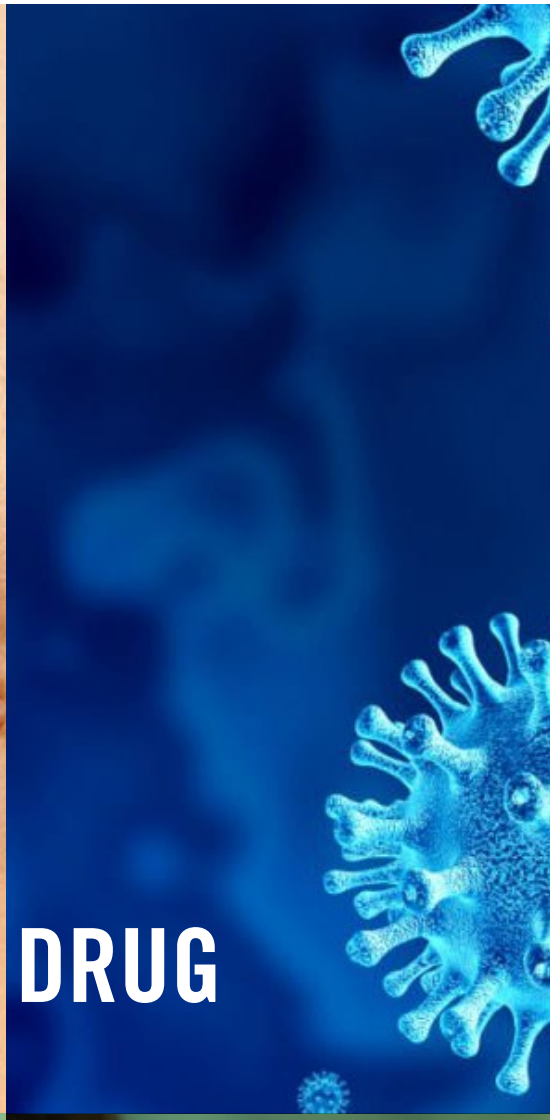


2022 PRESCRIPTION DRUG TREND REPORT

EXPRESS SCRIPTS CANADA

EXPRESS SCRIPTS®

Foreword

Over the past 20 years, it's fair to say Canada's pharmacy benefit management landscape has evolved greatly. Yet, in the past two years alone, a confluence of factors – technological, financial, political and others – have conspired to exert revolutionary change in our industry.

On the healthcare front, the pandemic catapulted digital health solutions into the mainstream. Virtual care apps saw wide adoption; Express Scripts Canada Pharmacy's online service alone saw double-digit growth.

A growing lineup of blockbuster drugs also came onstream with novel therapeutics continuing to emerge. While sophisticated gene therapies and biologics promise to more effectively treat diseases, including cancer, these drugs come with price tags that are straining benefit plans.

In 2021, overall private drug plan spend increased 4.3 per cent. Despite fewer plan members submitting claims, the per claimant cost grew. For example, while 29 per cent of all drug spend is on specialty drugs, this category represents fewer than one per cent of all claimants.

The COVID-19 pandemic also caused widespread disruption. Among the impacts, patients avoided hospitals and clinics, which led to a dramatic decrease in disease diagnoses. The resulting treatment backlog is only now beginning to dissipate.

Meanwhile, federal health policy saw delays in the anticipated implementation of Patented Medicine Prices Review Board changes. Similarly, a funding model to tackle rare diseases and a proposed framework for a pan-Canadian formulary remain in development – all against an inflation-fuelled economic backdrop now exacerbated by the war in Ukraine.

For plan sponsors, and their employer clients seeking to attract and retain workers, in part, by offering best-in-class

Foreword

In a quest to help make prescription medications more accessible and affordable for Canadians, Express Scripts Canada is committed to working with private payors and delivering innovative solutions, new ideas and approaches, for everyone's benefit.

drug benefits programs, the question of drug-plan sustainability looms large.

At Express Scripts Canada (ESC) we believe managed drug plans that balance comprehensiveness and affordability are key to the solution. For example, tools like managed care formularies, PLAs and step therapy – an approach that covers expensive drugs only after proven, lower-cost drugs have failed – can help plan sponsors ensure their members have equitable access to medication provided through plans that also promise long-term sustainability.

For managed plans to work, however, they need three key elements: 1) drug choices aligned with clinical guidelines, 2) engaged patients who make better choices and 3) an ability to serve the needs of patients with complex health issues.

ESC's Dynamic Therapeutic Formulary (DTF), for example, covers certain drugs at a different reimbursement level than others, encouraging doctors and patients to choose clinically effective drugs that are also affordable.

While DTF and other programs provide financial incentives, other options focus on convenience and clinical support.

ESC Pharmacy patients enjoy 24/7 access to an online pharmacy that can analyze their prescription history and, where needed, recommend options to co-ordinate treatments that improve health outcomes and save money. Our Pharmacy can also identify plan members who would benefit from more reimbursement options and, in some cases, direct patients to find alternative funding sources for their treatment.

Without question, today's pharmacy benefit management landscape is complex and evolving.

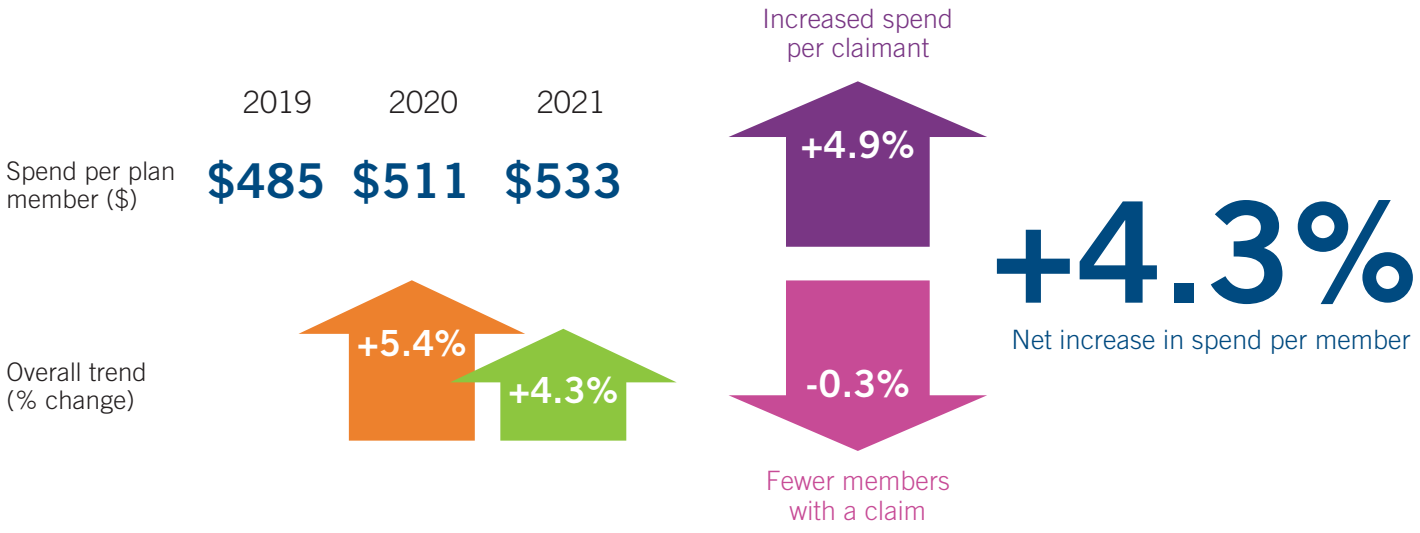
In a quest to help make prescription medications more accessible and affordable for Canadians, Express Scripts Canada is committed to working with private payors and delivering innovative solutions, new ideas and approaches, for everyone's benefit.

