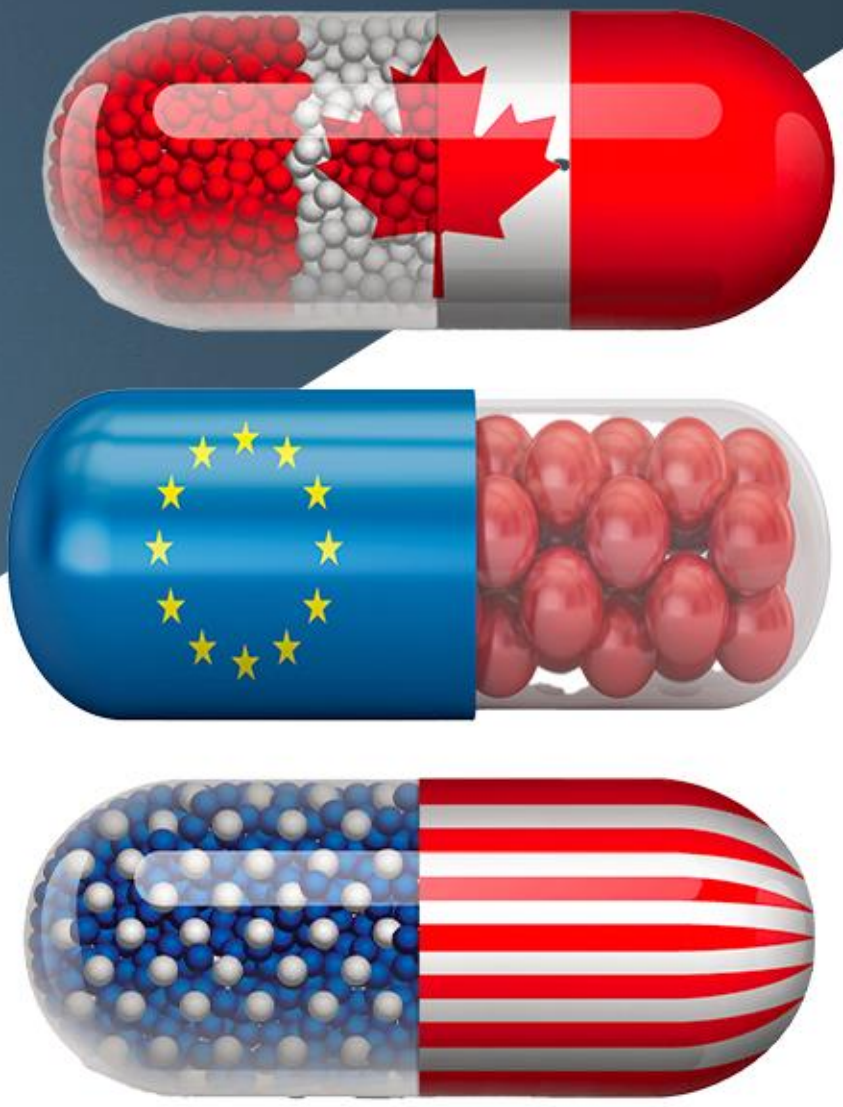
Waiting for new medicines in Canada, Europe and the United States

2018-2023



CANADIAN HEALTH POLICY INSTITUTE

TITLE

Waiting for new medicines in Canada, Europe, and the United States 2018-2023

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ATTRIBUTION

This paper is corporately authored and edited based on proprietary template models and methods that are intended to facilitate regular updates. The design and content are a cumulative reflection of the diverse contributions collectively attributable to the CHPI affiliated researchers who may have variously participated in updating each edition. Data sources, methods and editorial presentation may evolve from previous editions.

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.

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REVISED

This paper was revised on 14 APR 2024 to include additional data omitted from the original version published on 11 APR 2024. The revisions appear on pages 10 and 11.

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Highlights

- Canada is a low priority market for new drug launches:
    - During 2018-2022 Health Canada (HC) received 208 new drug applications (NDA) for new active substances (NAS), compared to 335 received by the European Medicines Agency (EMA) and 386 received by the US Food and Drug Administration (FDA).
    - Pharmaceutical companies waited an average of 327 days after submitting a new drug application to the EMA or the FDA to file an application for the same drug to Health Canada.
- Regulatory approval added significantly to the overall wait for access to new medicines:
    - During 2018-2022 Health Canada reported 166 marketing authorizations (MA) for NAS, while the FDA accrued 241 MA and the EMA accrued 214 MA that were comparable to the HC cohort.
    - On average, the time consumed from the NDA submission to the issuance of a marketing authorization, was 379 days in Canada, 442 days in the EU, and 321 days in the US.
- The process leading to public drug insurance coverage in Canada delayed access to new medicines:
    - CADTH's health technology assessment (HTA), PCPA's centralized reimbursement negotiations, and the provincial and federal public drug plans' formulary listing process collectively added 770 days to the overall wait time for access to new medicines.
- Overall, the total number of new drugs accessible in public drug plans was lower in Canada, and wait times were longer:
    - Of the 166 NAS authorized for marketing in Canada during 2018-2022, only 30 (18%) on average were listed on provincial and federal public drug formularies as of 31 DEC 2023. Counting NAS matching, accruing, or uniquely corresponding to the Canadian study cohort there were 214 comparable public drug formulary listings in the EU and 241 in the US.
    - The average total wait time from the first global new drug application to formulary listing in a public drug plan was 1476 days in Canada, 647 days in the EU, and 530 days in the US.
- Patent term restoration should be extended to compensate for all time lost due to government regulations and processes. Canada's PTR currently compensates for a maximum two years lost patent time attributable to Health Canada's approval process. PTR does not compensate for subsequent delays caused by HTA, and federal-provincial formulary processes.

