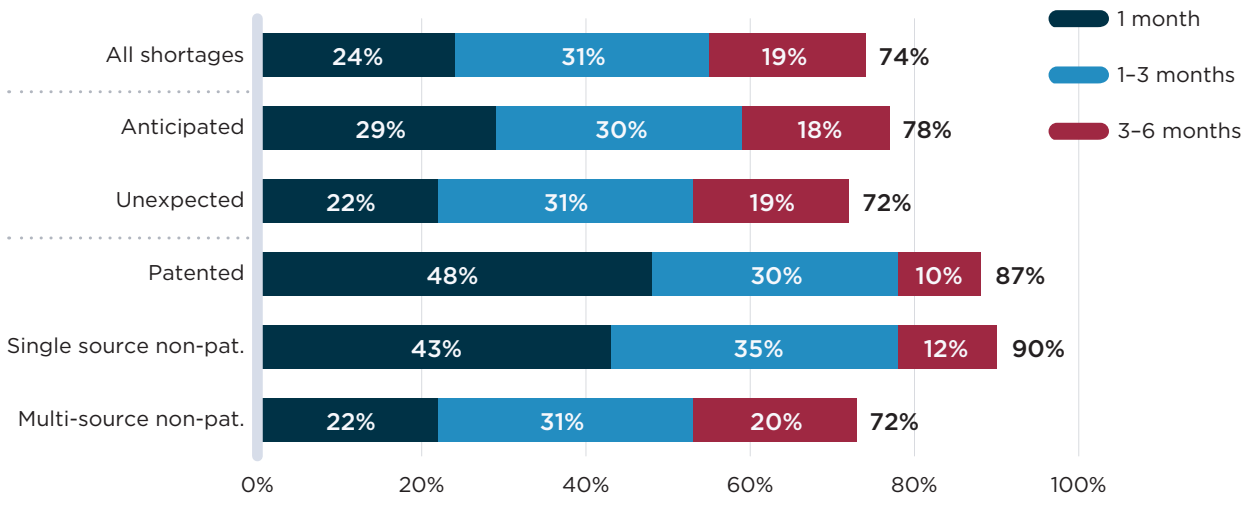
This section documents resolution rates of shortages during the year following their onset by measuring the proportion of shortages that achieved a "resolved" status by a given date. Most shortages were resolved within a 3-month period, but some groups of drugs displayed slower resolution than others and a minority remained unresolved a year after the shortage's onset.

Based on the reports filed by manufacturers, most drug shortages are resolved within three months of their onset. As shown in Figure C1, 55% of reports were updated to "resolved" by the company that filed the report within a three-month period and about three quarters (74%) were updated to "resolved" within a six-month period.

Two factors were associated with faster shortage resolution. Shortages that were anticipated (i.e., shortage reports that had an "anticipated" status at creation) were resolved faster than unexpected shortages (i.e., those with an "actual" status at creation). By one month after the shortage onset, "anticipated" shortages were seven percentage points more likely to be resolved than unexpected shortages. Shortages of drugs with fewer competitors were also resolved faster. Shortages of patented and single-source non-patented medicines had greater resolution rates at one, three, and six months after onset than those of multi-source non-patented medicines.

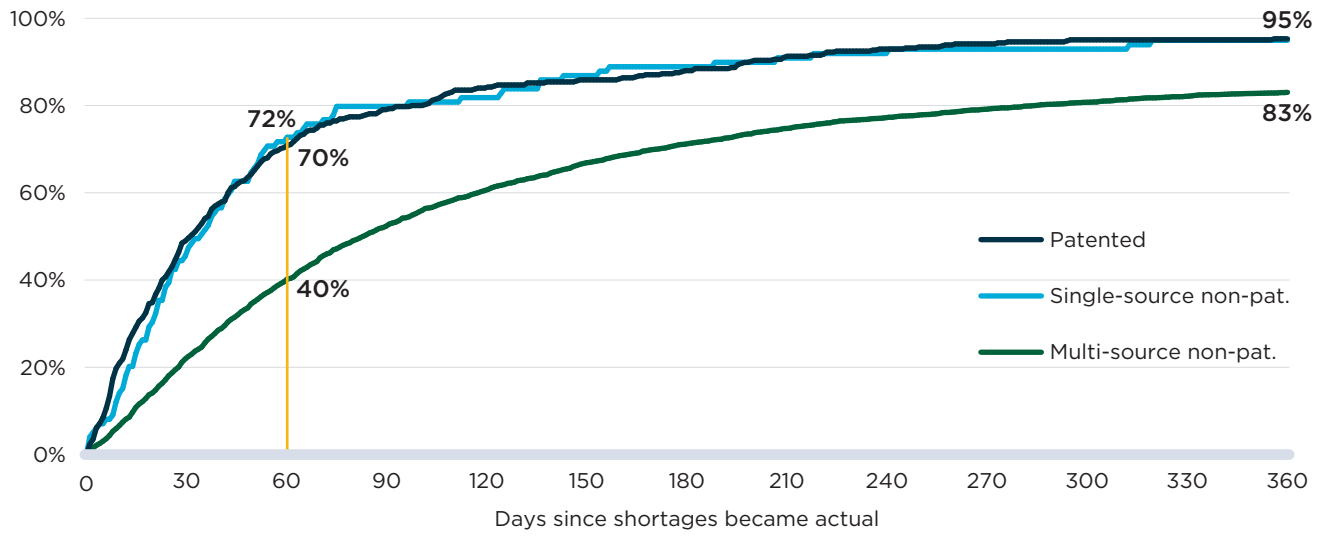
Figure C2 shows cumulative resolution rates for drug shortages in the year after their onset. The first 60 days after onset had the steepest rates of resolution for all market segments shown, with the pace slowing in the following months. Throughout, resolution rates were markedly lower for multi-source non-patented medicines, and their end-of-year resolution rate (83%) was below the rate for patented and single-source non-patented medicines (96%).

FIGURE C1. Resolution rates for drug shortages in the first six months following onset, 2017/18 to 2019/20



Note: The figure excludes shortages with an onset less than six months prior to the data export as well as those for drugs with a discontinuation report created within one month of the report being resolved.
Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; PMPRB.

FIGURE C2. Cumulative resolution rates for drug shortages by market segment, 2017/18 to 2019/20



Note: The figure excludes shortages with an onset less than 365 days prior to the data export as well as shortages for drugs with a discontinuation report created within one month of the report being resolved.
Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; PMPRB.

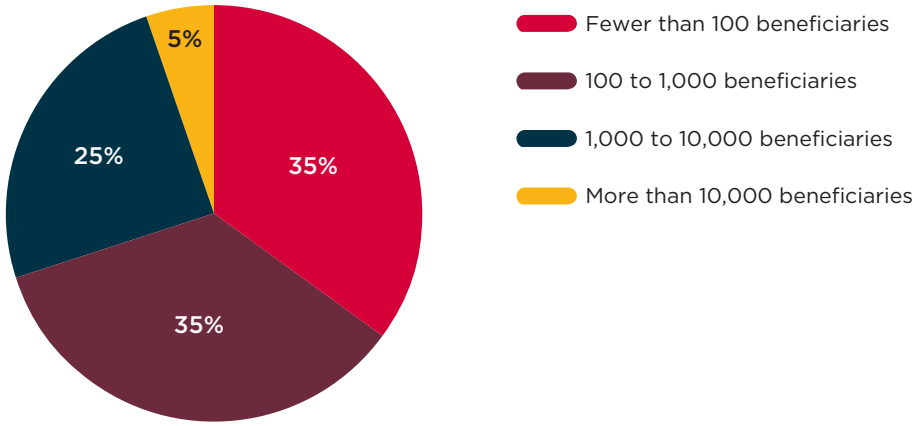
D. Impact of shortages on public plan beneficiaries

This section documents the change in public plan beneficiaries during shortages by comparing the number of active monthly beneficiaries for a given drug before and during the shortage. Shortages are considered at the drug level and at the chemical subgroup level, which accounts for substitutions made to similar drugs within the same therapeutic class. At the drug level, 40% of shortages were followed by a steep decline (>20%) in beneficiaries. However, when considering the chemical subgroup of drugs impacted by shortages, only 8% of shortages were associated with a similar decline.

