Potential impact of U.S. demand on the Canadian supply of 46 prescription drugs.

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DISCLAIMER

This study uses data from IQVIA Inc. The analysis, conclusions and opinions expressed in this paper do not necessarily reflect the views of the data supplier.

ABSTRACT

Canadian prices for patented medicines are regulated and are lower than American market prices on average, creating an incentive for Americans to import prescription drugs that were intended to be sold to Canadians. Importation on a commercial scale has not been allowed due to concerns of the U.S. FDA about the safety and effectiveness of products sold through foreign resale channels. Recent policy changes in the U.S. have introduced legal pathways allowing commercial scale importation of prescription drugs. This study estimates the impact that U.S. importation will have on the Canadian supply of a sample of medicines that are likely to be targets for purchase by American states, wholesalers and pharmacists. The purpose is to gauge the urgency of the threat that U.S. importation poses for the Canadian drug supply and to examine how this may affect specific patient populations differently. The analysis shows that the Canadian drug supply cannot sustain increased demand from full-scale U.S. importation. Most of the drugs studied would have their total Canadian supply exhausted in less than 3 months. Half the molecules would have been exhausted in just over 1 month and many would have lasted less than 2 weeks. The potentially rapid depletion of the Canadian drug supply from U.S. importation puts the onus on Canada's federal government to act pre-emptively to prevent events from moving faster than the legislative or regulatory process can respond.

INTRODUCTION

Canadian prices for patented medicines (aka. innovative branded prescription drugs) are regulated by the federal government and are significantly lower than American market prices on average.[1] The differentiation in drug prices between the markets creates an economic incentive for regulatory arbitrage, whereby Americans import prescription drugs that were originally intended to be sold in Canada to Canadian patients. However, arbitrage-related importation (generally referred to simply as "importation") on a commercial scale has not been legally permitted in the United States due to concerns of the U.S. Food and Drug administration (FDA) about its capacity to ensure the safety and effectiveness of products sold through foreign resale channels.[2] Recent policy changes in the United States have proposed legal pathways to allow the commercial scale importation of prescription drugs from Canada.

On July 31, 2019 following an initiative launched by U.S. President Donald Trump, the U.S. Department of Health and Human Services (HHS) announced that HHS and the FDA planned to introduce rules for legal importation of certain drugs originally intended for foreign markets. The plan authorizes "states, wholesalers or pharmacists" to seek HHS

[1] Patented Medicine Prices Review Board (PMPRB). 2017 Annual Report.
[2] U.S. Food and Drug administration (FDA). Importations of Drugs. United States Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. section 331). https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/importations-drugs

approval to import certain drugs from Canada that are versions of FDA-approved drugs that are manufactured consistent with the FDA approval.[3,4]

The U.S. President's initiative is preceded by significant legislative activity supporting drug importation at the federal and state levels of government over the last 2 years. Since 2017 three legislative bills have been introduced in the U.S. Congress (House 2; Senate 1) that contained provisions that would have allowed legal importation of prescription drugs from Canada.[5] And as of August 1, 2019 at least 17 American states had filed a total of 30 legislative bills legalizing or seeking to legalize prescription drug importation from Canada.[6] The states include Colorado, Connecticut, Florida, Illinois, Indiana, Maine, Massachusetts, Minnesota, Missouri, New Mexico, New York, Oklahoma, Oregon, Utah, Vermont, West Virginia and Wyoming.