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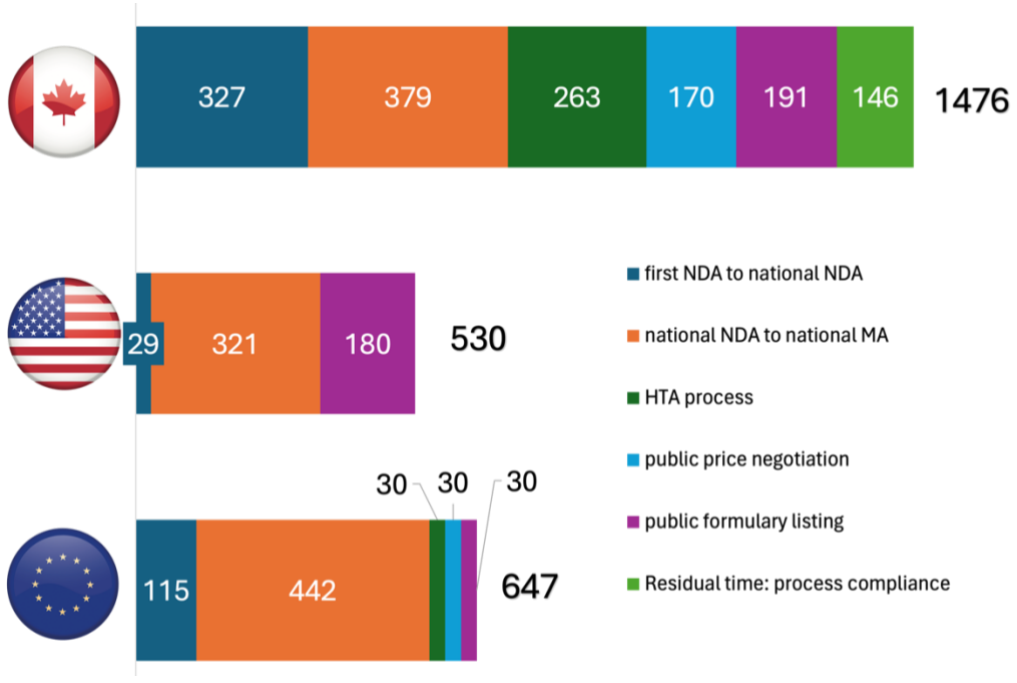
- The availability and wait for new drugs could be improved through regulatory harmonization under which, Health Canada would automatically and immediately recognize new drug approvals occurring first in either the EMA or the FDA. Over the five years from 2018-2022, regulatory harmonization could have potentially made an additional 171 new drugs available to Canadians and shortened average wait times by up to 58 days.
- Germany's system for pharmaceutical pricing and reimbursement, uses structured negotiation instead of regulation and is designed to allow immediate interim insurance coverage following marketing authorization, with permanent insurance coverage pending the outcome of negotiations. Expediting formulary listings using a similar approach in Canada would have shortened average wait times by 770 days.
- Research has shown that price regulation is a significant factor in company decisions about prioritizing markets for new drug launches. The federal government should end its price control regime.

Total wait for new medicines in Canada, the EU, and the US - Average time (days) from 1st global new drug application (NDA) to national public drug formulary listing: status 31 DEC 2023; for the study cohort of 166 new active substances (NAS) authorized for marketing (MA) by Health Canada 2018-2022 and comparable EU and US NAS MA matching, accruing, or uniquely corresponding to the CA study cohort.



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1.0 Introduction: Pathway to Access New Medicines in Canada

It takes a long time to develop a new drug that will prove safe and effective for use by patients. A 2016 estimate based on the United States experience found that the time between the start of clinical testing of a novel drug molecule, and submission of a new drug application for marketing authorization was 80.8 months or 6.7 years. **[1]** The end of the research and development phase is just the beginning of the wait for access to new medicines affected by government policies pertaining to new drug launches, regulatory approvals, and Insurance coverage/reimbursement processes.

Before a new drug can be sold in Canada, it must be authorized for marketing by the federal regulatory agency Health Canada, which reviews the clinical evidence to assess and certify the safety and therapeutic effectiveness of the product. The prices of new medicines are also federally regulated by a quasi-judicial agency known as the Patented Medicine Prices Review Board (PMPRB). PMPRB reviews the clinical evidence to determine the applicability of price control guidelines and sets the ceiling price for new drugs using international, domestic, and therapeutic reference prices.

Further, new drugs are subject to health technology assessment (HTA) by the Canadian Agency for Drugs and Technology in Health (CADTH), which again reviews clinical evidence to assess the cost-effectiveness of the product and make recommendations regarding reimbursement on behalf of all federal and provincial public drug plans, except Quebec which utilizes its own HTA agency known as the Institut national d'excellence en santé et en services sociaux (INESSS).

Manufacturers of new drugs then enter price negotiation with the pan-Canadian Pharmaceutical Alliance (PCPA), which acts as a monopsony on behalf of every federal and provincial public drug plan. Under the direction of their respective Ministers of Health, public drug plans make the final decision about listing a new drug on the formulary, and the reimbursement price and conditions, within a budget allocated by the Minister.

This complex process determines the availability of new drugs, and how long Canadian patients must wait for access to new medicines in public drug plans. Despite its importance, policy makers have failed to scrutinize the impact of the process on access. Access to new medicines should be a higher priority for federal and provincial governments. A literature review published by CHPI in 2019, found 68 studies published in peer-reviewed academic journals from 1990-2018 affirming that greater use of innovative pharmaceuticals is empirically associated with improved patient and population health outcomes, reduced potential health system costs, and reduced societal costs like economic productivity losses from untreated or under-treated illness. **[2]** There is a lot to be gained from improving access to new drugs.

This study compares access by examining the regulatory and reimbursement experience of new medicines in Canada, the European Union, and the United States. It uses an accrual-based analysis to account for drugs that matched a cohort of new active substances authorized for marketing by Health Canada during the years 2018-2022, but which were approved in previous years in Europe or the United States. The analysis comprehensively examines the total wait time for insured access to new medicines, measured from the first global application for marketing authorization to inclusion on a public drug plan formulary.

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2.0 Methods

2.1 New Medicines: Definition

A new medicine (i.e. innovative pharmaceutical) was defined as a patented prescription drug product (chemical or biologic) for human use and categorized as a new active substance (NAS) by the European Medicines Agency (EMA) and/or Health Canada, or as a new molecular entity (NME) by the US Food and Drug Administration (FDA). According to Health Canada, a new active substance is a new drug (pharmaceutical or biologic) that contains a medicinal ingredient not previously approved in a drug in Canada and that is not a variation of a previously approved medicinal ingredient. The EMA defines a new active substance as a drug not previously authorized as a medicinal product in the European Union. Similarly, the FDA defines a new molecular entity as an active ingredient that contains no active moiety that has been previously approved by the Agency or has been previously marketed as a drug in the United States. The study excluded radiopharmaceuticals and vaccines.

2.2 Access to New Drugs: Metrics

Access to new medicines was evaluated based on counts and time (days) in process for:

- New drug launches: new drug applications submitted to each jurisdiction.
- Marketing authorizations: regulatory approvals in each jurisdiction.
- Formulary listings: new drugs covered under public insurance in each jurisdiction.

2.2.1 New Drug Launches: Global v National

This study uses the terminology “new drug application (NDA)” synonymously to include Health Canada’s “new drug submission (NDS)”; the FDA’s “new drug application (NDA)” and “biologic license application (BLA)”; and the EMA’s “marketing authorisation application (MAA)”. A new drug was deemed to be globally launched from the date of the first submission of a new drug application for marketing authorization to any of the EMA, the FDA, or Health Canada. National launch was defined from the date of submission of a new drug application in each jurisdiction. The ‘launch’ definition used here differs from other analyses which define launch by the date of first sale. **[**3**]** CHPI’s definition is based on the view that the NDA represents the earliest signal that the pharmaceutical manufacturer believes that its product is safe and effective and ready for use by patients. Thereafter, availability of the drug is determined by processes external to the manufacturer.