Between 2017/18 and 2019/20, most of the drugs that experienced a shortage had relatively few beneficiaries in Canadian public plans. As seen in Figure D1, 70% of the drugs for which a shortage was reported had fewer than 1,000 monthly beneficiaries prior to the shortage, while just 5% of drugs with a shortage had over 10,000 monthly beneficiaries.

The implications of these results are two-sided: fewer beneficiaries may be directly impacted by a shortage for a drug with a lower number of active users, but drugs with fewer users often have fewer competitors, offering limited substitution options for those affected.

FIGURE D1. Distribution of drugs in shortage by number of active beneficiaries in the month preceding the shortage, 2017/18 to 2019/20



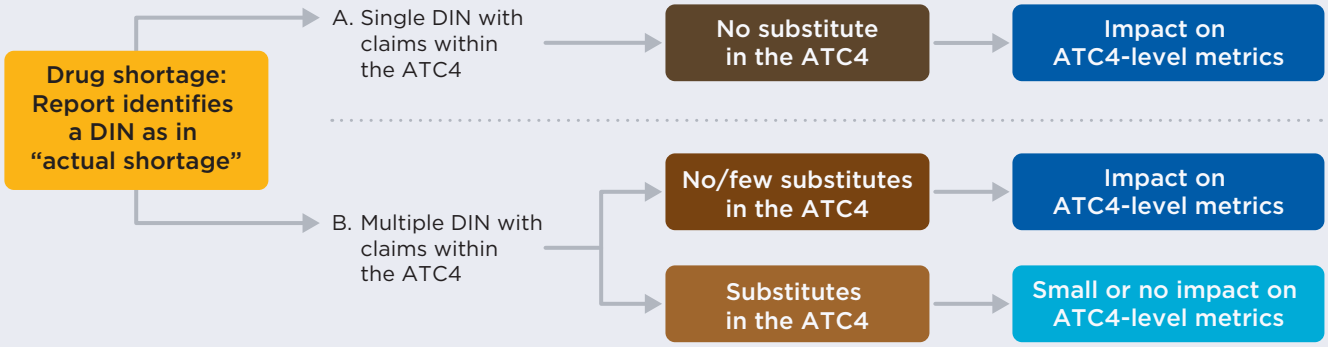
Note: This figure shows the 3,431 DINs with at least one shortage and at least one claim in the NPDUIS database one month prior to the shortage. When multiple shortages were reported for the same DIN, only the first was counted.
Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

In-depth: Drug substitutions during shortages

In some cases, drug shortages can be managed by substituting the drug in shortage for the same medicine with a different package size, strength, or form, or the same package size, strength, and form but supplied by another manufacturer. In those cases, the impact of shortages for beneficiaries is likely to be less severe than when there is no substitute available.

To better distinguish the shortages with fewer substitutes, this section studies two different levels of shortages. The first is **shortages at the drug level**, which considers outcomes at the drug identification number (DIN) level for shortage reports with an "actual" status. In most cases, shortages are expected to lead to a decline in the number of beneficiaries for the drug. However, if different package sizes for the same DIN exist or if the shortage is caused by an increase in the demand for the drug, there may not be a decline despite the shortage.

The second is **shortages at the chemical subgroup level**, which occur when shortages with an "actual" status are reported for at least one DIN within a group of drugs defined by the fourth level of the World Health Organization's Anatomical Therapeutic Chemical classification system (ATC4). The ATC4 classification level is the most granular level prior to chemical substance and includes drugs with similar chemical components used to treat identical or related indications. DINs for the same ingredient and indication but with different manufacturers, strengths, or forms are all included in the same ATC4.



As shown in the diagram, shortages impacting DINs with no or few substitutes are expected to impact both drug- and the ATC4-level metrics, while shortages impacting DINs with many substitutes are not expected to translate to important impact at the ATC4-level.

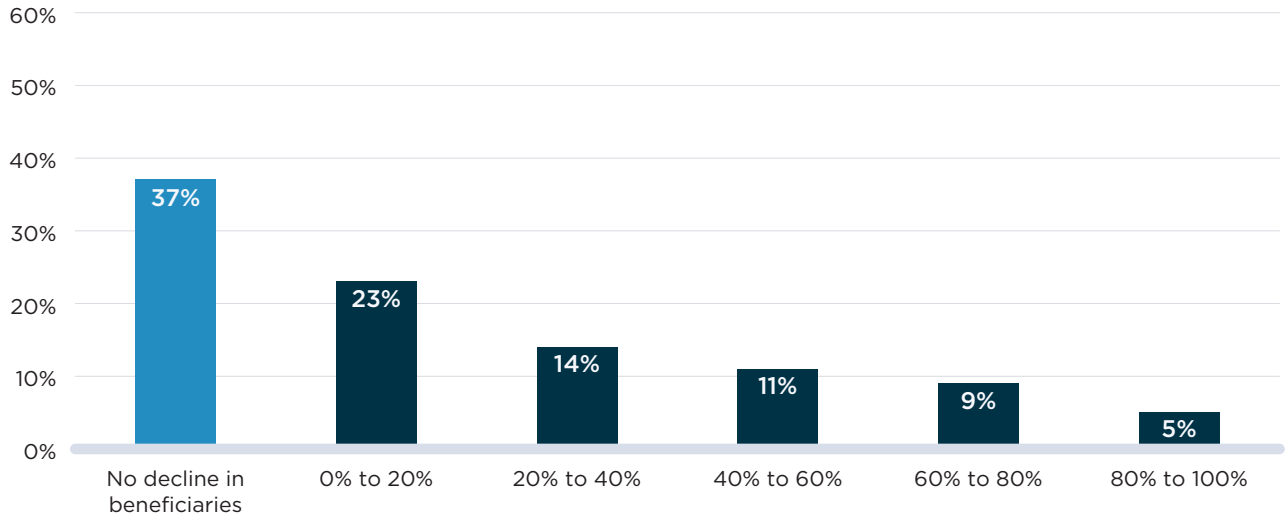
Figure D2 presents the distribution of shortages by the decline in active beneficiaries observed during the shortage relative to the months prior. Figure D2(a) shows the declines seen at the DIN level when a shortage report is created. For all but 37% of cases, shortages were accompanied by a decline in the number of active beneficiaries. For 23% of shortages, the decline was relatively modest (less than 20%), while the remaining 40% of shortages were associated with a decline of at least 20% of beneficiaries, meaning that at least 1 in 5 beneficiaries who expected to fill a prescription during the shortage had to find a substitute or go without treatment.

In Figure D2(b), shortages defined at the chemical subgroup (i.e., ATC4) level showed fewer and less severe declines in the number of beneficiaries impacted. About half (51%) of shortages were not accompanied by a decline in the number of beneficiaries of the ATC4s impacted. For another 41% of shortages, there was a modest decline (less than 20%) in the number of beneficiaries.

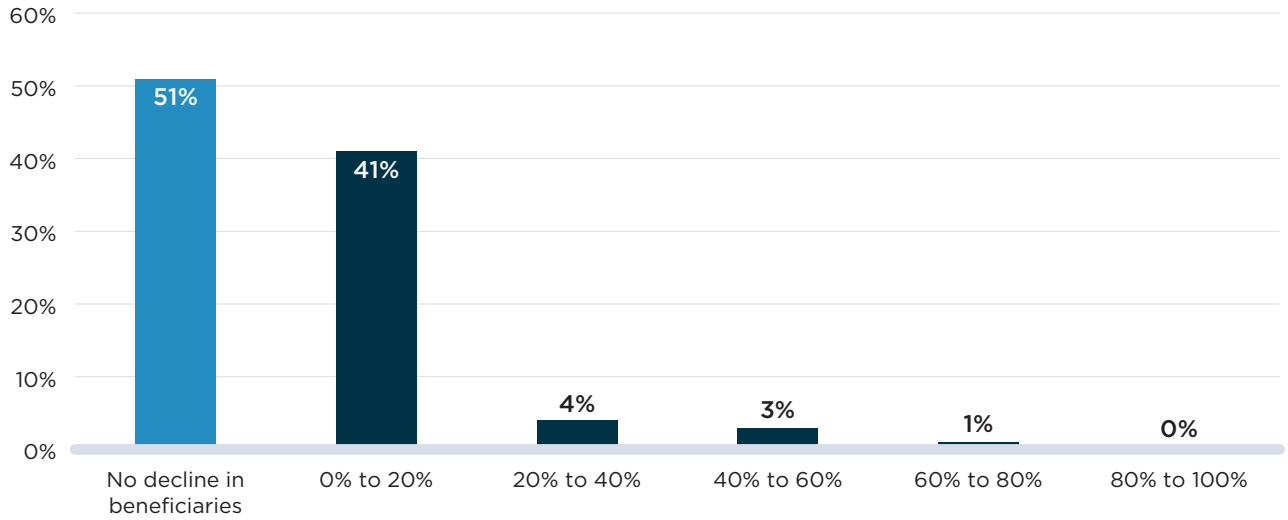
Declines in the number of beneficiaries were less severe when analyzed at the chemical subgroup level because beneficiaries can substitute other drugs within the subgroup and remain active beneficiaries of the ATC4 and because, within the larger frame of the subgroup, the beneficiaries of an affected drug make up a smaller fraction of the total. These factors are most impactful for ATC4 classes that include more drugs.