On July 25, 2019 the Alliance for Safe Online Pharmacies Canada (ASOP), a coalition of patient groups, health professionals and wholesale and retail pharmacies, wrote a letter to Canada's federal health minister expressing concern regarding the growth in legislation in the United States that seeks to permit the importation of Health Canada-approved medicines for U.S. patients. The group was comprised of Best Medicines Coalition, Canadian Patient Safety Institute, Canadian Medical Association, Canadian Nurses Association, Canadian Organization for Rare Disorders, Canadian Pharmacists Association, Canadian Society of Hospital Pharmacists, Diabetes Canada, HealthcareCAN, Health Charities Coalition of Canada, McKesson Canada, Neighbourhood Pharmacy Association of Canada, OnPharm-United and Shoppers Drug Mart/Loblaw Companies Limited. The letter stated in part:

> "The Canadian medicine supply is not sufficient to support both Canadian and U.S. consumers. Canada is allocated certain quantities of pharmaceuticals, based on estimated national requirements, by manufacturers with global supply chains. The Canadian industry, health system, and governments do not have the capacity to address the potential increased demand that could come from a direct supply relationship between Canada pharmacy and U.S. states. The supply simply does not and will not exist within Canada to meet such demands… we are deeply concerned by the implications of any legislation in the U.S. Congress and state legislatures that would allow for the draining of Canada's medicine supply to the United States. We respectfully request that Health Canada intervene where necessary to ensure continuity in the Canadian drug supply. We also believe Health Canada should provide clarity to Canadians regarding the implications of these U.S. laws on the Canadian drug supply. This could include

[3] U.S. Department of Health and Human Services (HHS). Media release: HHS Announces New Action Plan to Lay Foundation for Safe Importation of Certain Prescription Drugs. July 31, 2019. https://www.hhs.gov/about/news/2019/07/31/hhs-new-action-plan-foundation-safe-importation-certain-prescription-drugs.html

[4] U.S. Department of Health and Human Services (HHS) and the U.S. Food and Drug Administration (FDA). Safe Importation Action Plan. https://www.hhs.gov/sites/default/files/safe-importation-action-plan.pdf

[5] Improving Access to Affordable Prescription Drugs Act, H 1776, 115th Cong, 1st Sess (2017-1018). Affordable and Safe Prescription Drug Importation Act, H 1245, 115th Cong, 1st Sess (2017-1018). Affordable and Safe Prescription Drug Importation Act, S 469, 115th Cong, 1st Sess (2017-1018).

[6] National Academy for State Health Policy (NASHP). State Legislative Action to Lower Pharmaceutical Costs. Updated Aug. 1, 2019. State Prescription Drug Legislative Tracker 2019. https://nashp.org/rx-legislative-tracker-2019/

> the scope of laws and regulations currently in place to protect the Canadian drug supply from leaving our borders, and necessary measures that could be taken to address any current gaps in Canadian statute." [7]

The urgent tone of the coalition's letter is justified by a 2018 study that estimated the impact U.S. drug importation would have on the Canadian prescription drug supply. Using aggregate data on the total number of Canadian and U.S. prescriptions dispensed in 2015, the study forecasted that if 20% of U.S. prescriptions were filled using Canadian prescription drug sources, the 2015 Canadian drug supply would be exhausted in 183 days. Canada's drug supply would have lasted only 55 days if 100% of U.S. prescriptions were filled using Canadian suppliers.[8]

Previous analyses did not estimate supply and demand at the molecule-level. American and Canadian utilization varies by molecule. Therefore, estimates of how long it will take to exhaust the Canadian drug supply under U.S. importation will also vary by molecule. This means that the speed and severity of drug shortages will impact patient populations differently depending on their need for access to any particular molecule.

OBJECTIVE

Building on previous research by Shepherd (2018, 2010),[9,10] this study estimates the particular impact that U.S. importation will have on the Canadian prescription drug supply at the molecule-level for a sample of medicines that are likely to be targets for purchase by American states, wholesalers and pharmacists under the guidelines published by HHS. The purpose of this analysis is to estimate the urgency of the threat that U.S. importation poses for the Canadian drug supply and to examine how this may affect specific patient populations differently. Canadian policy implications are briefly discussed.