2.2.2 Marketing Authorizations: Cohort, Matched, Accrued, Unique

The study uses the terminology “marketing authorization (MA)” interchangeably with “regulatory approval(s)”. Both terms mean that the national/central regulator has issued formal permission to sell a new drug. The study focused on a cohort of new active substances authorized for marketing by Health Canada during the years 2018-2022. We used this group of drugs as a benchmark for comparison with marketing authorizations in the European Union and the United States during the same timeframe. Many of the new drugs approved by Health Canada during the

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study period, were approved by the FDA or the EMA in earlier years. Due to the Canadian focus of the study, products approved by the FDA or the EMA during the two years before the study cohort, were deemed to be accrued to the study period if they matched drugs approved by Health Canada during the study period. The comparative drugs from Europe and the United States were identified according to three criteria:

- New active substances (NAS) approved by the EMA and/or the FDA from 2018-2022 that were exact matches of NAS approved by Health Canada from 2018-2022.
- NAS approved by the EMA and/or the FDA during 2016-2017 that were exact matches of NAS approved by Health Canada from 2018-2022 (i.e. accrued marketing authorizations).
- NAS approved by the EMA and/or the FDA from 2018-2022 that were different from the drugs approved by Health Canada from 2018-2022.

2.2.3 Formulary Listings: Public Insurance

The study uses the terminology "formulary listings" interchangeably with "insurance coverage" or "reimbursement". Insured access to a new medicine was indicated by its inclusion on the formulary of a public drug plan by 31 DEC 2023. Insurance coverage was deemed to be the only meaningful concept of access because the cost of many pharmaceuticals would be financially unaffordable for most people without the risk pooling associated with private insurance plans or the subsidy associated with publicly funded drug plans.

2.3 Total Wait for New Medicines

The total wait for access to new medicines was measured in three consecutive time segments:

- Launch priority delay: the number of days lapsed between the date that the first new drug application was submitted to any of the national pharmaceutical regulators in Canada, the European Union, or the United States, and the date that a new drug application for the same new active substance was submitted to the national regulator in each jurisdiction.
- Regulatory process delay: the number of days lapsed between the date that the new drug application was submitted within each jurisdiction, and the date of marketing authorization in each jurisdiction.
- Insurance coverage delay: the number of days lapsed between the date of marketing authorization, and the date that the medicine was included on a public drug plan formulary in the jurisdiction.

2.4 Calculations

The availability status was verified, and wait times metrics were calculated, for the same drug across all three national jurisdictions. For each jurisdiction, the aggregate number of new drug launches, marketing authorizations, and formulary listings were calculated from counts of dates posted in the database. The delays associated with launch priority, regulatory process, and insurance coverage were measured in days and were calculated by subtracting earlier dates from later dates marking the beginning and ending of the respective segment. For each jurisdiction wait

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times were averaged across all drugs identified for comparison during the study period and aggregated at the national level. The analysis does not account for the conditional status of the formulary listing (i.e. full benefit versus special authorization/ limited use/ exceptional access). The study excluded radiopharmaceuticals and vaccines. Drugs missing vital data, or which had date reconciliation conflicts were also excluded.

2.5 Data Sources

The aggregate number of new drug launches (unadjusted for accruals) from 2018-2022 was determined from the annual performance reports of the EMA, FDA, and Health Canada. **[4] [5] [6]** The submission dates for new drug applications and the effective dates of regulatory approval were obtained by special request from Health Canada for all new active substances that were authorized for marketing from 1 JAN 2018 to 31 DEC 2022. **[APPENDIX EXHIBIT A]** Comparable European and US data for new drug applications and regulatory approvals are published by the EMA and the FDA and available online and covered the years 2016-2022. **[**7**] [**8**]**

To measure counts and wait times (days) associated with health technology assessment (HTA), data were obtained from CADTH and INESSS that contained the start and end dates of the manufacturer's submission and the issuance of a recommendation by the agency. The type of recommendation was also available. **[9] [10]** We extrapolated CADTH data to represent the national experience with HTA because all of the federal and provincial public drug plans except Quebec participate in CADTH.

For the counts and wait times associated with the PCPA, published online data were obtained from the PCPA website that contained the start and end dates marked respectively by the issuance of an engagement letter and the subsequent issuance of a letter of intent (LOI) to add a new drug to public formularies. **[11]**

Canadian formulary data were separately available for the 11 federal (Non-Insured Health Benefit NIHB) and provincial publicly funded drug plans from IQVIA Inc. **[12]** The data were supplemented and cross-referenced by accessing the publicly available formulary lists from the federal and provincial drug plans and cancer care agencies. Formulary status was assessed current to 31 DEC 2023 to allow at least one year for formulary listings data to mature. Comparable data for the insurance coverage experience of new drugs in the EU and the US were not available.

The data were compiled into CHPI's Canadian Access to Innovative Medicines Database (CA2IMD). The database includes the brand name, generic name, manufacturer, regulator, submission class (e.g. NAS/NME), biologic/chemical identifier, new drug application date, marketing authorization date for drugs approved by the EMA, FDA, and Health Canada, and Canadian reimbursement data including first claim date across private sector drug plans, formulary listing dates for each federal and provincial drug plan, and the reimbursement status of each formulary listing. The database is updated annually.

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3.0 Results and Analysis

3.1 Benchmark Cohort and Comparable Drugs

The study identified 166 new active substances which had been authorized for marketing by Health Canada during 2018-2022, excluding vaccines and radiopharmaceuticals. These were designated as the benchmark cohort for the study. Using an accrual method, we identified a total of 337 unique new active substances that met the comparability criteria for inclusion and were therefore defined as having received or accrued marketing authorization during the study period in at least one of the pharmaceutical regulators in Canada, the European Union, or the United States.

3.2 Launch Priority: New Drug Applications

The data indicate that Canada was a low priority market for new drug launches relative to the EU and the US. **CHART 1** displays data from each agency's annual report which shows the number of new drug applications received by the EMA, FDA, and Health Canada, during 2018-2022 for new active substances excluding advanced therapeutic medicinal products (ATMP), vaccines and radiopharmaceuticals. The data includes every NDA received by each jurisdiction from 2018-2022 and does not necessarily correspond to the study cohort. During the study period, Health Canada received 208 NDA submissions for marketing authorization, compared to 335 received by the EMA, and 386 by the FDA.