FIGURE D2. Distribution of drug shortages by percent decline in active beneficiaries during the shortage, 2017/18 to 2019/20

A. Shortages defined at the drug level (N=4,858)



B. Shortages defined at the chemical subgroup level (N=532)



Note: Shortages shown here are a situation in which either a (a) DIN or (b) DIN within an ATC4 is mentioned by at least one shortage report with an "actual" status during the study period. The percent decline in active beneficiaries compares the average monthly number of beneficiaries during the shortage and up to six months prior to the shortage.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

Of the 532 ATC4-level shortages shown in Figure D2(b), 41 shortages (8%) showed declines greater than 20% in the number of active beneficiaries. Table D1 compares characteristics of these shortages against shortages associated with more modest beneficiary declines or no decline at all. On average, the shortages that had the steepest declines in beneficiaries occurred in ATC4s with less spending and fewer beneficiaries prior to the shortage than shortages with more modest or no declines in beneficiaries. The shortages with steep declines in beneficiaries also impacted ATC4s with fewer DINs and more brand and single-source drugs, meaning fewer generic options that could be used as substitutes. These shortages also lasted longer, with an average duration of 10.4 months compared to 8.3 months for shortages with no decline and 7.2 months for shortages with modest declines. "Analgesics" were the most common therapies with

steep beneficiary declines, with six shortages impacting over 20% of beneficiaries, while "antibacterials for systemic use" were most represented in shortages impacting fewer patients.

The 41 shortages with declines greater than 20% in the number of active beneficiaries are described in further detail in Appendix 2.

TABLE D1. Descriptive statistics of chemical subgroup level shortages by decline in beneficiaries, 2017/18 to 2019/20

	Shortages with no decline in beneficiaries	Shortages with 0% to 20% decline in beneficiaries	Shortages with decline in beneficiaries greater than 20%
Number of shortages (N)	273	218	41
Spending prior to the shortage ($, mean)	$1,913,286	$1,158,360	$227,128
Number of beneficiaries prior to the shortage (mean)	26,275	16,749	6,345
Spending per beneficiary prior to the shortage ($, mean)	$337	$490	$163
Shortage duration in months (mean)	8.3	7.2	10.4
Characteristics of the chemical subgroups impacted			
Number of DINs (mean)	24.6	18.4	11.6
Proportion of the chemical subgroup composed of:			
Oral solid drugs	50%	46%	49%
Branded drugs	33%	38%	45%
Single-source drugs	19%	23%	32%
Patented medicines	11%	11%	2%
Therapeutic classes most impacted			
1	Antibacterials for systemic use (N=18)	Antibacterials for systemic use (N=16)	Analgesics (N=6)
2	Antineoplastic agents (N=17)	Ophthalmologicals (N=12)	Sex hormones and modulators of the genital system (N=4)
3	Sex hormones and modulators of the genital system (N=14)	Psycholeptics (N=11)	Anti-acne preparations (N=3)
4	Ophthalmologicals (N=13)	Sex hormones and modulators of the genital system (N=10)	Drugs for functional gastrointestinal disorders (N=3)
5	Drugs for obstructive airway diseases (N=12)	Antivirals for systemic use (N=9)	Ophthalmologicals (N=3)

Note: Shortages are defined here as a situation in which a DIN within an ATC4 is mentioned by at least one shortage report with an "actual" status during the study period. The decline in active beneficiaries compares the average monthly number of beneficiaries during the shortage and up to six months prior to the shortage. Proportions of drugs by formulation and market segment are calculated as the percentage of DINs with claims within the ATC4 with these attributes. Drugs for which the attributes are unknown are counted as not having the attribute.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

Case Study: Alpha-glucosidase inhibitors

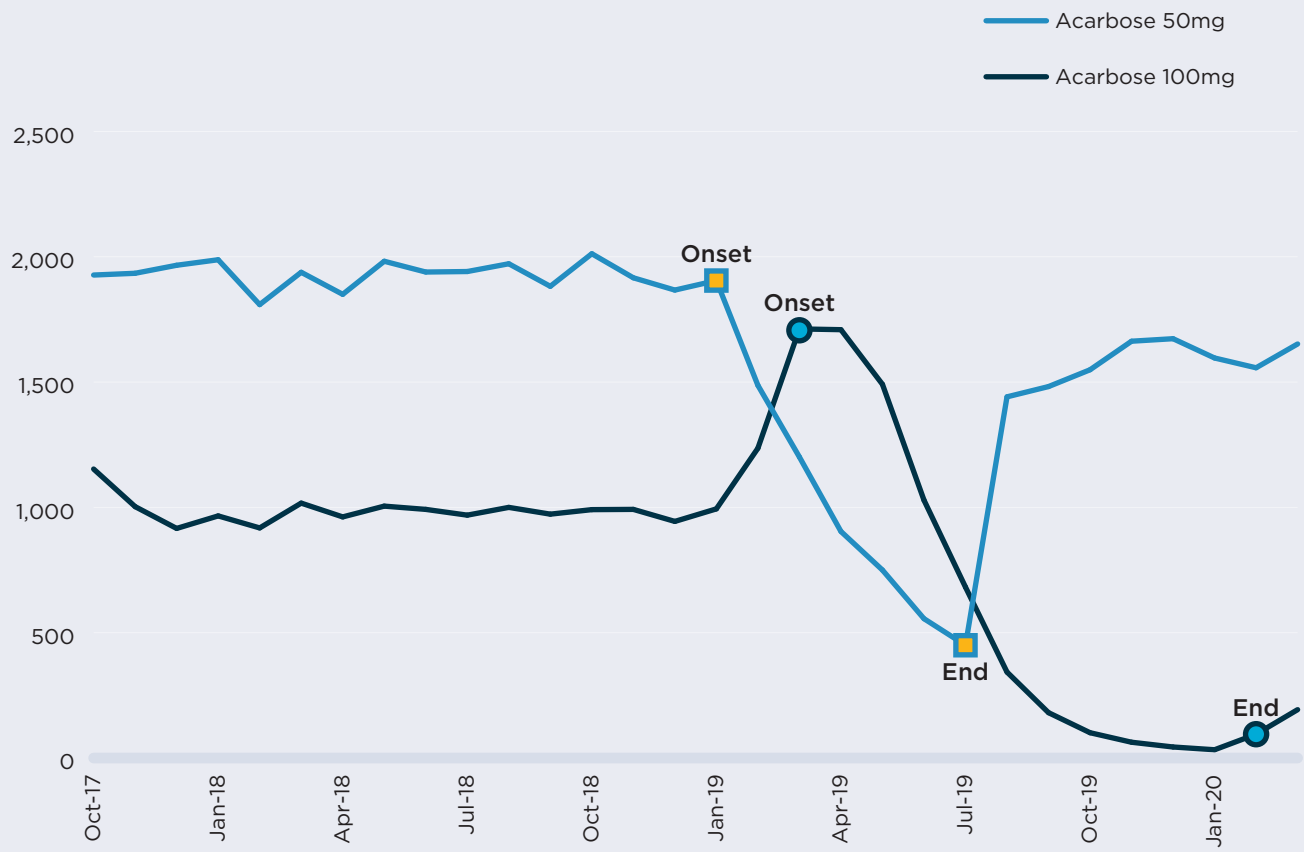
The ATC4 class of alpha-glucosidase inhibitors (A10BF), which are used to treat type 2 diabetes, can offer an example of a shortage that impacted a large proportion of active beneficiaries and public plan spending.