Dr. Dorian Lo
President

Drug Trend and Utilization

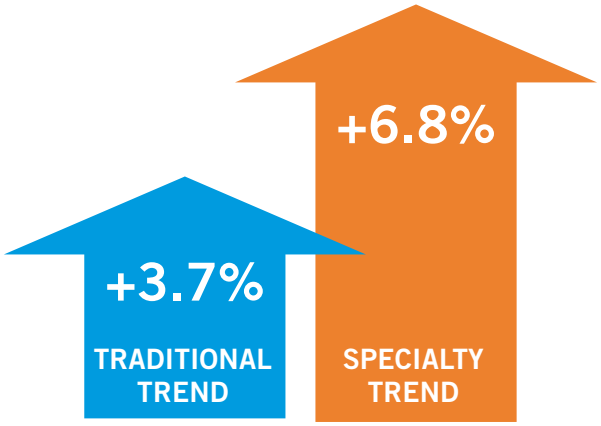
Overall Drug Trend

Overall private drug plan spend per member increased by 4.3%, with fewer plan members making claims, but with a higher amount per claimant. Specifically, the percentage of plan members who made a claim decreased 0.3% in 2021; however, spend per claimant increased 4.9%.



Traditional vs. Specialty Drug Trend

2021	Estimated annual spend per claimant	% Spend	% Claims	2021 Trend
Traditional Drugs	< $10,000	71%	99.1%	+3.7%
Specialty Drugs	≥ $10,000	29%	0.9%	+6.8%



Traditional Drug Trend

The year-over-year spend per plan member for traditional drugs increased by 3.7% in 2021, driven primarily by the 4.3% increase in spend per claimant. This is due, in part, to an increase in diabetes treatments (+5.6%) and migraine medications (+6.8%). Utilization increased by 1%, driven by 62.3% of all eligible plan members who had at least one claim for a traditional drug.

Top 10 Traditional Drugs (by overall spend)

Rank by overall spend	2020		2021	
	Drugs Chemical name (BRAND)	**Therapeutic class**	**Drugs** Chemical name (BRAND)	**Therapeutic class**
1	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes
2	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	isCGM** (flash glucose monitoring) (FREESTYLE LIBRE®)	Diabetic Supplies
3	Lisdexamfetamine (VYVANSE®)	ADHD	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD
4	Sitagliptin-metformin (JANUMET®)	Diabetes	Lisdexamfetamine (VYVANSE®)	ADHD
5	Rosuvastatin* (CRESTOR®)	High Cholesterol	Empagliflozin (JARDIANCE®)	Diabetes
6	isCGM** (flash glucose monitoring) (FREESTYLE LIBRE®)	Diabetic Supplies	Sitagliptin-metformin (JANUMET®)	Diabetes
7	Blood glucose test strips	Diabetic Supplies	Rosuvastatin* (CRESTOR®)	High Cholesterol
8	Budesonide-formoterol (SYMBICORT®)	Asthma/COPD	Blood glucose test strips	Diabetic Supplies
9	Empagliflozin (JARDIANCE®)	Diabetes	Budesonide-formoterol (SYMBICORT®)	Asthma/COPD
10	Esomeprazole* (NEXIUM®)	Ulcer/Reflux	Esomeprazole* (NEXIUM®)	Ulcer/Reflux

*Generic(s) available

**Intermittently Scanned Continuous Glucose Monitoring

Traditional Drug Trend cont'd

Some notable changes in 2021 drug spend included flash glucose monitoring supplies (now referred to by Diabetes Canada as intermittently scanned continuous glucose monitoring or isCGM), which jumped in spend from 6th to 2nd place. This increased spend may be due to their convenience; however, the cost is five times higher than traditional blood glucose monitoring supplies (see Diabetes section). Empagliflozin (JARDIANCE®) for diabetes moved from 9th to 5th place. This drug was already a popular treatment due to its cardiovascular benefits, in addition to glycemic control, while its new indication for use in patients with heart failure in 2021 expanded the patient population beyond those with diabetes.

Overall spend for migraine treatments increased by 12% due to a 4.8% increase in claimants and a 6.8% increase in spend per claimant. The primary driver is erenumab (AIMOVIG®) – first to market with a new mechanism of action, as a CGRP inhibitor, for migraine prevention. CGRP inhibitors cost approximately $5,000 per claimant per year. However, they prevent migraines, whereas older, lower-cost treatments only treat migraine symptoms.

Specialty Drug Trend

The trend, or year-over-year spend per plan member, for specialty drugs increased by 6.8% in 2021. The primary driver was utilization, with a 0.1% increase in plan members making specialty drug claims. The trend was driven by an 8.3% increase in claimants for treatments of inflammatory conditions and a 4.8% increase in claimants for drugs used to treat multiple sclerosis. This was offset by a 0.7% decrease in spend per claimant for specialty drugs.

Multiple Sclerosis

Overall spend for drugs used to treat multiple sclerosis (MS) increased by 6.2% due to a 4.8% increase in claimants. OCREVUS® (Ocrelizumab) can be used for two types of MS, both relapsing-remitting MS (RRMS) and primary progressive MS (PPMS). It is noted to be the first effective drug for PPMS, the less common form of MS, and offers convenient dosing for RRMS. Maintenance dosing is an infusion every six months, versus older treatments that require weekly to monthly maintenance dosing.

What to watch for in 2022: The approval of generic alternatives for dimethyl fumarate (TECFIDERA®) in fall 2021 may reduce overall spend in this class. A new monthly injectable therapy for RRMS – ofatumumab (KESIMPTA®) – was approved in spring 2021 and eliminates the need for long infusions required with some MS treatments.

Cancer

The number of claimants for cancer treatments grew 5.4% in 2021, but overall spend decreased by 18.7%. The top three cancer drugs by spend – REVLIMID® (lenalidomide), IBRANCE® (palbociclib) and LYNPARZA® (olaparib) – are all oral cancer drugs. Various provincial drug funding mechanisms will result in differing regional impacts to private plans.

What to watch for in 2022: Generic alternatives for lenalidomide (REVLIMID®) were approved in Q4 2021, which could reduce spend in this class.

Skin conditions

The drug spend for skin condition treatments grew 10% in 2021, driven primarily by dupilumab (DUPIXENT®). The approximate annual spend was $15,000 per claimant, and there was a 52% increase in claimants. This could be due to new indications approved in 2021 that include treatment for children as young as six years for atopic dermatitis, severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps. It is currently being investigated for additional indications that could potentially increase the eligible patient population.

Specialty Drug Trend cont'd

Cystic Fibrosis

Cystic Fibrosis is considered a rare disease, and drug spend in this class increased 9.6% in 2021. A new treatment, TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor) was approved in 2021. It has an annual cost of approximately $300,000, which is $30,000 more than the closest comparator. This new triple therapy for patients 12 years and older offers improvement in lung function and received a lot of publicity in 2021 due to patient advocacy and listing on several public plans. The potential impact on private plans will evolve as provincial drug plan funding for these treatments becomes available.

Top 10 Specialty Drugs (by overall spend)

Rank by overall spend	2020		2021	
	Drugs Chemical name (BRAND)	**Therapeutic class**	**Drugs** Chemical name (BRAND)	**Therapeutic class**
1	Adalimumab (HUMIRA®)	Inflammatory Conditions	Adalimumab* (HUMIRA®)	Inflammatory Conditions
2	Infliximab* (REMICADE®)	Inflammatory Conditions	Infliximab* (REMICADE®)	Inflammatory Conditions
3	Ustekinumab (STELARA®)	Inflammatory Conditions	Ustekinumab (STELARA®)	Inflammatory Conditions
4	Etanercept* (ENBREL®)	Inflammatory Conditions	Dupilumab (DUPIXENT®)	Skin Conditions
5	Omalizumab (XOLAIR®)	Asthma/COPD	Omalizumab (XOLAIR®)	Asthma/COPD
6	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease
7	Golimumab (SIMPONI®)	Inflammatory Conditions	Etanercept* (ENBREL®)	Inflammatory Conditions
8	Lenalidomide (REVLIMID®)	Cancer	Golimumab (SIMPONI®)	Inflammatory Conditions
9	Ocrelizumab (OCREVUS®)	Multiple Sclerosis	Ocrelizumab (OCREVUS®)	Multiple Sclerosis
10	Secukinumab (COSENTYX®)	Inflammatory Conditions	Secukinumab (COSENTYX®)	Inflammatory Conditions

*Biosimilar(s) available

Some notable spend ranking shifts in 2021 included dupilumab (DUPIXENT®), which was a new entrant to the top 10 specialty drugs. Etanercept (ENBREL®) fell from 4th place in 2020 to 7th place in 2021, driven by a 3% decrease in claimants and 7% decrease in spend, potentially due to the impact of biosimilars. Lenalidomide (REVLIMID®) dropped out of the top 10 in 2021 but continues to be the highest spend for cancer treatments.