Canada's status as a low priority market for new drug launches is also reflected by the infrequent occasions when Health Canada was first to receive a new drug application among the three national regulators. Looking only at the drugs that correspond to the study cohort, **CHART 2** shows the number of cases in which each national regulator was first to receive a new drug application for marketing authorization of the 337 new active substances approved by at least two of the EMA, the FDA, and Health Canada accruing during 2018-2022. Canada was first to receive an NDA for only 33 (10%) of 337 NAS corresponding to the cohort. The EMA was first to receive 79 (23%), and the FDA was first to receive 225 (67%). Narrowing this further, of the drugs corresponding to the cohort, 92 new drug applications were submitted in common to all three jurisdictions from 2018 to 2022. Of these 85 (92%) were launched first in the US, 6 (7%) we're launched first in the EU, and one (<1%) was launched in Canada.

The delay attributable to the national order of priority for launching a new drug was measured from first NDA in any jurisdiction, to the submission of an NDA to each of the national regulators. **CHART 3** shows the average number of days between the first NDA submitted among the EMA, the FDA and HC (aka "global launch") and submission of an NDA to each domestic regulator (aka "national launch") for the same NAS. Bilateral comparisons of the drugs launched in Canada and in at least one other of the EU or US, indicated pharmaceutical companies waited an average of 327 days after the first NDA submission to file an NDA for the same NAS to Health Canada. The corresponding bilateral comparisons show that the wait from the first global NDA to national NDA was 115 days for the EU, and 29 days for the US.

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CHART 1. New drug launches in the EU, US, and Canada 2018-2022.

CHART 2. First market to receive a new drug application 2018-2022: of NAS approved in at least 2 markets [left]; of NAS approved in 3 markets [right].

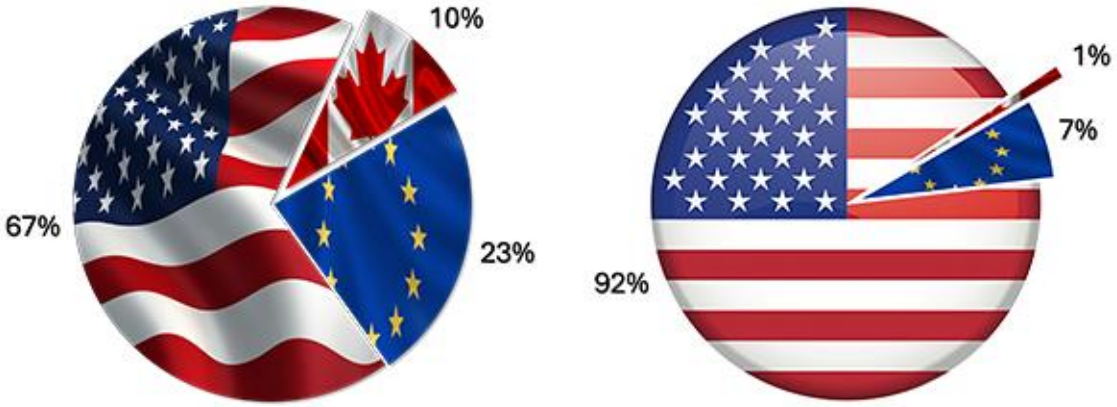

CHART 3. National launch delay: Mean time (days) - first NDA to national NDA 2018-2022.

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3.3 Regulatory Performance: Marketing Authorizations

CHART 4 displays the number of marketing authorizations for new drugs matching, accruing, or uniquely corresponding to the study cohort during 2018-2022. Results are shown separately by national regulator. The bars are segmented to separately show the number of drugs authorized for marketing in common with Health Canada during 2018-2022, the number of unique drugs authorized for marketing during the same period, and the number of drugs in common with drugs approved by Health Canada during 2018–2022, but which accrued marketing authorization before 2018. Health Canada reported 166 marketing authorizations for new active substances during 2018-2022. The FDA authorized 241 NAS, and the EMA authorized 214. The delay to access caused by the regulatory process is represented by the time between the date of the NDA and the date of marketing authorization by the national regulator. **CHART 5** shows the average number of days from NDA to national MA in the EMA, FDA, and Health Canada. Results are shown only for accrued MA for the drugs that were in common with the NAS approved by HC. Health Canada took 379 days on average to approve an NAS. The EMA took 442 days, and the FDA took 321 days.

CHART 4. Marketing authorizations (MA) corresponding to study cohort 2018-2022.

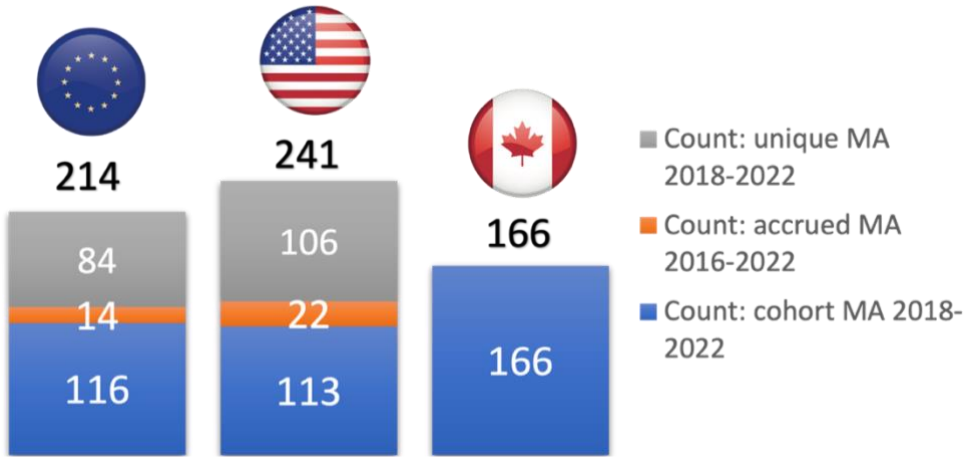

CHART 5. Mean time (days): national NDA submission to MA 2018–2022.

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3.4 Insurance Coverage Process: HTA, Pricing, Reimbursement

Comparison of publicly funded drug insurance in Canada, the European Union and the United States was limited by data availability and complicated by differences in each system. Formulary listing data were available only for Canada. However, we were able to compare across jurisdictions by applying some general assumptions based on the structure of pricing and reimbursement in publicly funded drug plans in the Europe and Medicare in the United States.

United States

In the United States publicly subsidized drug benefits are provided through Medicare Part D, which is financed from federal revenues (73%), beneficiary premiums (15%), and state contributions (11%). Medicare does not maintain a formulary or use HTA. Medicare Part D drug plan sponsors must review new drugs and decide on coverage within 180 days of FDA approval. Formularies must include at least two chemically distinct drugs for each therapeutic class, and any additional drugs presenting therapeutic advantages. [**13**] Part D plan sponsors typically list all NAS drugs on formulary immediately following marketing authorization from the FDA and adjust the level of insurance coverage by tiered premiums, deductibles, and copayments. One study showed that 90% of novel therapeutics were covered by at least 1 Medicare plan within 1 year following FDA approval but did not report the average time to list new drugs on part D formularies. [**14**]

Recently legislated provisions of the Inflation Reduction Act will allow the federal government to negotiate directly with drug companies to determine the prices that Medicare will pay for drugs covered under Part D starting in 2026. Previously Medicare was not permitted to negotiate prices. The Act is being challenged in court by the pharmaceutical industry. It is yet unclear how the negotiation process will be structured and what the impact will be on the time to access new medicines.