Acarbose was the only drug within this class with public drug plan claims during the study period. For most of the period, there were only two DINs with claims: a 50 mg strength version and a 100 mg strength, both sold by the same manufacturer. On average, there were 2,898 active monthly beneficiaries of the drugs in NPDUIS plans in the six months prior to the shortage.

The 50 mg strength option was reported as having gone into shortage on January 15, 2019, because of a "disruption of the manufacture of the drug." This report was followed by a sharp decline in the number of active beneficiaries for the DIN, from 1,932 per month in the six months prior to the shortage to an average of 891 during the shortage.

During the first two months of the shortage, beneficiaries were able to substitute their prescriptions with the 100 mg strength version of the same drug. However, on March 26, 2019, the 100 mg version also went into shortage due to a manufacture disruption. From March to July 2019, both strengths were simultaneously in shortage and the number of active beneficiaries of acarbose fell to 1,096 in July 2019, 62% lower than prior to the shortage.

Active beneficiaries of alpha-glucosidase inhibitors, October 2017 to March 2020



Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

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During the 13 months encompassing both drug-level shortages, from January 2019 to February 2020, monthly beneficiaries and spending for the chemical subgroup (ATC4) were 35% and 36% lower than their pre-shortage figures, respectively. The shortages of both strengths were resolved by February 2020, but beneficiaries did not immediately return to pre-shortage levels.

In February 2020, a new generic competitor offering both strengths entered the market and started recording claims. The introduction of more products into the chemical subgroup lowered the risk of all options being simultaneously in shortage.

Declines in beneficiaries and spending observed during the shortage

	DIN-level Shortages		ATC4-level Shortage
	2190885 Acarbose 50mg	02190893 Acarbose 100mg	A10BF Alpha glucosidase inhibitors
Shortage timeline			
Onset	1/15/2019	3/26/2019	1/15/2019
End	7/24/2019	2/5/2020	2/5/2020
Duration (days)	190	316	386
Monthly active beneficiaries (mean)			
Prior to the shortage	1,932	1,022	2,898
During the shortage	891	525	1,878
Decline (%)	54%	49%	35%
Monthly spending (mean, $)			
Prior to the shortage	$87,300	$62,900	$147,900
During the shortage	$34,000	$21,200	$94,400
Decline (%)	61%	66%	36%

Note: Shortages shown here are a situation in which a DIN or DIN within an ATC4 group is mentioned by at least one shortage report with an "actual" status. The percent decline in active beneficiaries compares the average monthly number of beneficiaries during the shortage and during the six months prior to the shortage.

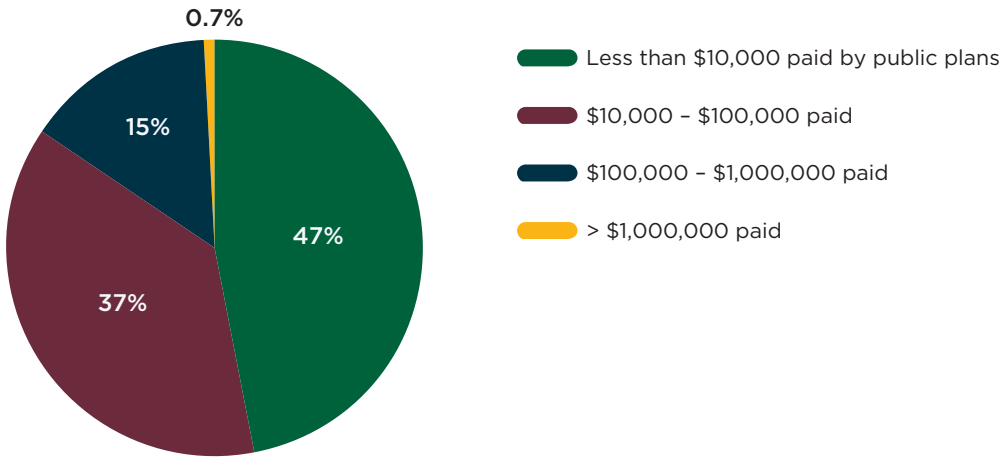
Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

E. Impact of shortages on public plan spending

Complementing the above analysis on public plan beneficiaries, this section documents changes in public spending by comparing drug spending by NPDUIS plans before and during a shortage. Shortages are considered at the drug level (by DIN) and at the chemical subgroup level (by ATC4). At the drug level, 62% of shortages were accompanied by an increase or decrease in spending greater than 20%. However, when considering the chemical subgroup, only 18% of shortages were associated with a similar shift in plan spending.

Figure E1 shows the distribution of drugs with a shortage between 2017/18 and 2019/20 by monthly public plan spending prior to the shortage. Approximately half of drugs (47%) had less than $10,000 in monthly spending across NPDUIS plans before the onset of their shortage, while less than 1% (23 drugs) had over $1 million in monthly plan spending.

FIGURE E1. Distribution of drugs in shortage by public drug plan spending in the month preceding the shortage, 2017/18 to 2019/20



Note: This figure shows the 3,431 DINs with at least one shortage and at least one claim in the NPDUIS database one month prior to the shortage. When multiple shortages were reported for the same DIN, only the first was counted.
Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

Drug shortages can result in a net increase, no significant change, or a decrease in public plan spending. In most cases, the most direct effect of shortages is a decline in utilization for the impacted drugs, which, excluding other factors, lowers spending. Substitutions can also lower spending in some cases, for instance when a generic drug is used as a substitute for a brand drug in shortage.

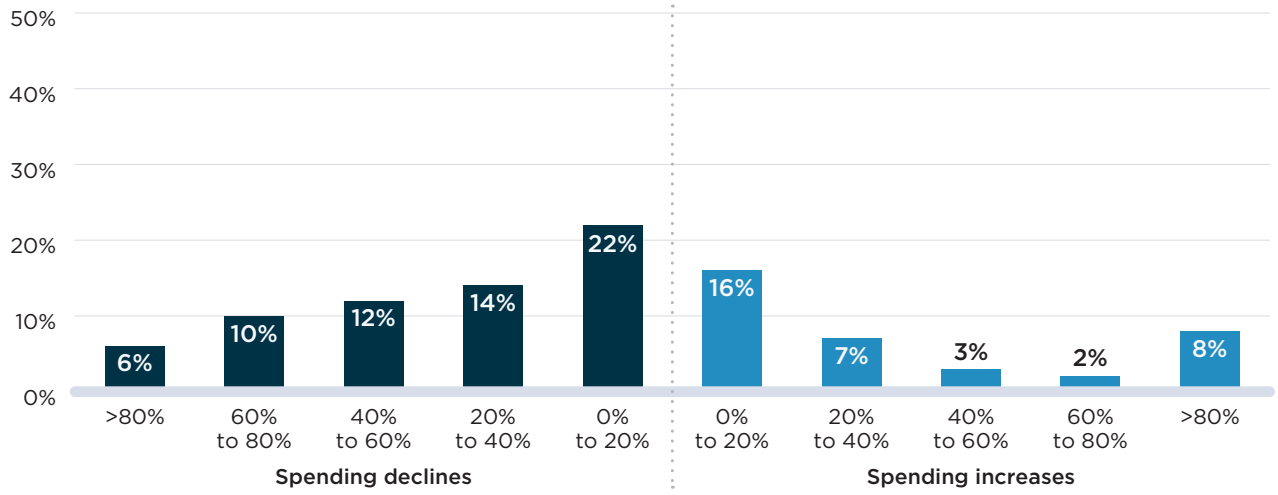
However, three factors can lead to a spending increase during a shortage. First, as shown in Figure A4, 13% of shortages reported by Canadian manufacturers cite a demand increase for the drug as a cause for the shortage, in which case there may be more utilization and spending during the shortage than prior. Second, shortages can lead to increases in the unit price of drugs impacted. Finally, substitutions can lead to higher spending, for instance when a branded drug is used as a substitute for a generic drug in shortage.