What to watch for in 2022: New efficacious biologic therapies for psoriasis may be approved (see the Drug Pipeline section) and more biosimilars for infliximab (REMICADE®) and adalimumab (HUMIRA®) could be marketed. This would impact the position of the top 10 specialty drugs next year.

Top Therapeutic Classes 2021

The top two 2021 therapeutic classes were the same as in 2020; however, spend on depression medications jumped from 4th to 3rd place. Skin conditions saw a significant increase from 11th to 8th place in 2021 (see Specialty Drug Trend section for further analysis of this class).

Top 10 Therapeutic Classes (by overall spend)

Rank by % of overall spend			Therapeutic class	% of overall spend	Trend	
2021	2020	Change			Spend	Volume of claims
1	1		Inflammatory Conditions	**13.3%**	8.2%	6.4%
2	2		Diabetes	**10.6%**	15.6%	1.5%
3	4	▲ 1	Depression	**5.1%**	7.3%	2.2%
4	3	▼ 1	Asthma/COPD	**5.0%**	-4.0%	-12.9%
5	5		High Blood Pressure	**4.7%**	-3.4%	-4.4%
6	6		Cancer	**3.7%**	-18.7%	-3.6%
7	7		Attention Deficit Disorder	**3.5%**	16.6%	11.4%
8	11	▲ 3	Skin Conditions	**3.2%**	10.1%	1.1%
9	8	▼ 1	Ulcer/Reflux	**3.1%**	1.3%	-0.5%
10	9	▼ 1	Multiple Sclerosis	**3.0%**	6.2%	1.1%

An increase in the number of claimants for several therapeutic classes led to an increased spend in 2021.

Rank by % of 2021 overall spend	Therapeutic class	Increase in # of claimants
1	Inflammatory Conditions	8.3%
2	Diabetes	9.4%
3	Depression	9.1%

Top Therapeutic Classes 2021 cont'd

Top 3 Therapeutic Classes Highlights

#1: Inflammatory conditions

- Spend driven almost entirely by an 8.3% increase in claimants.
- STELARA® (ustekinumab) had a 14% increase in claimants and 16.2% increase in spend.
- SKYRIZI® (risankizumab) was launched in mid-2019 and spend increased by 59% in 2021. Increased use may be due to better clinical results than STELARA® for moderate to severe plaque psoriasis.

#2: Diabetes

- Diabetes maintained 2nd position and spend continued to grow at more than 10% per year. Some of the growth is a result of a 9.4% increase in the number of claimants, which could potentially be due to:

  A) Increasing number of newly diagnosed patients with type 2 diabetes:

  - 1 in 4 Canadians lives with prediabetes or diabetes.
  - There has been a greater than 50% increase in diabetes prevalence over the past 10 years.
  - Six million Canadians have prediabetes, and if left untreated, more than 50% of them will develop type 2 diabetes within 8 to 10 years.

  B) Canadian diabetes treatment guidelines recommend that additional therapies be added to existing treatments as the condition progresses.[1]

  C) A possible clearing of the healthcare backlog to pre-pandemic levels, with more patients seeking medical care and filling prescriptions for diabetes medications (see COVID-19 Backlog section).

- Another cost driver was a 70% increase in semaglutide claimants. The annual cost was $1,400 per claimant and accounted for 24% of diabetes spend in 2021 versus 16% in 2020.

#3: Depression

- Drug spend for depression continued to grow, with a jump from 4th spot in 2020 to 3rd spot in 2021.
- The primary driver was a 9.1% increase in claimants in 2021.

[1] Diabetes Canada Clinical Practice Guidelines Expert Committee. *Diabetes Canada* 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 2018; 42(Suppl 1):S1-S325.

Diabetes

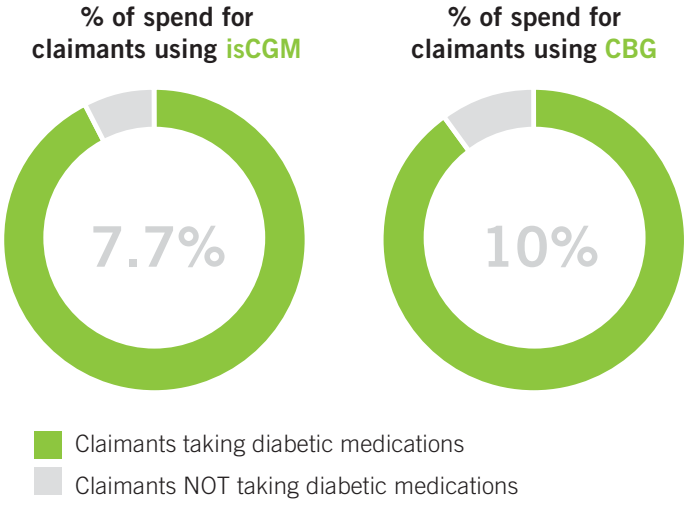
Flash glucose monitoring

Costs driven almost entirely by an 8.3% increase in flash glucose monitoring supplies, now known as intermittently scanned continuous glucose monitoring (isCGM), allow for frequent monitoring of glucose levels without finger pricks and test strips (capillary blood glucose testing or CBG testing). These are advantageous to those on intensive insulin regimens who require multiple daily tests and need to adjust insulin or food intake based on the results.

Updated Diabetes Canada guidelines[2] recommend isCGM as an alternative option for adult patients with type 2 diabetes using insulin therapy to reduce the frequency and duration of hypoglycemia. This is also recommended as a glucose monitoring alternative for patients with type 1 diabetes.

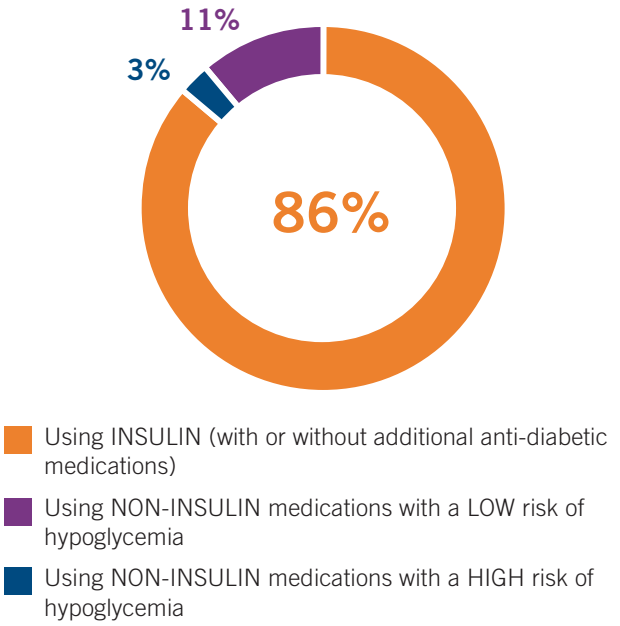
Claimants who do not take any diabetes medications accounted for 7.7% of total isCGM spend. These individuals may have been diagnosed with prediabetes and recommended to monitor their glucose levels. Prior to the availability of isCGM, these individuals would have used CBG testing. Comparatively, claimants who do not take any other diabetes medications accounted for 10.0% of the total spend on diabetes test strips for CBG testing.

Glucose Monitoring Claimants and use of Diabetic Medications



Analysis of diabetes drug spend for claimants using flash glucose monitors indicated that 11% of the spend is from those who took non-insulin diabetes therapies with a low risk of hypoglycemia, and 3% comes from claimants who took medications with a high risk of hypoglycemia.

Percentage of isCGM spend based on concurrent diabetes medication usage



Because the average annual cost of isCGM supplies was five times greater than test strips for traditional CBG testing, there may be an opportunity for plan savings by implementing criteria to ensure that these supplies are being used as per current guidelines.