During the period of the study the US did not have a central negotiator for drug prices and reimbursement under Medicare, and there was zero impact on the insurance coverage delay. We assumed that the average time between marketing authorization and listing on at least one Medicare part D formulary would not exceed 180 days.

European Union

In the EU, marketing authorization is centralized, but HTA, pricing, and reimbursement processes for public drug plans differ across its member states. However, the EU has taken steps to centralize HTA with new regulation scheduled for implementation in 2025. The regulation will allow health technology developers to make a single submission at the EU level. Member states currently retain independence to determine how and when to use EU HTA recommendations in their national processes for public drug reimbursement. [**15**] Our assumptions about pricing and reimbursement in Europe were based upon the French and German processes which apply HTA as a post-market process to expedite access, or as a concurrent process with marketing authorization.

In France, HTA runs as a concurrent process with marketing authorization to minimize delays. The prices of drugs authorized for marketing are freely established by the pharmaceutical companies. The prices of publicly reimbursed medicines are subsequently determined through negotiation between the manufacturer and the ministry of health. France has an expedited access policy to

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facilitate immediate market entry under public reimbursement on a temporary basis for novel drugs with significant therapeutic benefit. Pricing is the responsibility of the Economic Committee for Health Products (CEPS) following HTA conducted by the national health authority known as HAS. The HTA and pricing process together account for a maximum 90 days for drugs not granted expedited market access. [**16**]

In Germany, new medicines are added to public formularies immediately following EMA marketing authorization. Under the German Medicines Market Reorganization Act (AMNOG) 2011, pharmaceutical manufacturers launching a new drug on the market, are free to set the price for a maximum of twelve months. Public pricing is a post-market event in Germany. Manufacturers must submit clinical evidence to the Federal Joint Committee (G-BA) that proves the additional benefit of the drug. If there is additional therapeutic benefit, the price at which the drug will be reimbursed by the statutory health insurance funds is negotiated by the federal health insurance association known as GKV-Spitzenverband. Price negotiations must reach agreement within six months. If no agreement can be reached, an arbitration board decides on the reimbursed price using European reference prices. There is an appeal process. **[17] [**18**]**

We assumed for analysis that public pricing was a post-market process in the EU and the public drug insurance coverage delay ranged from zero up to 90 days maximum.

Canada

In Canada, provincial governments offer publicly funded drug benefits to seniors and low-income households, with special programs for select diseases. The federal government offers public benefits to the aboriginal population. About 1/3 of the population is eligible under these programs. In addition, provincial governments are the universal payer of last resort for people who incur uninsured out-of-pocket costs exceeding income-based deductibles. Detailed data were available for Canada that allowed us to analyze the insurance coverage process in segments looking separately at HTA, pricing, and reimbursement. In Canada HTA is a stepwise consecutive process leading up to listing on a public formulary. Manufacturers submit new drug products to the Canadian Agency for Drugs and Technology in Health (CADTH) for HTA following marketing authorization from Health Canada. The HTA process adds significant time to the wait for access to new medicines in Canada. **TABLE 1** shows the number of HTAs completed by CADTH from 2018-2023 corresponding to the study cohort. CADTH completed 276 HTAs for unique drug products (including only one indication) in total during 2018-2023 and 110 of these assessments were for drugs that matched the 166 NAS authorized for marketing by Health Canada during 2018-2022. The distribution of recommendations issued by the agency was: 1 “reimburse”, 85 “reimburse with conditions”, and 24 “do not reimburse”. The time from the manufacturer’s submission to the issuance of a recommendation was significant, adding 263 days on average to the total wait for access to new medicines under public drug plans.

In Canada, the pan-Canadian Pharmaceuticals Alliance (PCPA) negotiates reimbursement prices with pharmaceutical manufacturers on behalf of all provincial, territorial, and federal publicly funded drug plans. **TABLE 1** shows few of the drugs authorized for marketing by Health Canada successfully completed negotiations with the PCPA during the study period. The PCPA completed 201 negotiations for unique drug products in total from 2018-2023. Only 81 (49%) of the 166 NAS approved by Health Canada during 2018-2022 were issued a letter of intent (LOI) to list the drug product on the public formularies as of 31 DEC 2023. Measured from the issuance of an

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engagement letter to the issuance of an LOI, the PCPA process added 170 days on average to the wait for new medicines under public drug plans across the country. Following the issuance of an LOI by the PCPA the federal, provincial drug plans extend the delay by an average of 191 days to complete the process of listing new drugs on public formularies.

TABLE 1. CADTH HTA and PCPA negotiations completed 2018-2023.

	COUNT	%
Study cohort: NAS authorized for marketing by Health Canada 2018-2022	166	100%
Total CADTH HTA completed 2018-2023	276	-
CADTH HTA matching study cohort, by recommendation type:		
Do not reimburse	24	14.5%
Reimburse	1	0.6%
Reimburse with conditions	85	51.2%
Total	110	66.3%
Total PCPA LOI completed 2018-2023	201	-
PCPA LOI matching study cohort	81	48.8%
Mean time (days): from CADTH submission to recommendation	263	
Mean time (days): from PCPA engagement letter to LOI issuance	170	
Mean time (days): from LOI issuance to formulary listing	191	