Figure E2 shows the distribution of shortages by the percent variation in public plan spending during the shortage relative to the months prior. Figure E2(a) shows the spending variations at the drug level (by DIN). In 65% of cases, shortages were associated with a decline in spending, with 43% of shortages leading to a decline of over 20%. The remaining 35% of shortages were associated with an increase in spending at the drug level. For 1 in 5 shortages (20%), the increase in spending was greater than 20% of pre-shortage spending.

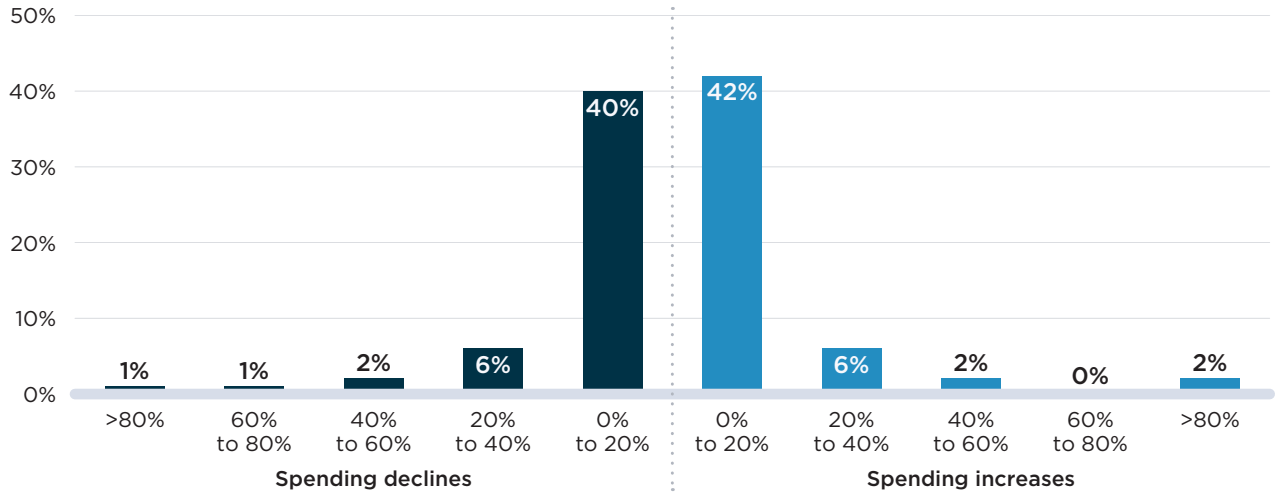
As seen in Figure E2(b), few shortages had a major impact on spending at the chemical subgroup level (by ATC4). Only 10% and 9% of shortages were accompanied by increases and declines in spending greater than 20% of pre-shortage levels, respectively. As was the case in Section D, the less pronounced variations in spending can be attributed to two factors: substitutions may have been made to other drugs with the same ATC4, which would limit the effect on spending for the class, and the drugs in shortage likely account for a relatively small proportion of the spending within the chemical subgroup, leading to smaller degrees of variation overall.

FIGURE E2. Distribution of drug shortages by change in spending during the shortage, 2017/18 to 2019/20

A. Shortages defined at the drug level (N=4,858)



B. Shortages defined at the chemical subgroup level (N=532)



Note: Shortages are defined here as a situation in which a DIN (Panel A) or DIN within an ATC4 group (Panel B) is mentioned by at least one shortage report with an "actual" status during the study period. The percent change in spending compares the average monthly spending during the shortage and up to six months prior to the shortage.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

Table E1 takes a closer look at the 100 ATC4-level shortages with an increase or decline in spending greater than 20%. Shortages that were accompanied by a large decline in spending tended to feature lower spending prior to the shortage, more brand and single-source medicines, and fewer DINs. Conversely, shortages that showed an increase in spending tended to have higher spending prior to the shortage, fewer brand drugs in the subgroup and a relatively high number of DINs to use as substitutes.

Detailed characteristics of the 44 ATC4-level shortages with spending variations greater than 40% are shown in Appendix 2.

TABLE E1. Descriptive statistics of chemical subgroup level shortages by change in spending, 2017/18 to 2019/20

	Shortages with declines in spending		Shortages with increases in spending	
	Greater than 20%	0% to 20%	0% to 20%	Greater than 20%
Number of shortages (N)	48	211	221	52
Spending prior to the shortage (mean)	393,653	1,098,734	2,092,515	1,365,153
Number of beneficiaries prior to the shortage (mean)	12,280	17,520	27,547	13,655
Spending per beneficiary prior to the shortage ($, mean)	$132	$488	$351	$361
Shortage duration in months (mean)	10.5	7.8	7.1	10.8
Characteristics of the chemical subgroups impacted				
Number of DINs (mean)	15.0	18.0	25.1	21.9
Proportion of the chemical subgroup composed of				
Oral solid drugs	52%	45%	51%	46%
Branded drugs	44%	38%	34%	28%
Single-source drugs	33%	23%	18%	23%
Patented medicines	6%	11%	11%	12%
Therapeutic classes most impacted				
1	Analgesics (N=6)	Antibacterials for systemic use (N=20)	Ophthalmologicals (N=12)	Antibacterials for systemic use (N=6)
2	Ophthalmologicals (N=5)	Psycholeptics (N=11)	Psycholeptics (N=11)	Antineoplastic agents (N=5)
3	Anti-acne preparations (N=3)	Sex hormones and modulators of the genital system (N=10)	Sex hormones and modulators of the genital system (N=11)	Sex hormones and modulators of the genital system (N=4)
4	Antiinflammatory and antirheumatic products (N=3)	Antivirals for systemic use (N=8)	Antineoplastic agents (N=10)	Drugs for obstructive airway diseases (N=3)
5	Drugs for obstructive airway diseases (N=3)	Ophthalmologicals (N=8)	Drugs for obstructive airway diseases (N=9)	Ophthalmologicals (N=3)

Note: Shortages are defined here as a situation in which a DIN within an ATC4 is mentioned by at least one shortage report with an "actual" status during the study period. The decline in active beneficiaries compares the average monthly number of beneficiaries during the shortage and up to six months prior to the shortage. Proportions of drugs by formulation and market segment are calculated as the percentage of DINs with claims within the ATC4 with these attributes. Drugs for which the attributes are unknown are counted as not having the attribute.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

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Appendix 1: Compounding

In Sections D and E, the impact of drug shortages on beneficiaries and spending are analyzed at the drug level (by DIN) and chemical subgroup (by ATC4) levels. The latter set of analyses aims to account for substitutions made during shortages. However, these substitutions may still be underestimated as they do not capture all cases where drugs were compounded to fill the need created by the shortage. Compounding is typically the process of combining or altering ingredients to create a medication tailored to an individual patient's need (U.S. Food and Drug Administration, 2018), but this process is also used to alleviate shortages when no marketed substitutes are available.

Because compounded drugs do not originate from a licensed manufacturer, they do not have DINs and cannot be directly linked to shortage reports. They are typically coded using artificial identifiers created by public plans to report claims with no matching DIN in Health Canada's Drug Product Database.

Of the compounded drugs that can be identified in the data, the majority are assigned a World Health Organization Anatomical Therapeutic Chemical Classification System (ATC) code. This code identifies exactly which ingredient, strength, and form was compounded. In those cases, the chemical subgroup analysis correctly captures substitutions to compounds. However, when the ATC code is not available, substitutions can be missed in the analysis.

Table 1.1 gives the number of NPDUIS claims that mentioned a compound between 2017/18 and 2019/20. Of 1.9 million claims attributable to compounds during the three-year period, 1.1 million (58%) had an ATC code.