DATA AND METHOD

To identify a sample of prescription drug molecules that are likely to be targets for U.S. importation this study reviewed published HHS guidelines, as well as publicly available documents in the 17 states that have introduced or passed legislation that would allow importation from Canada. 60 molecules were initially identified as meeting the HHS guidelines and were expected to have significant U.S.-Canada price differentials and substantial U.S. sales volumes in 2018, making them likely cost containment targets for importation. 2018 was selected because it was the most recent full calendar year available at the time of study. Data were obtained from IQVIA™ that included molecule,

[7] Alliance for Safe Online Pharmacies Canada. July 25, 2019. Letter to The Hon. Ginette Petitpas Taylor, Minister of Health.
[8] Shepherd M (2018) U.S. Drug Importation: Impact on Canada's Prescription Drug Supply. Health Econ Outcome Res Open Access 4: 146.
[9] See note 8.
[10] Shepherd M. The Effect of U.S. Pharmaceutical Drug Importation on the Canadian Pharmaceutical Supply. *Canadian Pharmaceutical Journal*, Vol 143, No.5, September/October 2010, 226-232.

innovative status (branded, branded generic, generic), international product name, local product name, formulation, strength, pack size, sales dollars and standard units sold (tabs, caps, etc.) by country. Of the 60 molecules that were requested, 9 had no sales recorded in Canada in 2018 and were therefore eliminated from the data set. The remaining 51 molecules had recorded sales in both Canada and the United States in 2018. The 51 molecules were comprised of 52 products in Canada: 51 branded, 1 branded generic, 0 generic; and 58 products in the United States: 51 branded, 2 branded generic, 5 generic. Of the U.S. products, 2 had both branded generic and generic products available. It was assumed that if a generic product was available in the United States that there would be little reason to include it on the list of drugs likely to be targeted for importation and therefore those molecules were removed from the analysis. Five were removed leaving 46 molecules remaining in the analysis. [see TABLE 1]

Canadian regulations prevent drug prices from fluctuating in response to increased market demand. The analysis assumes that drug companies will continue to supply the Canadian market at levels that are consistent with normal Canadian demand. Diversion of the Canadian drug supply to Americans via importation will therefore result in equivalent shortages for Canadian patients. The analysis also assumes maximum potential American demand for the Canadian prescription drug supply. HHS rules are open-ended regarding eligible importers, specifying only "states, wholesalers and pharmacists" which does not preclude any public institution or private-sector entity. Total potential demand for the Canadian drug supply was assumed to be the sum of Canadian demand plus maximum potential American demand.

RESULTS

Table 1 shows the data that were used to calculate the retrospective hypothetical maximum potential impact of U.S. importation on the 2018 Canadian prescription drug supply of the 46 molecules that were identified as likely to be eligible for U.S. importation under HHS guidelines. The number of standard units sold in 2018 is shown for each molecule as a total for the year and as a calculated average per day. The last column in the table shows the calculated number of days until the Canadian drug supply for each molecule would have been exhausted under the maximum potential impact of U.S. importation in 2018.

Across all 46 molecules, the number of days to exhaust the Canadian drug supply ranged from less than one day up to 149 days. Half the molecules would experience the total exhaustion of their Canadian supply in about 5 weeks. Almost 90% of the molecules would have experienced total exhaustion of their Canadian supply in less than 3 months. The number of days until total exhaustion of the aggregate Canadian drug supply across all 46 molecules together was 60 days. The average number of days until total exhaustion of the Canadian drug supply observed for each of the 46 molecules was 43 days.

The results are illustrated in Charts 1a, 1b and 2. Chart 1a shows the aggregate daily erosion of the Canadian drug supply across the 46 molecules likely to be eligible for U.S.

importation. The chart plots the aggregate supply across all 46 molecules, stated as the number of standard units available, along the vertical axis and plots a calendar timeline along the horizontal axis. Under importation beginning on January 1, 2018, the Canadian drug supply of the 46 molecules studied would have lasted until approximately March 1. Chart 1b shows the aggregate daily erosion of the Canadian drug supply across the 46 molecules assuming only one-third of the maximum potential American demand under U.S. importation. Under importation beginning January 1, 2018, the aggregate Canadian supply on the 46 molecules studied would've lasted 135 days or until approximately May 15. Chart 2 illustrates the number of days to exhaust the Canadian drug supply for each of the 46 molecules likely to be eligible for U.S. importation.