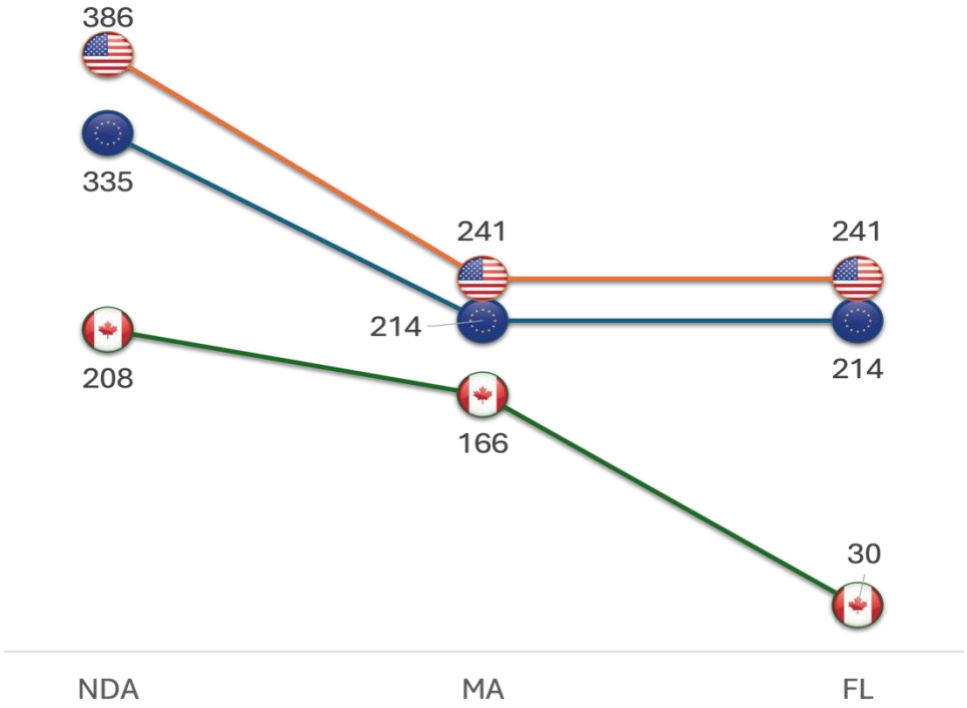
4.0 Summary Metrics

4.1 Final Availability of New Drugs in Public Drug Plans

We assumed that EU public drug plans cover all new active substances approved by the EMA, and that most US Medicare Part D drug plans covered all NAS approved by the FDA. Detailed data were available for formulary listings in each of the federal and provincial public drug plans in Canada. The data were aggregated at the national level by averaging across the jurisdictional totals. **CHART 6** displays the count of NAS surviving from new drug application (NDA) to marketing authorization (MA) to listing on a public formulary (FL). Formulary status was current as of 31 DEC 2023. The NDA data include all submissions. The MA and FL data include only the drugs in each jurisdiction that were matched, accrued or uniquely corresponding to the study cohort and period of time.

From 1 JAN 2018 to 31 DEC 2022 the EU received 335 NDA, and authorized 214 NAS for marketing, and subsequently listed all of them on public drug plan formularies as of 31 DEC 2023. During the same timeframe, the US received 386 NDA, authorized 241 NAS for marketing, and all were listed on Medicare part D plan formularies. By comparison, over the same period, Canada received only 208 NDA, and authorized only 166 NAS for marketing, and subsequently listed only 30 of the approved drugs on average across federal and provincial public drug plans as of 31 DEC 2023.

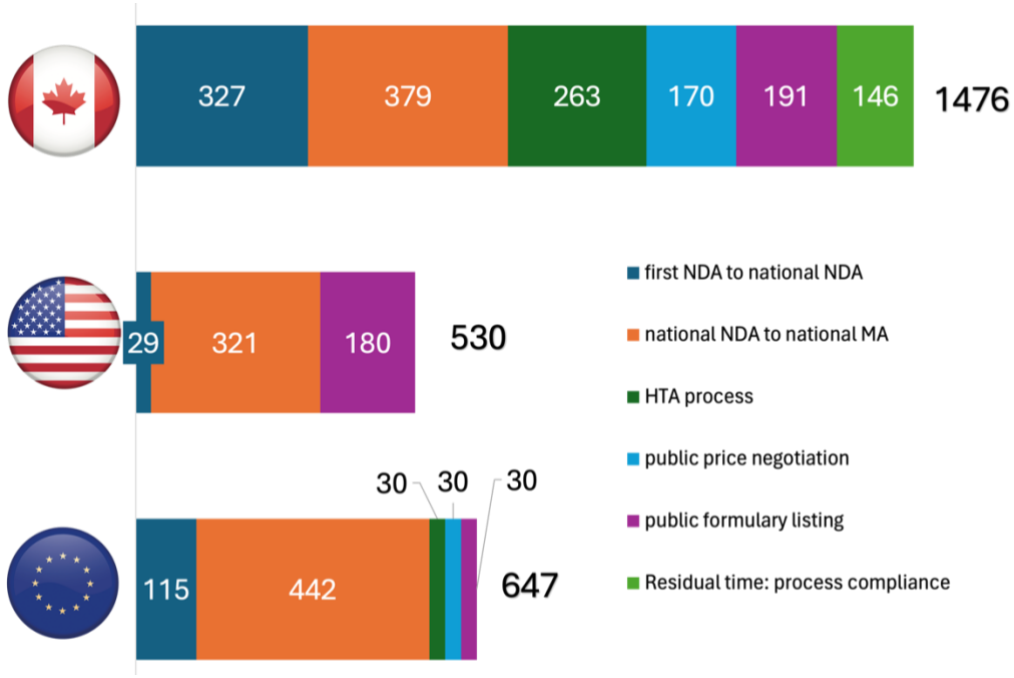
CHART 6. Count of NAS surviving from new drug application (NDA) to marketing authorization (MA) to listing on a public formulary (FL): status 31 DEC 2023.



4.2 Total Wait for Coverage of New Medicines in Public Drug Plans

The total wait time for access to new medicines is displayed in **CHART 7** showing the average number of days between first global launch and insured access in a public drug plan, for new active substances matched, accruing, or uniquely corresponding to the study cohort defined by Health Canada marketing authorizations issued during 2018-2022. The bars are presented in three segments showing the time from (1) global NDA to national NDA, (2) national NDA to national marketing authorization (MA), and (3) national marketing authorization to public insurance coverage in Canada, the EU (using France and Germany as proxy models), and the US, as of 31 DEC 2023. For the EU and the US, the third segment represents assumptions based on the structure of the insurance coverage process in those jurisdictions. For Canada, the third segment is subdivided to show the time spent in health technology assessment (263 days), centralized price negotiation (170 days), and formulary listing (191 days), plus residual time attributable to process compliance (146 days): subtotal 770 days. Measured from the date of the first global NDA to the date of a national public formulary listing, the overall total wait time to access new medicines in a public drug plan averaged 1476 days in Canada, 647 days in the European Union, and 530 days in the United States.

CHART 7. Total wait for new medicines in Canada, the EU, and the US 2018-2023.



5.0 Policy Discussion

5.1 Americans and Europeans get Better, Faster Access to New Medicines

The analysis conducted for the study confirms that Canadians get access to only a fraction of the new drugs that are available to Europeans and Americans. The contrast is especially sharp in bilateral comparisons between Canada and the United States. Only 54% of the new drugs launched in the United States were also launched in Canada during the study. Only 69% of the new drugs authorized for marketing in the United States were also approved in Canada. The average Canadian public drug plan covers less than 13% of the new medicines covered by US Medicare part D drug plans.

Canadians also wait much longer than Europeans and Americans for new drug launches, and for insurance coverage of new medicines. On average, Canadians waited almost one year after a new drug was launched in Europe or in the United States for the same new drug to be launched in Canada. In total, on average publicly insured Canadians waited 4 years to get access to a new medicine under their drug plan, which is 2.5 years longer than Americans insured under Medicare, and 2.2 years longer than publicly insured Europeans.