Increased spend on GLP-1 agonists

Newer diabetes medications, glucagon-like peptide-1 (GLP-1) agonists such as semaglutide (OZEMPIC®) and liraglutide (VICTOZA®), have gained popularity. This is due to convenient dosing schedules (e.g., once weekly), positive impact on weight and improved cardiovascular outcomes in addition to glycemic control. In 2021, GLP-1 agonists made up 41% of the diabetes medication spend.

[2] Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 2018; 42(Suppl 1):S1-S325.

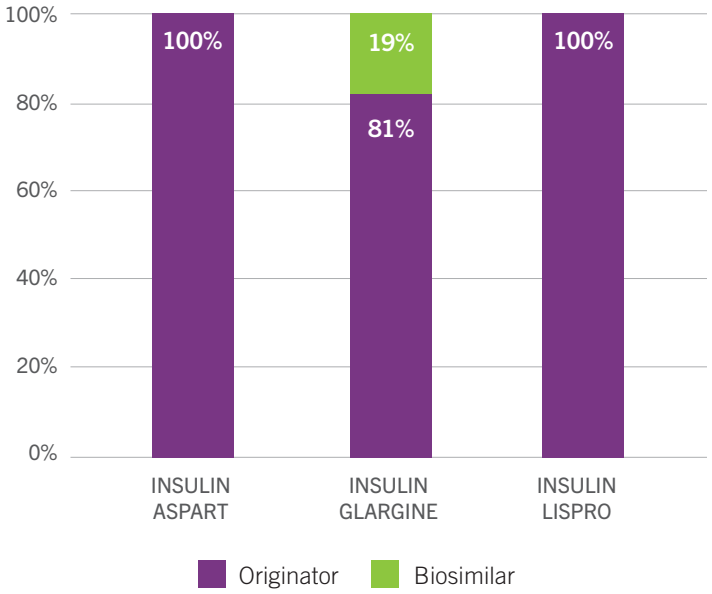
Diabetes cont'd

Insulin biosimilar penetration remains low

The use of originator biologics for insulin products remained high despite the availability of biosimilars. The biosimilar for insulin glargine has been available in Canada since 2015 and has been targeted by multiple provincial biosimilar programs; its biosimilar penetration increased from 15% of spend in 2020 to 19% in 2021. The biosimilar usage of insulin lispro was much lower because the first biosimilar was only recently marketed in Canada.

What to watch for in 2022: The use of insulin lispro and insulin aspart biosimilars may increase in 2022 due to being targeted by biosimilar switching programs in Quebec, New Brunswick, British Columbia and Alberta. Although these biosimilars had previously received Health Canada approval, they were only recently launched in Canada.

National insulin biosimilar penetration



Obesity

Anti-obesity drugs are not typically covered by private plans; if covered, there may be limits attached.

About obesity: Many organizations, including Obesity Canada, the Canadian and American medical associations and the World Health Organization, consider obesity to be a chronic disease. In 2018, Statistics Canada estimated that 26.8% of Canadians were living with obesity and an additional 36.3% were classified as overweight.[3]

Obesity increases the risk of serious chronic illnesses such as heart disease, cancer, stroke, type 2 diabetes, and non-alcoholic fatty liver disease (NASH), among others.

Anti-obesity drugs in Canada: There are only a few anti-obesity drugs available in Canada. These include liraglutide (SAXENDA®), an injectable drug also available in a lower dose for the treatment of type 2 diabetes under the tradename VICTOZA®, naltrexone-bupropion (CONTRAVE®) and orlistat (XENICAL®).

All are recommended as an adjunct to a reduced-calorie diet and increased physical activity for weight management. Newer drugs may be more effective and have a positive impact on other related conditions.

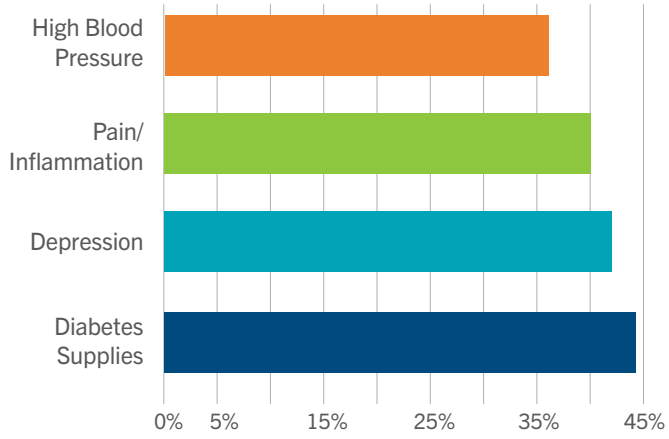
What to watch for in 2022: Semaglutide (WEGOVY®) was approved by Health Canada in 2021 and is expected to be available in 2022. This injectable drug is available in a lower dose for the treatment of type 2 diabetes under the tradename OZEMPIC®, which was the #1 traditional drug in terms of spend in 2020 and 2021 (see Traditional Drug Trend section).

[3] Statistics Canada (2018). *Overweight and obese adults.*

Obesity cont'd

In 2021, the spend for anti-obesity drugs increased by 23% due to a 22% increase in claimants, which is much greater than the 2% increase in spend in 2020. Obesity is a known risk factor for type 2 diabetes and high blood pressure and has a high correlation with pain/inflammation and depression.

Percentage of anti-obesity drug claimants who also had claims for drugs to treat:



Given the prevalence of obesity, we would expect claims data to be more equally split between genders. However, 80% of 2021 claimants for anti-obesity drugs were female.

50%

of Canadians living with obesity are female[4]

80%

of claimants reimbursed for anti-obesity drugs were female

26.8% of adult Canadians[4] reported height and weight that might classify them as living with obesity, which suggests that the size of this population exceeds the small proportion who are claiming anti-obesity medications. Although drug therapy is not the only solution for weight reduction, coverage for these drugs seems to be limited.

The small proportion of claimants may be due to a variety of factors, such as the small number of plans that provide coverage for anti-obesity medications, the shortage of health professionals who specialize in obesity care and the potential stigma with seeking anti-obesity treatment.

26.8%

of Canadians live with obesity

<1%

of claimants were reimbursed for an anti-obesity drug

[4] Statistics Canada (2018). *Overweight and obese adults.*

Pharmacy Landscape

Legislative Updates

Rare Disease National Strategy

Federal government committed up to $1 billion for drugs for rare diseases

The 2019 federal budget committed to help Canadians with rare diseases access the drugs they need, with funding of up to $1 billion over two years, starting in 2022-2023, and up to $500 million per year thereafter. The federal government is working with provinces and stakeholders to establish the national strategy, and the proposed program is expected to be announced in 2022.

What to watch: Although drugs for rare disease generally have high annual costs, they can be life-altering for patients. The impact on medication access and private plan costs will be dependent on the program scope.

Patented Medicine Prices Review Board (PMPRB) changes

Proposed PMPRB changes further delayed until July 1, 2022

Amendments to PMPRB regulations initially published in 2019 were intended to lower the price of patented medications in Canada. After legal challenges and a series of delays, the changes that were to come into effect on January 1, 2022, have been further delayed to July 2022, and some proposed changes have been dropped.

What to watch: The proposed changes may lower plan costs due to lower drug prices. Ongoing stakeholder engagement will ultimately shape the timeline and implementation of these changes.

Legislative Updates cont'd

Pan-Canadian Prescription Drug List

The Canadian Advisory Council on the Implementation of National Pharmacare 2019 report included recommendations to develop a "pan-Canadian formulary to include a broad range of safe, effective, evidence-based drugs and related products that meet the health care needs of Canada's diverse population."

The Canadian Agency for Drugs and Technologies in Health (CADTH) was engaged by Health Canada to develop processes and highlight best practices for formulary management. CADTH invited stakeholders to provide input on a proposed framework, which will be incorporated into final recommendations to Health Canada.

What to watch: The pan-Canadian formulary may be considered a preliminary step toward the development of a national pharmacare program. It is too early to assess the potential impact on private plans.

COVID-19

COVID-19 vaccinations for children as young as five years old were approved by Health Canada in November 2021. An oral treatment for COVID-19 was approved by Health Canada in January 2022. When started within a specific interval after the onset of symptoms, this new drug may reduce the risk of hospitalization and death.

What to watch: Because COVID-19 vaccinations and treatments are currently government funded, there is likely little impact to private drug plans.