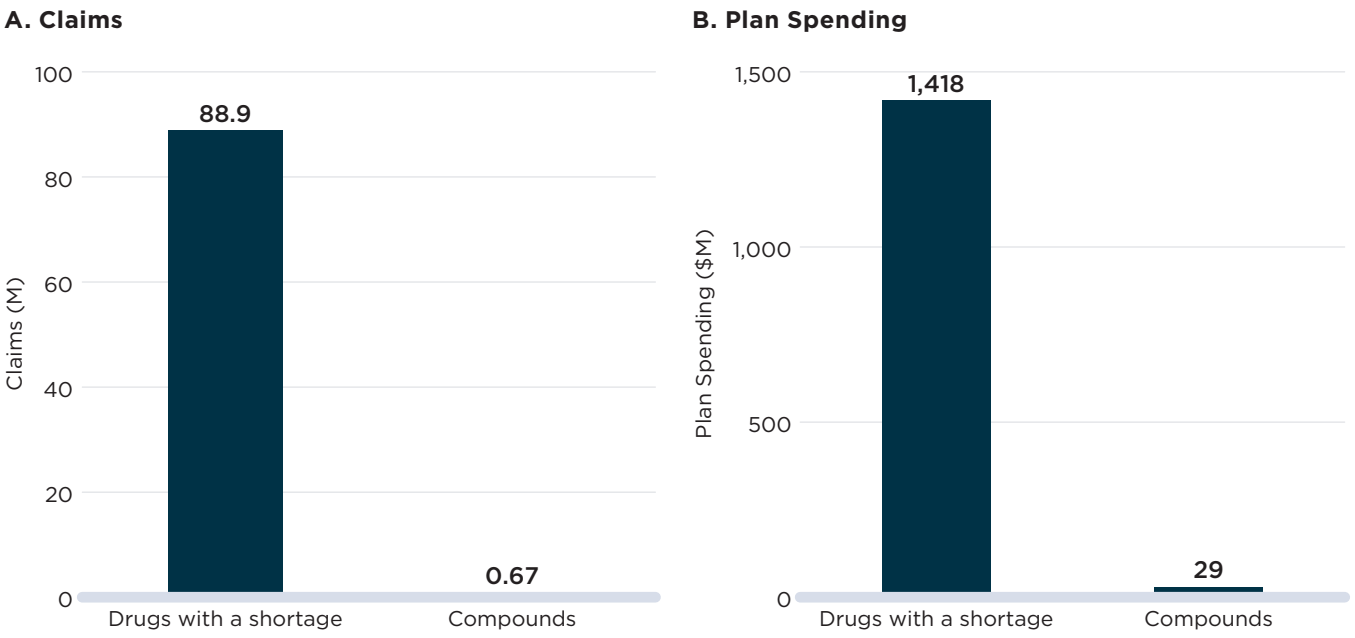
Figure 1.1 provides perspective on the volume of compounds relative to the number of drugs in shortage. In 2019/20, both claims and spending for compounds were dwarfed by those for drugs in shortage. However, because compounds are not coded systematically in the database, their true volume is unknown.

TABLE 1.1 Claims and plan spending for compounded drugs, 2017/18 to 2019/20

	2017/18	2018/19	2019/20	Total
Claims				
Compounds	592,266	630,385	671,217	1,893,868
Compounds with an ATC code	329,694	369,789	406,313	1,105,796
Plan spending ($M)				
Compounds	$22.3	$25.9	$29.1	$77.3
Compounds with an ATC code	$9.4	$11.7	$14.0	$35.2

Note: ATC: World Health Organization Anatomical Therapeutic Chemical Classification System.
Compounds are identified based on a "compound" or "medicine in shortage" mention in the description of the claim.
Data source: NPDUIS database, Canadian Institute for Health Information (CIHI).

FIGURE 1.1 Comparison of claims and plan spending for drugs in shortage and for compounded drugs, 2019/20



Note: Compounds are identified based on a "compound" or "medicine in shortage" mention in the description of the claim. Drugs with a shortage are drugs for which a shortage report had an "actual" status in 2019/20.
Data source: www.drugshortagescanada.ca; NPDUIS database, Canadian Institute for Health Information (CIHI).

Appendix 2: Additional Exhibits

TABLE 2.1 Descriptive statistics of the sample used for the FTC analysis, 2019/20

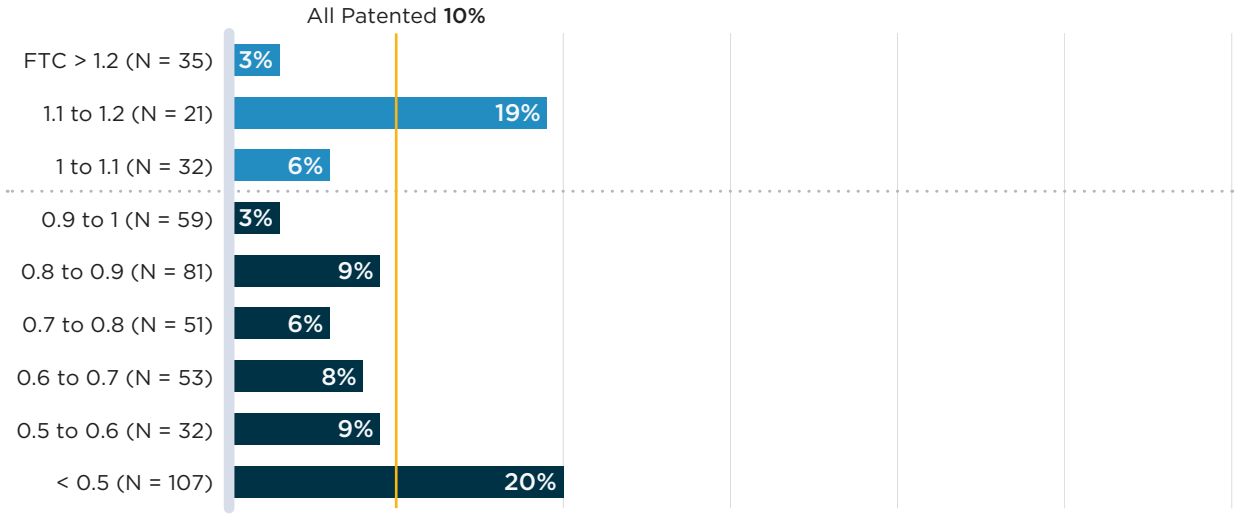
	All oral solid drugs with sales in Canada		Included in analysis: oral solid drugs with 3+ international price comparisons	
	N	%	N	%
Total count	6,098	100%	1,409	100%
Market segment				
Patented	726	12%	471	33%
Single-source non patented	261	4%	50	4%
Multi-source non patented	5,111	84%	888	63%
Generic status				
Generic	4,768	78%	665	47%
Brand	1,199	20%	737	52%
Uncategorized	131	2%	7	0%
Market size (molecule level)				
Less than $1M	1,261	21%	258	18%
$1M to $5M	2,152	35%	469	33%
$5M to $10M	1,010	17%	234	17%
$10M and over	1,645	27%	448	32%
Form				
Tablet	4,923	81%	1,139	81%
Capsule	1,175	19%	270	19%
Total revenue ($B)		**13.5**		**8.3**

Note: The 1,409 drugs with sales in Canada and three or more countries among the PMPRB11 were included in the international price analysis.

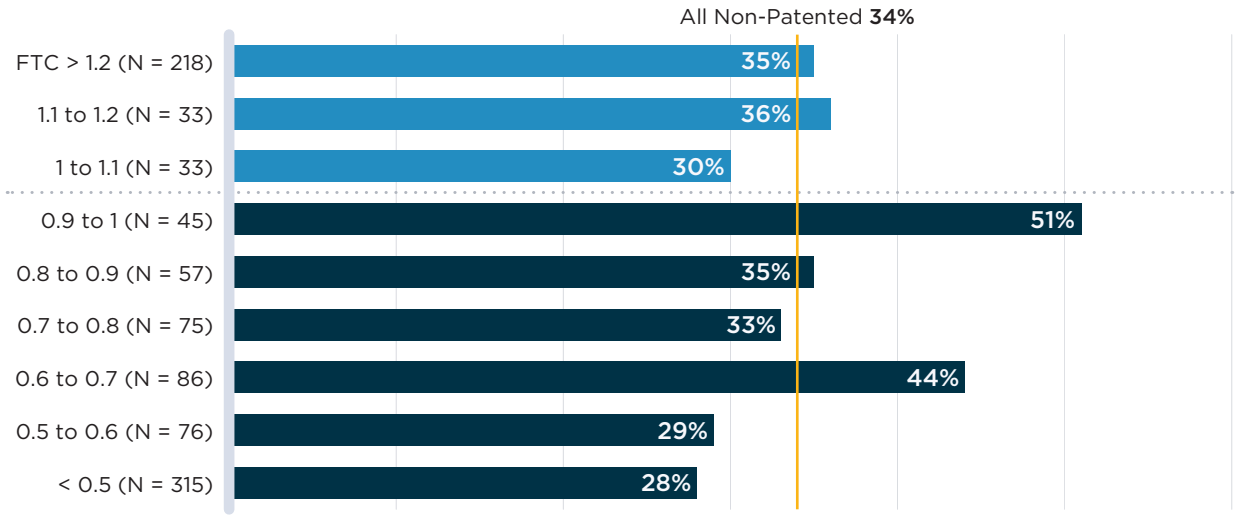
Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database; IQVIA Private Drug Plan database; PMPRB.