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5.2 Market Size

The country's lagging performance on these metrics can be explained by both structural and policy related factors. The size of the Canadian market is one determinant of the country's low priority for new drug launches. Canada's market is characterized by a small population (not shown) with relatively high income but counts for less than 2% of the global market for pharmaceutical sales. By comparison, the United States accounts for almost 40%, and the top four European jurisdictions (Germany, France, Italy, and Spain) collectively account for 11.5% of the global market for pharmaceutical sales. **[19] [20]** Canada is not an insignificant market, but it is much less important than the United States and Europe. The structural disadvantage makes it imperative that federal and provincial governments address the policy determinants of new drug launches.

5.3 Price Regulation

Small markets can minimize their structural disadvantage by avoiding price controls. Research has shown that price regulation is a significant factor in company decisions about prioritizing markets for new drug launches. **[21] [22] [23] [24] [25] [26]** The federal government should end its price control regime, revoke the regulations and decommission the PMPRB. The Board's function is redundant. Several other agencies are involved in regulating the efficacy and price of new drugs. Moreover, total spending on patented medicines has accounted for a stable, small percentage of national health expenditures for 33 years, totaling only 4.7% net of rebates to public payers in 2022. [**27]**

5.4 Regulatory Harmonization

The availability and wait for new drugs could be improved through regulatory harmonization under which, Health Canada would automatically and immediately recognize new drug approvals occurring first in either the EMA or the FDA. Health Canada could implement this policy unilaterally without requiring mutual recognition. Scientific standards for new drug applications are the same for Health Canada, the EMA and the FDA. Regulatory harmonization could have potentially made an additional 171 new drugs available to Canadians, equal to the difference between the total number of unique marketing authorizations across all three jurisdictions (337) and the number of NAS marking authorizations issued by Health Canada (166). The policy also could have reduced the overall wait by 58 days, which represents the current average time spent from national NDA to marketing authorization by Health Canada, which was 379 days, minus the same timeframe for the US which was 321 days.

5.5 Expedited Formulary Listing

Removing price regulation would increase incentives for companies to prioritize the Canadian market for new drug launches. Germany provides a real-world model for expediting insurance coverage for new medicines that could be useful to inform discussion of this issue in Canada. The German system for pharmaceutical pricing and reimbursement in its public drug plans is based on structured negotiation instead of regulation and is designed to allow immediate interim insurance coverage following marketing authorization, with permanent insurance coverage pending the outcome of negotiations.

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Applying this model to Canada, the federal price regulations would be eliminated. New active substances would be listed on drug plan formularies immediately following the first market authorization issued by the EMA/FDA/Health Canada. The initial formulary list price would be the manufacturer's suggested price and would be used as a benchmark for rebates negotiated directly with the drug plans. Negotiations would be confidential and could be informed, but not determined, by publicly available international reference prices and the HTA process. When negotiations were complete, the difference between the manufacturer's suggested price and the negotiated price would be retrospectively applied to sales that occurred in the interim period. Negotiations would be time limited and if agreement could not be reached, would progress to arbitration. The formulary listing would expire if either party rejected the arbiter's price and revenues earned under the interim price would be rebated according to the arbiter's price. Manufacturers would have the option to request renegotiation in the future if new clinical or cost effectiveness data emerged, or any other circumstances changed the value proposition of the drug product. The pCPA would be obliged to accommodate a second round of negotiation.

The proposed changes would expedite insured access to new drugs while leaving the bargaining leverage of the payer (formulary exclusion) and the seller (withholding product) ultimately intact. Adopting this policy change could reduce wait time by up to 770 days for publicly insured Canadians, equal to the current average time spent from Health Canada marketing authorization to formulary listing in a public drug plan.

5.6 Patent Term Restoration (PTR)

Intellectual property (IP) protection is another policy determinant of company decisions about prioritizing markets for new drug launches. **[28]** Canada currently has a patent term restoration regime that offers research-based pharmaceutical companies the potential to recover up to two years of time lost on their patent because of lengthy regulatory and government approval processes. Restoration is calculated from the filing date of the patent application to the date of marketing approval, up to a maximum of two years. PTR does not compensate for subsequent delays caused by HTA, pCPA negotiations and federal-provincial public formulary listing agreements. The data indicate the delay caused by reimbursement processes is as significant as the delay from regulatory processes. The erosion of time under market exclusivity is likely a major reason why pharmaceutical companies deprioritize the Canadian market for new drug launches. Extending patent term restoration to compensate for a full recovery of all time lost from the filing of a new drug application to formulary listing would remove IP related disincentives to launching new drugs earlier in Canada.

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Appendix

EXHIBIT A. Study cohort: 166 new active substances (NAS) authorized for marketing by Health Canada 2018-2022 excluding vaccines and radiopharmaceuticals.

NAS BRAND NAME	ACTIVE INGREDIENT GENERIC NAME
ABECMA	IDECABTAGENE VICLEUCEL
ADBRY	TRALOKINUMAB
ADDYI	FLIBANSERIN
ADTRALZA	TRALOKINUMAB
AIMOVIG	ERENUMAB
AJOVY	FREMANEZUMAB
AKLIEF	TRIFAROTENE
ALBRIOZA	URSODOXICOLTAURINE, SODIUM PHENYLBUTYRATE
ALUNBRIG	BRIGATINIB
ANTHIM	OBILTOXAXIMAB
BALVERSA	ERDAFITINIB
BELSOMRA	SUVOREXANT
BEOVU	BROLUCIZUMAB
BESPONSA	INOTUZUMAB OZOGAMICIN
BIKTARVY	EMTRICITABINE, TENOFOVIR ALAFENAMIDE HEMIFUMARATE, BICTEGRAVIR SODIUM
BIMZELX	BIMEKIZUMAB
BRAFTOVI	ENCORAFENIB
BREYANZI	LISOCABTAGENE MARALEUCEL
BRINEURA	CERLIPONASE ALFA
BRUKINSA	ZANUBRUTINIB
CABLIVI	CAPLACIZUMAB
CABOMETYX	CABOZANTINIB
CALQUENCE	ACALABRUTINIB
CAMZYOS	MAVACAMTEN
CIBINQO	ABROCITINIB
CORZYNA	RANOLAZINE
CRESEMBA	ISAVUCONAZONIUM SULFATE
CRYSVITA	BUROSUMAB
DACOGEN	DECITABINE
DAURISMO	GLASDEGIB
DAYVIGO	LEMBOREXANT
DOJOLVI	TRIHEPTANOIN
EMGALITY	GALCANEZUMAB
EMPAVELI	PEGCETACOPLAN
ENHERTU	TRASTUZUMAB DERUXTECAN
ENSPRYNG	SATRALIZUMAB
ERLEADA	APALUTAMIDE