POLICY IMPLICATIONS

The findings of this study are consistent with previous research and validate the urgency of the concerns raised by the ASOP letter to Canada's federal health minister. The analysis shows that the Canadian drug supply cannot sustain increased demand from the American market under U.S. importation. Time to exhaustion of the Canadian drug supply under U.S. importation also varies by molecule. This study demonstrates that the speed and severity of drug shortages will impact patient populations differently depending on their need for access to any particular molecule. Most of the drugs studied would have seen their total Canadian supply exhausted in less than 3 months. Half the molecules would have been exhausted in just over one month and many would have lasted less than 2 weeks. If the aggregate estimate is calculated taking into account only one-third of the maximum potential American demand under importation, the Canadian drug supply of the 46 molecules studied would have been exhausted in 4.5 months. This study also did not account for regional distribution differences that could cause shortages to occur earlier for patients depending on where they live. The potentially rapid depletion of the Canadian drug supply from U.S. importation puts the onus on Canada's federal government to act pre-emptively in order to avoid a situation in which events move faster than the legislative or regulatory process can respond.

TABLE 1. Retrospective hypothetical maximum potential impact of U.S. importation on the 2018 Canadian drug supply of 46 molecules likely to be eligible for U.S. importation.

MOLECULE[11]	STANDARD UNITS SOLD 2018				NUMBER DAYS TO EXHAUST CAN SUPPLY[12]
	CAN TOTAL/YR[11]	CAN AVG/DAY[12]	USA TOTAL/YR[11]	USA AVG/DAY[12]	
ERTUGLIFLOZIN	30	0	3,092,940	8,474	0
EMPAGLIFLOZIN-LINAGLIPTIN	7,800	21	12,172,440	33,349	0
COBICISTAT-DARUNAVIR-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	600	2	686,070	1,880	0
BICTEGRAVIR-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	47,250	129	14,745,870	40,400	1
EMTRICITABINE-TENOFOVIR DISOPROXIL	297,510	815	67,155,800	183,988	2
GLECAPREVIR-PIBRENTASVIR	109,368	300	13,016,724	35,662	3
DORAVIRINE	240	1	28,110	77	3
DOLUTEGRAVIR-RILPIVIRINE	27,810	76	2,131,830	5,841	5