Pharmacists' Scope of Practice

Some provinces expanded the scope of practice for pharmacists in 2021. In part, this was to reduce the burden to primary care and emergency healthcare services. Some provinces provided public funding for certain services, with the remaining services optional for private plans to reimburse. In Quebec, certain services are publicly funded, and others must be reimbursed by private plans in accordance with the *Régie de l'assurance maladie du Québec (RAMQ)*.

What to watch: Although these services could lead to increased plan costs, better access to medications could lead to improved productivity due to avoidance of treatment delays or missed work to attend physician appointments.

Legislative Updates cont'd

Provincial Biosimilar Policies

Several lower-cost biosimilar drugs have come to market in recent years for high-cost biologics. Several provinces implemented biosimilar policies in 2021, and the impact on private plans varies depending on the type of province and program, as well as plan design.

Pharmacare provinces are different

In pharmacare provinces (Manitoba, Saskatchewan and British Columbia), government drug coverage is available for all patients who reach an income-tested deductible, even those with private plans.

Opportunities exist to synchronize biosimilar policies with provincial programs.

Summary of provincial biosimilar policies

Targeted molecule	British Columbia	Alberta	Quebec	New Brunswick	Northwest Territories
Infliximab	Completed 2020	January 15, 2021	April 13, 2022	November 30, 2021	June 22, 2022
Rituximab	February 19, 2021	January 15, 2021 March 1, 2021*	April 13, 2022	November 30, 2021	June 22, 2022
Adalimumab	October 6, 2021	May 1, 2021	April 13, 2022	November 30, 2021	June 22, 2022
Etanercept	November 25, 2019* October 6, 2021*	January 15, 2021 May 1, 2021*	April 13, 2022	November 30, 2021	June 22, 2022
Insulin lispro	May 29, 2022	April 1, 2022	April 13, 2022	November 30, 2021	June 22, 2022
Insulin aspart	May 29, 2022	April 1, 2022	July 6, 2022	May 31, 2022	June 22, 2022
Insulin glargine	Completed 2019	January 15, 2021	April 13, 2022	November 30, 2021	June 22, 2022
Glatiramer Acetate	Completed 2019	January 15, 2021	April 13, 2022	November 30, 2021	June 22, 2022
Teriparatide	Not on formulary	Not on formulary	April 13, 2022	Not on formulary	Not on formulary

*A single reference biologic may have multiple transition periods because the policy is based on health indications.

Legislative Updates cont'd

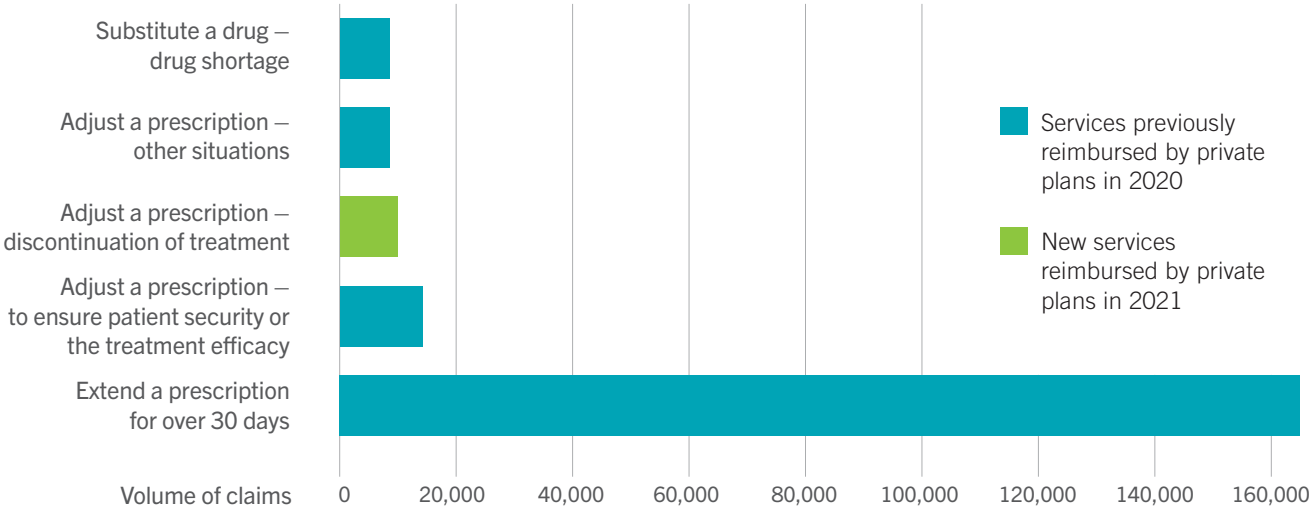
Quebec Pharmacist Clinical Services

Quebec expanded the scope of practice for pharmacists in 2021, and because of the unique nature of RAMQ requirements for private drug plans they must reimburse 100% of the cost of certain clinical services.

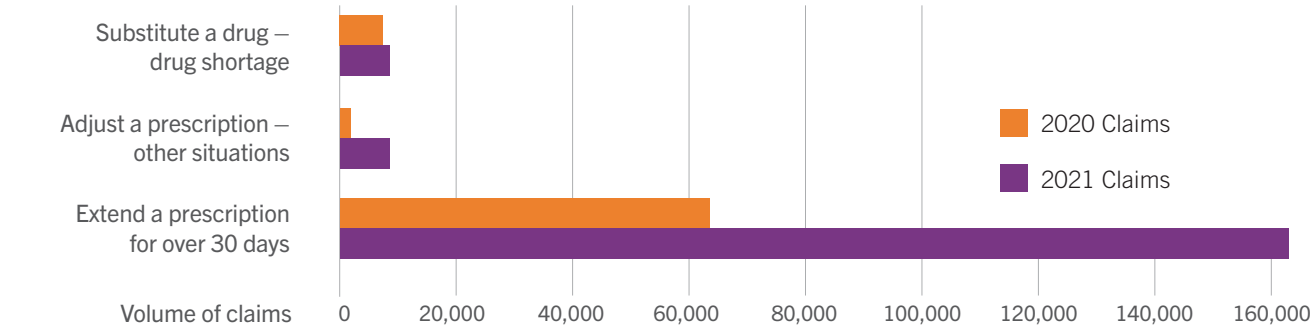
Additionally, effective January 2021, some clinical services previously paid by private plans are now provincially funded. Prior to this funding shift, two of the clinical services (prescribing when a diagnosis is not required and for minor conditions) were the 2nd and 3rd ranked reimbursed clinical services by claims volume in private plans in 2020. This change resulted in the costs for these services being shifted to the provincial budget.

Prescription extensions grew in 2021 and continued to be the most widely used clinical service for private plans in Quebec, followed by adjusting prescriptions.

Top 5 Quebec pharmacist clinical services reimbursed by private drug plans in 2021



Top 3 Quebec pharmacist clinical services reimbursed by private drug plans – 2020 vs. 2021



COVID-19 Backlog

Due to the COVID-19 pandemic, there was a backlog of Canadians who, for a variety of reasons, may not have received necessary diagnoses or treatments. Prior to the pandemic, there were many who were already unaware they had a chronic condition and remained undiagnosed.[5][6][7]