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ESPEROCT	ANTIHEMOPHILIC FACTOR VIII (RECOMBINANT, B-DOMAIN TRUNCATED), PEGYLATED
EUCRISA	CRISABOROLE
EVENITY	ROMOSOZUMAB
EVRYSDI	RISDIPLAM
FASENRA	BENRALIZUMAB
FOLOTYN	PRALATREXATE
GAVRETO	PRALSETINIB
GIVLAARI	GIVOSIRAN
HEMLIBRA	EMICIZUMAB
HYQVIA	HYALURONIDASE (HUMAN RECOMBINANT), IMMUNOGLOBULIN (HUMAN)
IBSRELA	TENAPANOR
IDHIFA	ENASIDENIB MESYLATE
ILUMYA	TILDRAKIZUMAB
INCRELEX	MECASERMIN
INQOVI	CEDAZURIDINE, DECITABINE
INREBIC	FEDRATINIB HYDROCHLORIDE
INTRAROSA	PRASTERONE
JEMPERLI	DOSTARLIMAB
JIVI	ANTIHEMOPHILIC FACTOR (RECOMBINANT, B-DOMAIN DELETED, PEGYLATED)
KERENDIA	FINERENONE
KIMMTRAK	TEBENTAFUSP
KISQALI	RIBOCICLIB SUCCINATE
KORSUVA	DIFELIKEFALIN
KOSELUGO	SELUMETINIB SULFATE
KYMRIAH	TISAGENLECLEUCEL
LEQVIO	INCLISIRAN SODIUM
LIBTAYO	CEMIPLIMAB
LIVTENCITY	MARIBAVIR
LOKELMA	SODIUM ZIRCONIUM CYCLOSILICATE
LONSURF	TIPIRACIL HYDROCHLORIDE, TRIFLURIDINE
LORBRENA	LORLATINIB
LUMAKRAS	SOTORASIB
LUXTURNA	VORETIGENE NEPARVOVEC
MAYZENT	SIPONIMOD
MEKTOVI	BINIMETINIB
MONJUVI	TAFASITAMAB
MOUNJARO	TIRZEPATIDE
MYLOTARG	GEMTUZUMAB OZOGAMICIN
NERLYNX	NERATINIB MALEATE
NEXTSTELLIS	DROSPIRENONE, ESTETROL MONOHYDRATE
NEXVIAZYME	AVALGLUCOSIDASE ALFA
NGENLA	SOMATROGON
NUBEQA	DAROLUTAMIDE

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ODOMZO	SONIDEGIB
OLUMIANT	BARICITINIB
ONPATTRO	PATISIRAN SODIUM
ONSTRYV	SAFINAMIDE
ORILISSA	ELAGOLIX
ORLADEYO	BEROTRALSTAT HYDROCHLORIDE
OSPHENA	OSPEMIFENE
OXERVATE	CENEGERMIN
OXLUMO	LUMASIRAN SODIUM
OZEMPIC	SEMAGLUTIDE
PADCEV	ENFORTUMAB VEDOTIN
PALYNZIQ	PEGVALIASE
PANHEMATIN	HEMIN
PEMAZYRE	PEMIGATINIB
PIFELTRO	DORAVIRINE
PIQRAY	ALPELISIB
POLIVY	POLATUZUMAB VEDOTIN
PONVORY	PONESIMOD
POTELIGEO	MOGAMULIZUMAB
QINLOCK	RIPRETINIB
QULIPTA	ATOGEPANT
RADICAVA	EDARAVONE
RAYALDEE	CALCIFEDIOL
REBLOZYL	LUSPATERCEPT
REKOVELLE	FOLLITROPIN DELTA
RETEVMO	SELPERCATINIB
RHOLISTIQ	BELUMOSUDIL MESYLATE
RINVOQ	UPADACITINIB
ROZLYTREK	ENTRECTINIB
RUKOBIA	FOSTEMSAVIR TROMETHAMINE
RUZURGI	AMIFAMPRIDINE
RYBREVANT	AMIVANTAMAB
SAPHNELO	ANIFROLUMAB
SARCLISA	ISATUXIMAB
SCEMBLIX	ASCIMINIB HYDROCHLORIDE
SILIQ	BRODALUMAB
SKYRIZI	RISANKIZUMAB
SOHONOS	PALOVAROTENE
SOTYKTU	DEUCRAVACITINIB
STEGLATRO	ERTUGLIFLOZIN
SUNLENCA	LENACAPAVIR SODIUM
SUNOSI	SOLRIAMFETOL HYDROCHLORIDE
SYMDEKO	IVACAFTOR, TEZACAFTOR
TABRECTA	CAPMATINIB HYDROCHLORIDE

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TAKHZYRO	LANADELUMAB
TALZENNA	TALAZOPARIB
TAVALISSE	FOSTAMATINIB DISODIUM
TAVNEOS	AVACOPAN
TECARTUS	BREXUCABTAGENE AUTOLEUCEL
TEGSEDI	INOTERSEN SODIUM
TEPMETKO	TEPOTINIB HYDROCHLORIDE
TEZSPIRE	TEZEPELUMAB
TIBELLA	TIBOLONE
TOMVI	ETOMIDATE
TRIFERIC AVNU	FERRIC PYROPHOSPHATE CITRATE
TRIKAFTA	ELEXACAFTOR, IVACAFTOR, TEZACAFTOR
TRODELVY	SACITUZUMAB GOVITECAN
TRULANCE	PLECANATIDE
TRUSELTIQ	INFIGRATINIB PHOSPHATE
TUKYSA	TUCATINIB
UBRELVY	UBROGEPANT
ULTOMIRIS	RAVULIZUMAB
UNITUXIN	DINUTUXIMAB
VABYSMO	FARICIMAB
VASCEPA	ICOSAPENT ETHYL
VELPHORO	SUCROFERRIC OXYHYDROXIDE
VELTASSA	PATIROMER SORBITEX CALCIUM
VERZENIO	ABEMACICLIB
VITRAKVI	LAROTRECTINIB
VIZIMPRO	DACOMITINIB
VRAYLAR	CARIPRAZINE HYDROCHLORIDE
VYEPTI	EPTINEZUMAB
VYNDAQEL	TAFAMIDIS MEGLUMINE
VYZULTA	LATANOPROSTENE BUNOD
WAKIX	PITOLISANT HYDROCHLORIDE
WELIREG	BELZUTIFAN
XENLETA	LEFAMULIN ACETATE
XERMELO	TELOTRISTAT ETIPRATE
XOSPATA	GILTERITINIB FUMARATE
XPOVIO	SELINEXOR
XYDALBA	DALBAVANCIN
YESCARTA	AXICABTAGENE CILOLEUCEL
ZEJULA	NIRAPARIB
ZEPOSIA	OZANIMOD HYDROCHLORIDE
ZEPZELCA	LURBINECTEDIN
ZOLGENSMA	ONASEMNOGENE ABEPARVOVEC

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