EMTRICITABINE-RILPIVIRINE-TENOFOVIR ALAFENAMIDE	239,790	657	17,999,940	49,315	5
CANAGLIFLOZIN-METFORMIN	942,780	2,583	38,332,620	105,021	9
EMTRICITABINE-TENOFOVIR ALAFENAMIDE	960,570	2,632	35,364,210	96,888	10
COBICISTAT-DARUNAVIR	534,150	1,463	14,859,180	40,710	13
LEDIPASVIR-SOFOSBUVIR	114,044	312	2,839,340	7,779	14
APREMILAST	1,702,170	4,663	35,765,865	97,989	17
COBICISTAT-ELVITEGRAVIR-EMTRICITABINE-TENOFOVIR ALAFENAMIDE	2,558,430	7,009	50,777,940	139,118	18
DOLUTEGRAVIR	2,125,470	5,823	37,020,120	101,425	20
MARAVIROC	283,320	776	4,160,724	11,399	23
RALTEGRAVIR	2,795,820	7,660	28,728,748	78,709	32
INSULIN ASPART-INSULIN ASPART PROTAMINE CRYSTALLINE	930,225	2,549	9,254,911	25,356	33
ABACAVIR-DOLUTEGRAVIR-LAMIVUDINE	3,616,860	9,909	34,319,310	94,026	35
ETHINYLESTRADIOL-ETONOGESTREL	740,349	2,028	6,610,170	18,110	37
RILPIVIRINE	281,340	771	2,478,600	6,791	37
EMTRICITABINE-RILPIVIRINE-TENOFOVIR DISOPROXIL	612,870	1,679	5,212,410	14,281	38
SOFOSBUVIR-VELPATASVIR-VOXILAPREVIR	48,020	132	385,560	1,056	40
SOFOSBUVIR	2,016	6	15,680	43	42
FINGOLIMOD	1,213,296	3,324	9,151,380	25,072	43
APIXABAN	144,076,800	394,731	1,086,701,726	2,977,265	43
SITAGLIPTIN	59,741,850	163,676	448,744,092	1,229,436	43
EMPAGLIFLOZIN-METFORMIN	3,221,880	8,827	24,045,660	65,879	43
INSULIN GLARGINE	14,603,172	40,009	108,410,666	297,016	43
INSULIN ASPART	6,674,985	18,288	48,773,882	133,627	44
DIMETHYL FUMARATE	4,233,908	11,600	30,127,050	82,540	45
TOFACITINIB	2,779,350	7,615	19,720,230	54,028	45
DACLATASVIR	1,904	5	11,144	31	53
DAPAGLIFLOZIN-METFORMIN	6,257,460	17,144	36,259,800	99,342	54
LINAGLIPTIN	25,608,390	70,160	130,190,300	356,686	60
DAPAGLIFLOZIN	25,036,770	68,594	115,923,600	317,599	65
CANAGLIFLOZIN	32,532,330	89,130	125,797,380	344,650	75
TIOTROPIUM BROMIDE	92,483,442	253,379	348,930,218	955,973	76
SOFOSBUVIR-VELPATASVIR	928,032	2,543	3,181,892	8,718	82
EMPAGLIFLOZIN	46,319,970	126,904	156,693,480	429,297	83
ELBASVIR-GRAZOPREVIR	199,584	547	430,710	1,180	116
METFORMIN-SITAGLIPTIN	169,101,090	463,291	345,768,230	947,310	120
LINAGLIPTIN-METFORMIN	16,530,420	45,289	33,099,240	90,683	122
METFORMIN-SAXAGLIPTIN	12,804,000	35,079	19,366,440	53,059	145
SAXAGLIPTIN	19,000,350	52,056	27,411,650	75,100	149
TOTAL	**702,327,815**	**1,924,186**	**3,555,893,882**	**9,742,175**	**60**
				AVERAGE	**43**