FIGURE 2.1 Subgroup analysis: proportion of oral solid drugs in shortage by median foreign-to-Canadian (FTC) price ratio and patented status, PMPRB11, 2019/20

A. Patented medicines



B. Non-patented medicines



Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database.

TABLE 2.2 Shortage rates by therapeutic class, 2019/20

Therapeutic class	Drugs	Drugs with a shortage report	%
Agents acting on the renin-angiotensin system	711	395	56%
Drugs for acid related disorders	179	92	51%
Topical corticosteroids	158	78	49%
Calcium channel blockers	144	70	49%
Anti-Parkinson drugs	107	46	43%
Vaccines	67	28	42%
Anti-acne preparations	66	26	39%
Nasal preparations	27	10	37%
Ophthalmologicals	226	82	36%
Lipid modifying agents	368	131	36%
Endocrine therapy	93	32	34%
Urologicals	246	83	34%
Antivaricosis/anti-haemorrhoidal preparations	33	11	33%
Antibacterials for systemic use	472	141	30%
Antimycotics for systemic use	61	18	30%
Other nervous system drugs	282	83	29%
Corticosteroids for systemic use	63	18	29%
Sex hormones and modulators of the genital system	147	42	29%
Antiinflammatory and antirheumatic products	207	59	29%
Vitamins	36	10	28%
All other therapeutic products	88	23	26%
Psychoanaleptics	601	157	26%
Antipsoriatics	39	10	26%
Antithrombotic agents	160	40	25%
Drugs for treatment of bone diseases	92	23	25%
Anti-asthmatics	162	40	25%
Cough and cold preparations	41	10	24%
Antihypertensives	37	9	24%
Antiepileptics	437	104	24%
Psycholeptics	659	156	24%
Thyroid therapy	31	7	23%
Drugs used in diabetes	244	55	23%
Antivirals for systemic use	210	47	22%
Drugs for functional gastrointestinal disorders	51	11	22%
Antidiarrheals, intestinal antiinflammatory/antiin	42	9	21%
Muscle relaxants	57	12	21%

Therapeutic class	Drugs	Drugs with a shortage report	%
Antineoplastic agents	439	91	21%
Antiemetics and antinauseants	79	16	20%
Anesthetics	159	32	20%
Antibiotics and chemotherapeutics for dermatologic	20	4	20%
Beta blocking agents	194	37	19%
Analgesics	476	89	19%
Immunosuppressive agents	91	16	18%
Diuretics	73	12	16%
Antigout preparations	26	4	15%
Cardiac therapy	127	19	15%
Antiprotozoals	27	4	15%
Other gynecologicals	30	4	13%
Other hormones	74	9	12%
Diagnostic tests	27	3	11%
Immunomodulating agents	20	2	10%
Antianemic preparations	44	4	9%
Antihistamines for systemic use	24	2	8%
Pituitary and hypothalamic hormones	34	2	6%
Other cardiovascular products	35	2	6%
Antihemorrhagics	38	2	5%
Cardiovascular multitherapy combination products	24	1	4%
Intravenous solutions	43	1	2%
ATC2 classes with n < 20 (30 classes)	**220**	**47**	**21%**

Note: Therapeutic classes are defined based on the second level of the Anatomical Therapeutic Chemical (ATC) Classification System maintained by the World Health Organization (WHO). Therapeutic classes with fewer than 20 drugs with sales in Canada are presented in the last row.

Data source: www.drugshortagescanada.ca; IQVIA MIDAS® database.

TABLE 2.3 Detailed statistics of shortages defined at the chemical subgroup (ATC4) level with a decline greater than 20% in the number of public plan active beneficiaries during the shortage

Chemical Subgroup (ATC4)	Therapeutic Class (ATC2)	Shortage onset date	Shortage duration (months)	DINs	Active beneficiaries prior to the shortage	Decline in active beneficiaries during the shortage	Oral Solid (%)	Brand (%)	Single-source (%)	Patented (%)
S01AD	Ophthalmologicals	Jun-17	33	1	386	88%	0%	100%	92%	0%
H05BA	Calcium homeostasis	Dec-18	6	1	32	76%	0%	100%	95%	0%
M01CB	Antiinflammatory and antirheumatic products	Dec-17	19	4	216	75%	25%	100%	95%	0%
A03ED	Drugs for functional gastrointestinal disorders	Oct-17	8	1	31	68%	100%	100%	95%	0%
A03BB	Drugs for functional gastrointestinal disorders	Jan-18	19	3	4,547	67%	33%	67%	0%	0%
N02AD	Analgesics	Oct-18	6	1	31	62%	100%	100%	91%	0%
S01FA	Ophthalmologicals	Feb-18	8	12	3,669	54%	0%	25%	26%	0%
D10AA	Anti-acne preparations	Jan-19	2	1	26	54%	0%	100%	98%	0%
G03AB	Sex hormones and modulators of the genital system	Mar-19	13 (ongoing)	19	25,199	51%	89%	79%	21%	11%
G03GA	Sex hormones and modulators of the genital system	Feb-19	5	1	<5	50%	0%	0%	56%	0%
P02BA	Anthelmintics	Jan-18	4	1	<5	50%	100%	100%	64%	0%
S01HA	Ophthalmologicals	Aug-17	2	2	<5	50%	0%	50%	0%	0%
D10BA	Anti-acne preparations	Apr-19	2	8	6,270	50%	100%	75%	0%	0%
N02BA	Analgesics	Aug-19	8 (ongoing)	38	1,980	46%	92%	3%	0%	0%
N05CM	Psycholeptics	Jan-19	3	6	1,783	45%	0%	0%	93%	0%
D10BA	Anti-acne preparations	Jul-19	9 (ongoing)	8	5,607	45%	100%	75%	0%	0%
M01AX	Antiinflammatory and antirheumatic products	Oct-17	11	3	113	45%	67%	0%	32%	0%
L01CB	Antineoplastic agents	Sep-18	7	4	103	43%	25%	25%	18%	0%
N02BA	Analgesics	Jul-17	13	38	13,495	41%	92%	3%	0%	0%
P02CC	Anthelmintics	Dec-17	5	4	84	40%	50%	0%	41%	0%
C09BB	Agents acting on the renin-angiotensin system	May-19	2	1	<5	40%	100%	100%	0%	0%
G03AA	Sex hormones and modulators of the genital system	Dec-18	16 (ongoing)	53	77,575	37%	98%	57%	11%	7%