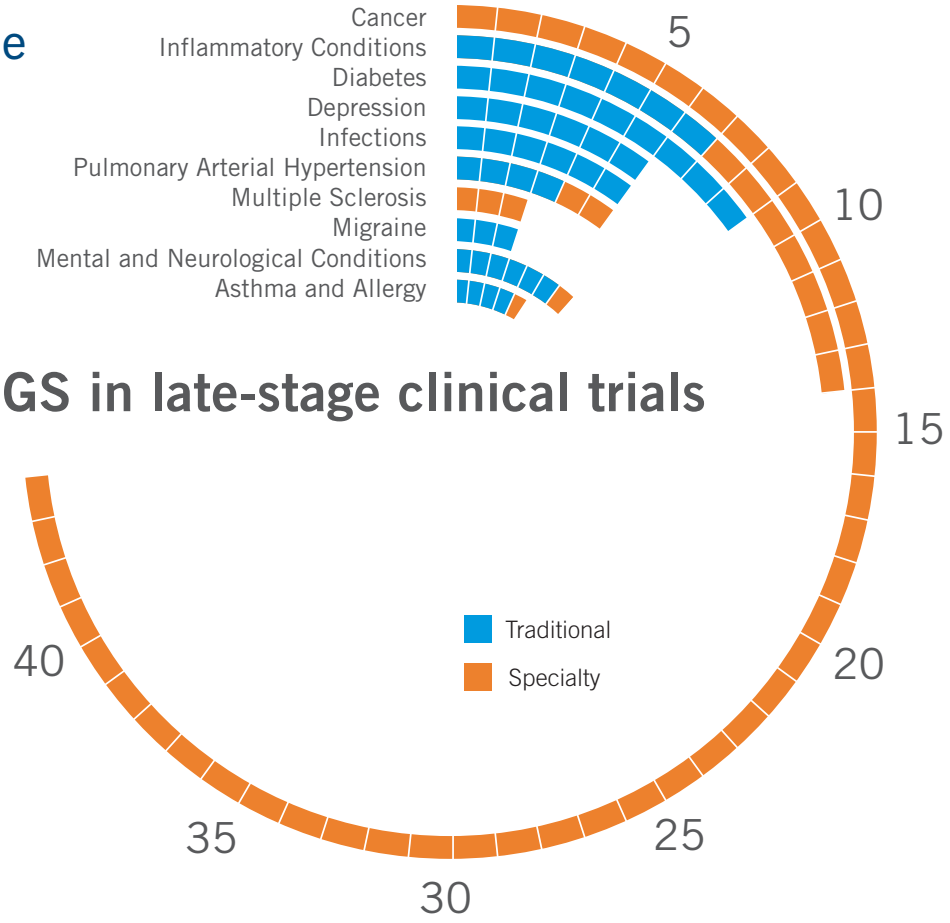
Due to the pandemic, and its significant burden on Canada's healthcare system, the backlog was further amplified by healthcare resources being redirected to urgent pandemic patient needs. Analysis of Express Scripts Canada drug claims data suggested a reduction in the backlog for some chronic conditions due to a gradual increase in access to healthcare services in 2021.

The backlog estimates are based on drug claims data. This would not factor in instances where members are receiving non-drug-therapy treatments. For example, members may be treating their diabetes with diet and exercise, or depression with counselling.

Therapeutic class	Estimated backlog	Details
Diabetes	Returned to pre-pandemic levels	In 2021, the estimated backlog returned to pre-pandemic levels. A 9.4% increase in claimants suggests more members are seeking treatments.
Cancer	Approximately 10,000 Canadians	In 2021, the estimated backlog decreased to approximately 10,000 Canadians due to a 5.4% increase in claimants.
Depression	Approximately 50,000 Canadians	Although there was an increase of 9.1% in claimants in 2021, and a 50% reduction in backlog, approximately 50,000 Canadians have not yet started drug treatment for depression.

[5] Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 2018;42(Suppl 1):S1-S325.
[6] Statistics Canada (2021). Blood pressure of adults, 2016-2019.
[7] Statistics Canada (2021). Cholesterol levels of adults, 2016-2019.

Drug Pipeline



NEW DRUGS in late-stage clinical trials

Biosimilars: The first biosimilar for the ophthalmic drug LUCENTIS® (ranibizumab) may be approved in 2022. The impact of this biosimilar could be significant because it may reduce the annual treatment cost, which currently ranges from $10,000 to $19,000. In addition, a second biosimilar for insulin glargine (LANTUS®) is also under review.

Dementia: Aducanumab (ADUHELM®) was approved amid controversy in July 2021 by the U.S. Food and Drug Administration (FDA) for mild cognitive impairment and mild dementia. The approval was marred by outstanding questions on the true degree of benefit and the pathway to approval in Canada remains uncertain.

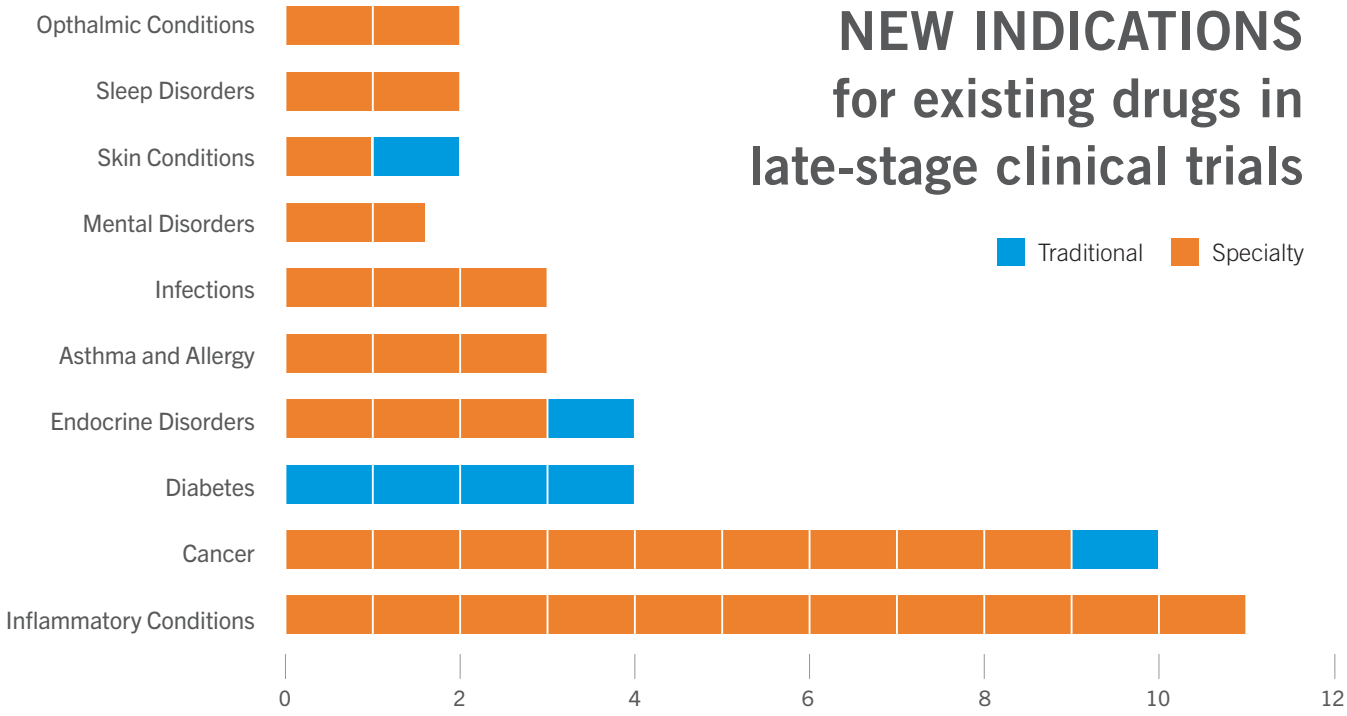
Diabetes: New treatment options – such as tirzepatide – could change how diabetes is treated. This drug offers a dual-action synergistic effect, resulting in greater improvement in blood glucose levels and a reduction of body weight.

Inflammatory conditions: Bimekizumab (BIMZELX®) is a biologic immunosuppressant that significantly outperforms the top biologics used to treat plaque psoriasis and potentially psoriatic arthritis. Deucravacitinib is an oral therapy under review for the treatment of moderate to severe plaque psoriasis and is more effective and better tolerated than current treatments. It is also under investigation for related conditions such psoriatic arthritis, lupus and inflammatory bowel disease.

Asthma: Tezepelumab is a first-in-class monoclonal antibody for the treatment of severe, uncontrolled asthma. Current biologic asthma treatments are approved for severe eosinophilic or allergic phenotype asthma. However, this treatment has demonstrated efficacy beyond these subtypes, offering a new treatment option for patients uncontrolled with traditional inhalers.

Women's health: Linzagolix is a potential first oral treatment of uterine fibroids, which may help with adherence and adoption versus current injectable treatments.

Drug Pipeline cont'd



Non-alcoholic steatohepatitis (NASH): OCALIVA® (obeticholic acid) may finally be approved in 2022 by the FDA for the additional indication for the treatment of NASH. There are currently no drugs approved for this condition; however, several are in the pipeline. This approval could lead to higher plan costs, as NASH currently affects 3% to 5% of Canadians.