[11] Source: IQVIA MIDAS database. Drug molecules selected by author.
[12] Author's calculation.

CHART 1a. Aggregate daily erosion of the Canadian drug supply of 46 molecules likely to be eligible for U.S. importation: 100% potential U.S. demand.

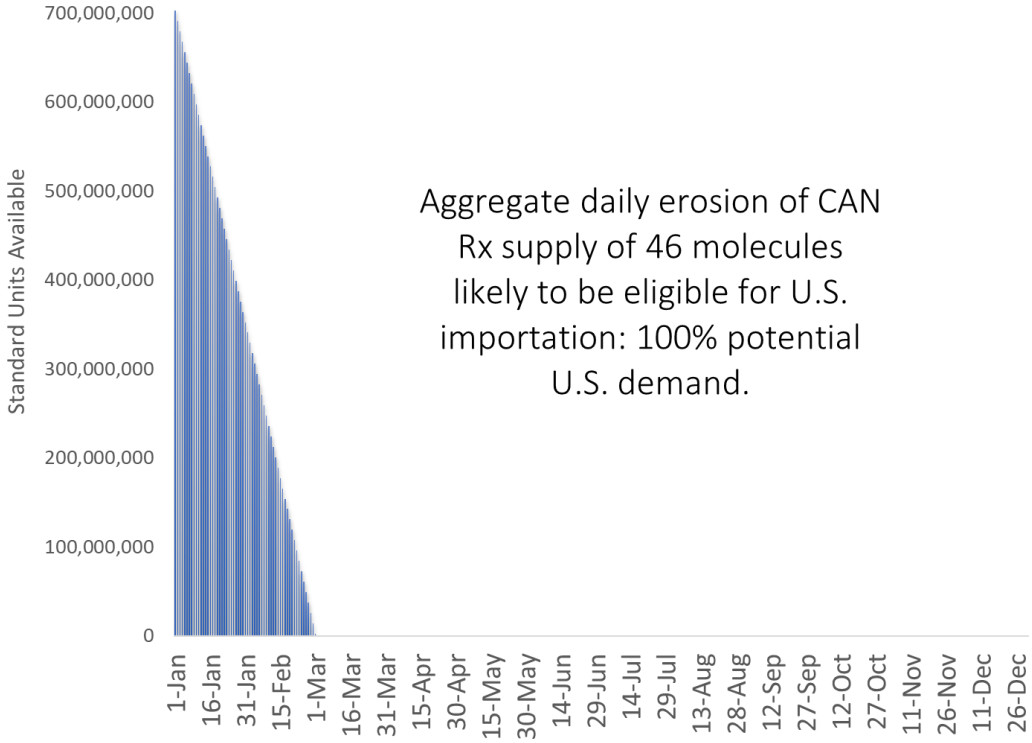

CHART 1b. Aggregate daily erosion of the Canadian drug supply of 46 molecules likely to be eligible for U.S. importation: 33.3% potential U.S. demand.

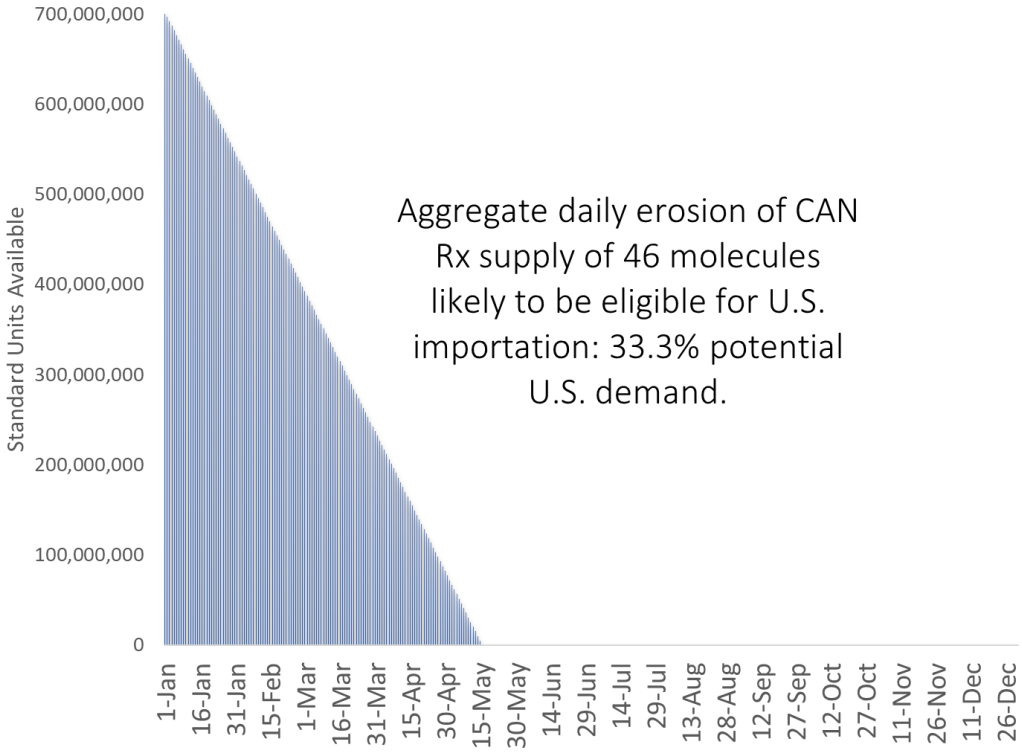

CHART 2. Number of days to exhaust the Canadian drug supply of 46 molecules likely to be eligible for U.S. importation: 100% potential U.S. demand.