Chemical Subgroup (ATC4)	Therapeutic Class (ATC2)	Shortage onset date	Shortage duration (months)	DINs	Active beneficiaries prior to the shortage	Decline in active beneficiaries during the shortage	Oral Solid (%)	Brand (%)	Single-source (%)	Patented (%)
R03BC	Drugs for obstructive airway diseases	Nov-17	2	3	22	36%	0%	0%	32%	0%
G03XA	Sex hormones and modulators of the genital system	Sep-18	18	4	203	36%	100%	100%	72%	0%
M05BB	Drugs for treatment of bone diseases	Sep-17	31 (ongoing)	10	26,394	36%	80%	30%	1%	0%
A10BF	Drugs used in diabetes	Jan-19	14	4	2,898	35%	100%	50%	35%	17%
J02AA	Antimycotics for systemic use	Apr-18	14	4	10	34%	0%	50%	0%	0%
N02AF	Analgesics	Jul-17	3	2	16	31%	0%	50%	50%	0%
J01XA	Antibacterials for systemic use	Nov-17	8	18	84	29%	11%	0%	0%	0%
A03AA	Drugs for functional gastrointestinal disorders	May-17	19	11	1,959	26%	91%	36%	18%	0%
C08DA	Calcium channel blockers	Sep-18	19 (ongoing)	23	8,459	24%	87%	13%	0%	0%
A07EA	Antidiarrheals, intestinal antiinflammatory/ antiinfective agents	Jul-18	21 (ongoing)	7	1,285	24%	29%	86%	22%	8%
J01XD	Antibacterials for systemic use	May-17	11	9	77	24%	22%	11%	7%	0%
N02BA	Analgesics	Mar-19	4	38	3,278	24%	92%	3%	0%	0%
N02AX	Analgesics	Jan-18	2	22	21	24%	100%	73%	13%	8%
R05DA	Cough and cold preparations	May-18	3	36	25,238	23%	33%	22%	2%	0%
R03CB	Drugs for obstructive airway diseases	Jan-19	4	1	1,823	23%	0%	0%	95%	0%
D07AA	Corticosteroids, dermatological preparations	Apr-19	12 (ongoing)	36	45,691	22%	0%	22%	0%	3%
R01AX	Nasal preparations	Jun-19	2	22	1,007	22%	0%	14%	8%	0%
R05CB	Cough and cold preparations	Oct-18	18 (ongoing)	7	513	22%	0%	29%	14%	14%
N06DX	Psychoanaleptics	Aug-17	21	8	17	21%	100%	13%	0%	13%

Note: Shortages are defined here as a situation in which a DIN within an ATC4 group is mentioned by at least one shortage report with an "actual" status during the study period. The decline in active beneficiaries compares the average monthly number of beneficiaries during the shortage and up to six months prior to the shortage.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).

TABLE 2.4 Detailed statistics of shortages defined at the chemical subgroup (ATC4) level for which public plan spending changed by more than 40% during the shortage

A. Shortages accompanied by spending increases larger than 40% (N=22)

Chemical Subgroup (ATC4)	Therapeutic Class (ATC2)	Shortage onset date	Shortage duration (months)	DINs	Monthly spending prior to the shortage ($)	Change in spending during the shortage (%)	Oral Solid (%)	Brand (%)	Single-source (%)	Patented (%)
G03AA	Sex hormones and modulators of the genital system	Jan-18	10	53	710,400	272%	98%	57%	11%	7%
G03AB	Sex hormones and modulators of the genital system	Jan-18	2	19	333,100	240%	89%	79%	21%	11%
M09AB	Other drugs for disorders of the musculo-skeletal system	Nov-18	2	1	1,200	172%	0%	0%	0%	0%
G03XB	Sex hormones and modulators of the genital system	Jul-17	7	2	98,200	150%	50%	100%	97%	47%
V04CF	Diagnostic agents	Jun-17	2	1	50	149%	0%	0%	42%	0%
L01AB	Antineoplastic agents	Dec-19	2	1	400	123%	100%	0%	100%	0%
S01FB	Ophthalmologicals	Aug-17	2	3	20	118%	0%	0%	23%	0%
A16AA	Other alimentary tract and metabolism products	Oct-19	2	19	114,000	104%	11%	42%	31%	4%
C01CA	Cardiac therapy	Sep-17	31 (ongoing)	22	1,128,600	85%	18%	27%	3%	0%
B05XA	Blood substitutes and perfusion solutions	Jun-17	34 (ongoing)	27	9,600	84%	0%	0%	18%	0%
L01XX	Antineoplastic agents	Dec-18	16 (ongoing)	27	800,400	78%	70%	56%	35%	30%
V03AB	All other therapeutic products	Apr-19	4	21	1,127,800	67%	0%	10%	3%	0%
J01AA	Antibacterials for systemic use	May-17	35 (ongoing)	30	379,900	58%	93%	7%	5%	2%
H01BA	Pituitary and hypothalamic hormones and analogues	May-17	16	19	212,900	54%	68%	63%	0%	31%

Chemical Subgroup (ATC4)	Therapeutic Class (ATC2)	Shortage onset date	Shortage duration (months)	DINs	Monthly spending prior to the shortage ($)	Change in spending during the shortage (%)	Oral Solid (%)	Brand (%)	Single-source (%)	Patented (%)
R03CB	Drugs for obstructive airway diseases	Mar-18	2	1	22,200	53%	0%	0%	95%	0%
N06DX	Psychoanaleptics	Nov-19	3	8	1,000	48%	100%	13%	0%	13%
J01DC	Antibacterials for systemic use	Jan-18	27 (ongoing)	43	379,000	46%	47%	26%	1%	5%
S01EE	Ophthalmologicals	Sep-18	2	25	2,895,600	45%	0%	44%	4%	14%
B05CB	Blood substitutes and perfusion solutions	May-17	5	13	9,000	44%	0%	0%	2%	0%
L01CB	Antineoplastic agents	May-19	4	4	67,600	43%	25%	25%	18%	0%
H05BX	Calcium homeostasis	Jan-18	13	18	88,400	42%	100%	17%	0%	15%
D11AF	Other dermatological preparations	May-18	3	11	2,200	41%	0%	36%	0%	0%

B. Shortages accompanied by spending declines larger than 40% (N=22)

Chemical Subgroup (ATC4)	Therapeutic Class (ATC2)	Shortage onset date	Shortage duration (months)	DINs	Monthly spending prior to the shortage ($)	Change in spending during the shortage (%)	Oral Solid (%)	Brand (%)	Single-source (%)	Patented (%)
S01AD	Ophthalmologicals	Jun-17	33	1	12,400	-89%	0%	100%	92%	0%
V04CF	Diagnostic agents	Jun-18	2	1	200	-88%	0%	0%	42%	0%
H05BA	Calcium homeostasis	Dec-18	6	1	9,400	-86%	0%	100%	95%	0%
A03ED	Drugs for functional gastrointestinal disorders	Oct-17	8	1	3,500	-74%	100%	100%	95%	0%
C09BB	Agents acting on the renin-angiotensin system	May-19	2	1	200	-70%	100%	100%	0%	0%
N02AD	Analgesics	Oct-18	6	1	2,800	-69%	100%	100%	91%	0%
A03BB	Drugs for functional gastrointestinal disorders	Jan-18	19	3	141,400	-68%	33%	67%	0%	0%
D10AA	Anti-acne preparations	Jan-19	2	1	600	-62%	0%	100%	98%	0%
M01CB	Antiinflammatory and antirheumatic products	Dec-17	19	4	25,400	-59%	25%	100%	95%	0%
N05CM	Psycholeptics	Jan-19	3	6	110,800	-56%	0%	0%	93%	0%
D10BA	Anti-acne preparations	Apr-19	2	8	676,500	-55%	100%	75%	0%	0%
D10BA	Anti-acne preparations	Jul-19	9 (ongoing)	8	603,500	-52%	100%	75%	0%	0%
G03AB	Sex hormones and modulators of the genital system	Mar-19	13 (ongoing)	19	1,206,100	-51%	89%	79%	21%	11%
S01HA	Ophthalmologicals	Aug-17	2	2	30	-50%	0%	50%	0%	0%
N02BA	Analgesics	Aug-19	8 (ongoing)	38	17,900	-46%	92%	3%	0%	0%
M01AX	Antiinflammatory and antirheumatic products	Oct-17	11	3	5,200	-43%	67%	0%	32%	0%
P02CC	Anthelmintics	Dec-17	5	4	1,700	-41%	50%	0%	41%	0%

Note: Shortages are defined here as a situation in which a DIN within an ATC4 group is mentioned by at least one shortage report with an "actual" status during the study period. The percent change in spending compares the average monthly spending during the shortage and up to six months prior to the shortage.

Data source: www.drugshortagescanada.ca; NPDUIS Database, Canadian Institute for Health Information (CIHI).