Asthma and allergy: DUPIXENT® (dupilumab) is being investigated for additional indications that could potentially increase the eligible patient population. The new indications are spontaneous urticaria and prurigo nodularis (chronic inflammatory skin diseases). DUPIXENT® is already approved for atopic dermatitis, asthma and nasal polyps, and entered the Top 10 Specialty Drug list in 2021.

HIV: Cabotegravir, an injectable antiviral, was approved by the FDA in 2021 for the additional indication of pre-exposure prophylaxis (PrEP). The current treatments are once daily oral medications, and this new injectable lasts for three months, which may improve patient adherence and the efficacy of PrEP treatment.

Biosimilars

Several provinces implemented biosimilar policies in 2021, and the impact on private plans varies depending on the type of province and program, as well as plan design.

Private plans may experience a spillover effect from the provincial biosimilar policies. If physicians are required to prescribe or switch to biosimilars for patients to be reimbursed by the provincial drug plan, they may also follow suit with patients reimbursed by private drug plans, even if no private biosimilar policy exists.

Biosimilar quick reference chart

Chemical name	Corresponding originator(s)	Short-term or maintenance
Adalimumab	HUMIRA®	Maintenance
Bevacizumab	AVASTIN®	Short term
Etanercept	ENBREL®	Maintenance
Filgrastim	NEUPOGEN®	Short term
Glatiramer acetate	COPAXONE®	Maintenance
Infliximab	REMICADE®	Maintenance
Insulin aspart	NOVORAPID®	Maintenance
Insulin glargine	LANTUS®	Maintenance
Insulin lispro	HUMALOG®	Maintenance
Pegfilgrastim	NEULASTA®	Short term
Rituximab	RITUXAN®	Maintenance
Somatropin	HUMATROPE®, GENOTROPIN®, NORDITROPIN®, SAIZEN®	Maintenance
Teriparatide	FORTEO®	Maintenance
Trastuzumab	HERCEPTIN®	Short term

Maintenance drugs Short-term drugs

Impact of provincial biosimilar switching policies on private plans

Provincial drug plans have pioneered biosimilar switching programs since 2019. However, private plans have not implemented switching policies on a large scale except in British Columbia.

Manitoba, Saskatchewan and British Columbia are considered pharmacare provinces where government drug coverage is available for all patients who reach an income-tested deductible, including those with private plans. Because of the availability of publicly funded coverage, private payors develop protocols to integrate the programs to reduce overall spend by sharing costs, where possible, with the public plan. BC is the only pharmacare province that has implemented a biosimilar transition program and the spillover effect resulted in a higher proportion of biosimilar claims on private plans. Since 2019, many Canadian private payors have aligned their biosimilar transition policies accordingly for plan members in BC.

There has been less spillover effect of provincial biosimilar switching policies on biosimilar claims for private plans in non-pharmacare provinces.

Impact of short-term versus maintenance drugs

Short-term use drugs have generated a much higher biosimilar uptake, due to the greater influx of new patients and payors' biosimilar-first policies.

Maintenance or long-term use drugs have had lower biosimilar penetration. Although recent new patients for maintenance drugs may have been started on biosimilars due to the biosimilar-first policy, overall there are fewer new claimants. Existing claimants make up the bulk of the originator claims for maintenance treatments, and increased biosimilar penetration may be possible if they are switched to biosimilars.

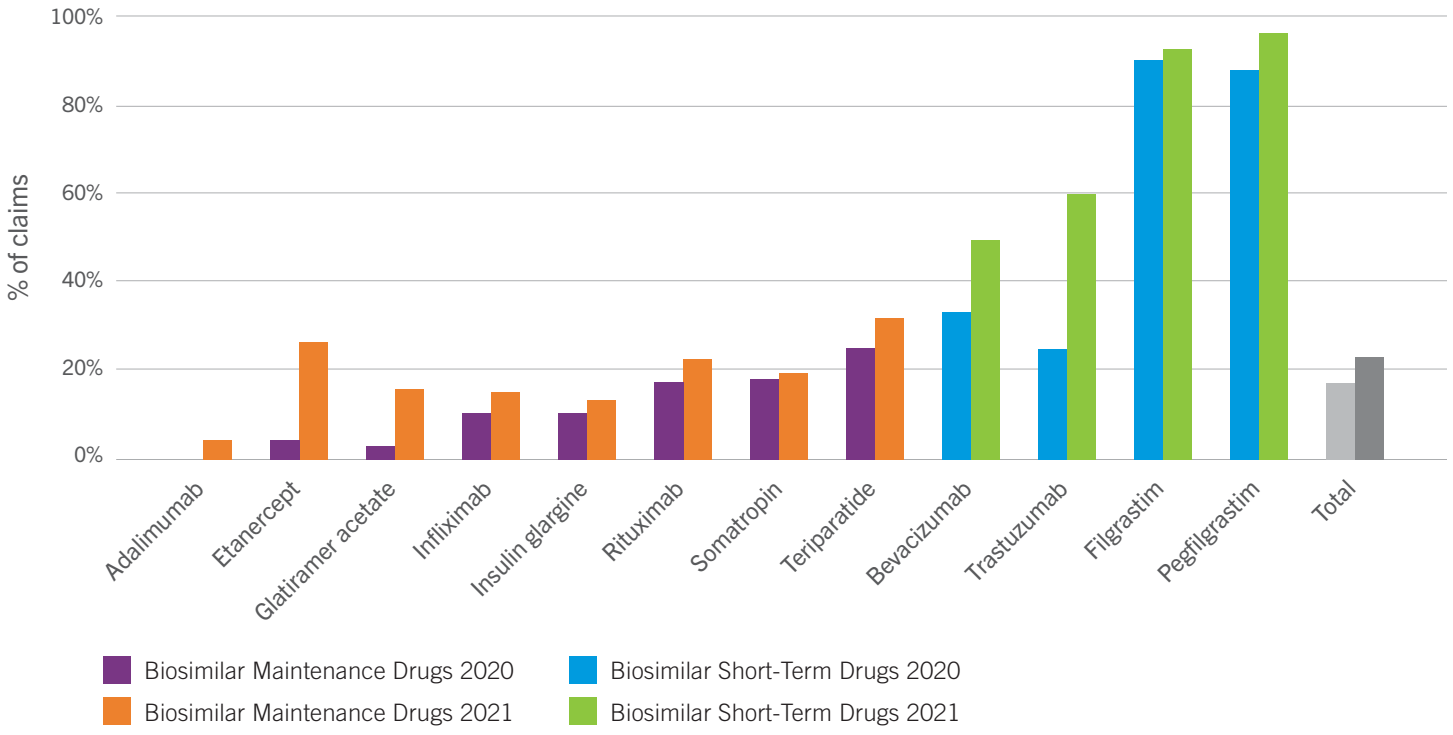
Biosimilars cont'd

2022 Provincial Biosimilar Policies (Q1)

Biosimilar First:
To be reimbursed by the provincial drug plan; naïve patients must use a biosimilar

Biosimilar First and Biosimilar Transitioning or Switching:
To be reimbursed by the provincial drug plan, patients on originator biologics must switch to a biosimilar

National biosimilar penetration rate – % of claims in 2020 and 2021



Biosimilars cont'd

British Columbia

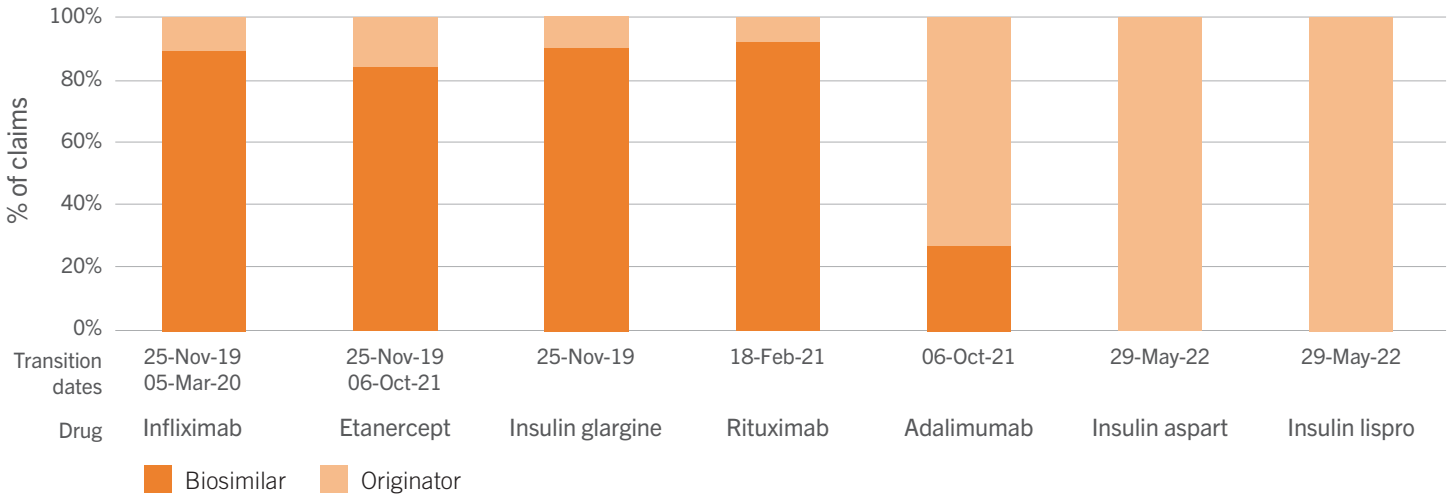
BC Pharmacare was the first public plan to implement biosimilar transitioning. Some biosimilar transitions for a single originator occurred in two phases with different transition periods for the drug's different indications.

Adalimumab (HUMIRA®) was the top drug based on spend for Express Scripts Canada in 2020 and 2021, and the second-highest-cost drug for BC Pharmacare in 2019/2020. The BC six-month transition period for this drug was April 7 to October 6, 2021, and private biosimilar claim uptake grew as expected during the transition period.

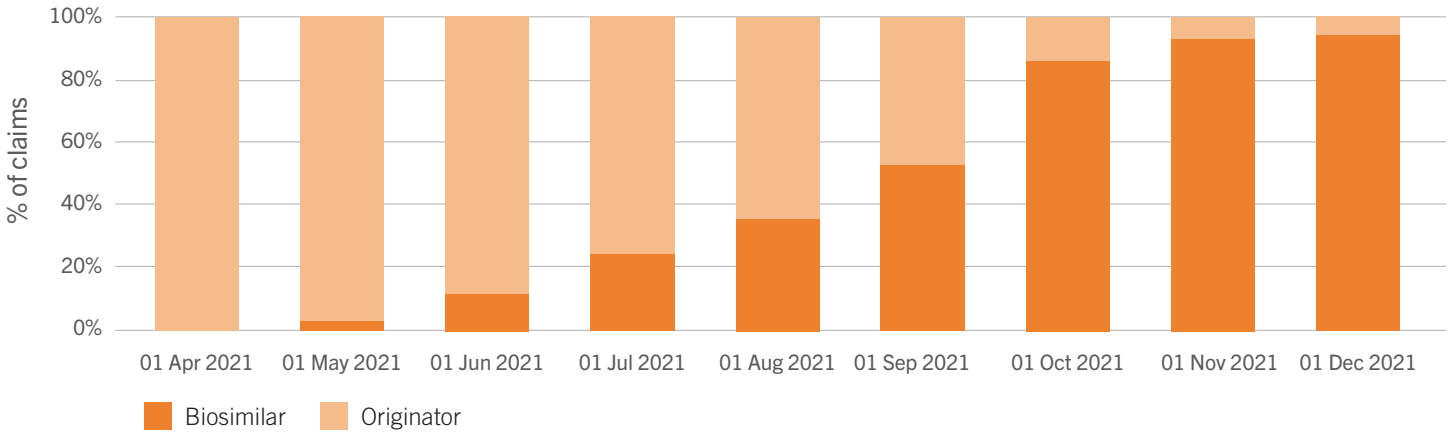
What to watch for in 2022:

BC Pharmacare biosimilar transition programs for insulin aspart and insulin lispro were announced in December 2021 with the transition period ending on May 29, 2022. There have been few private biosimilar claims to date; however, the impact will likely grow as the deadline nears.

British Columbia biosimilar claims penetration in 2021



British Columbia biosimilar adalimumab claims penetration in 2021



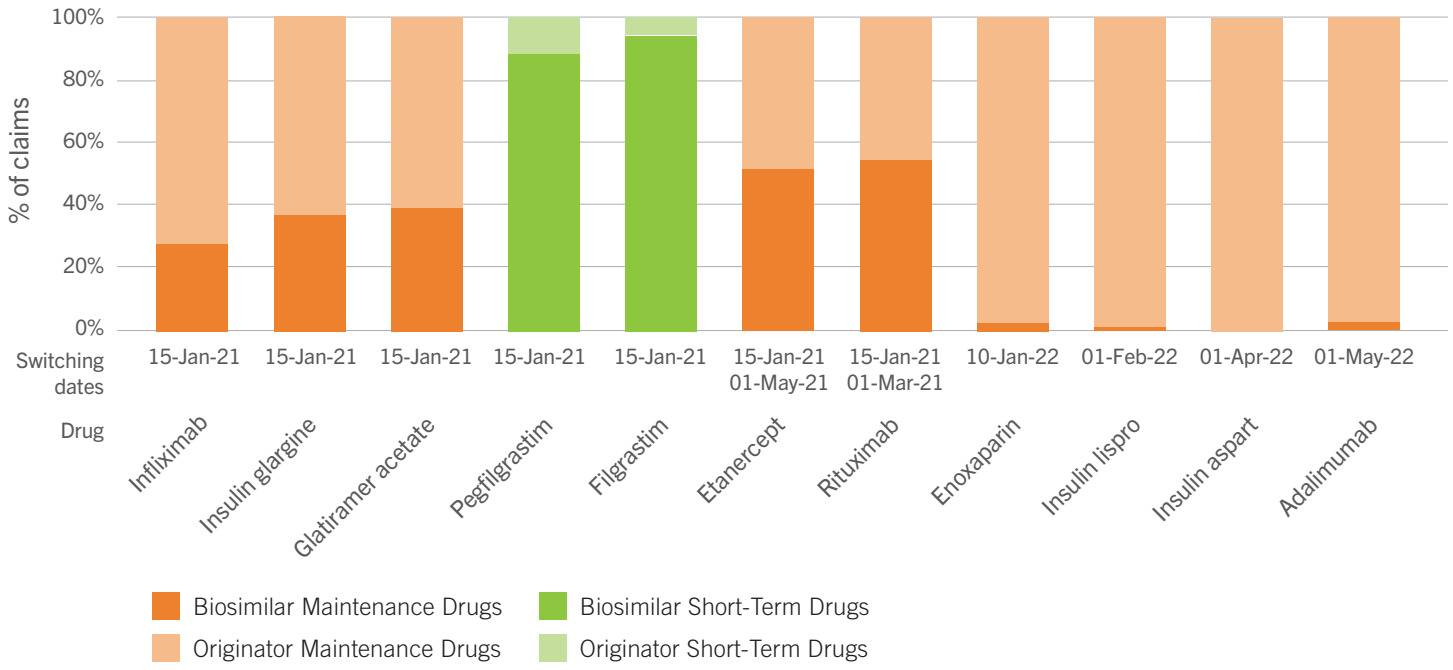
Biosimilars cont'd

Alberta

Provincial biosimilar switching policies in non-pharmacare provinces, such as Alberta, have less spillover effect on private drug plan claims. In Alberta, private plan short-term drug claims had a higher biosimilar uptake, probably due to the greater influx of new patients and the spillover effect of the provincial biosimilar-first policy.

What to watch for in 2022: Alberta's biosimilar switch program transition period for adalimumab (HUMIRA®) ends in 2022, so the impact of the provincial policy on private drug plan claims will likely be realized in 2022. Adalimumab (HUMIRA®) was the top drug based on overall spend in 2020 and 2021, so the provincial policy may increase biosimilar uptake for private drug plans.

Alberta biosimilar claims penetration in 2021



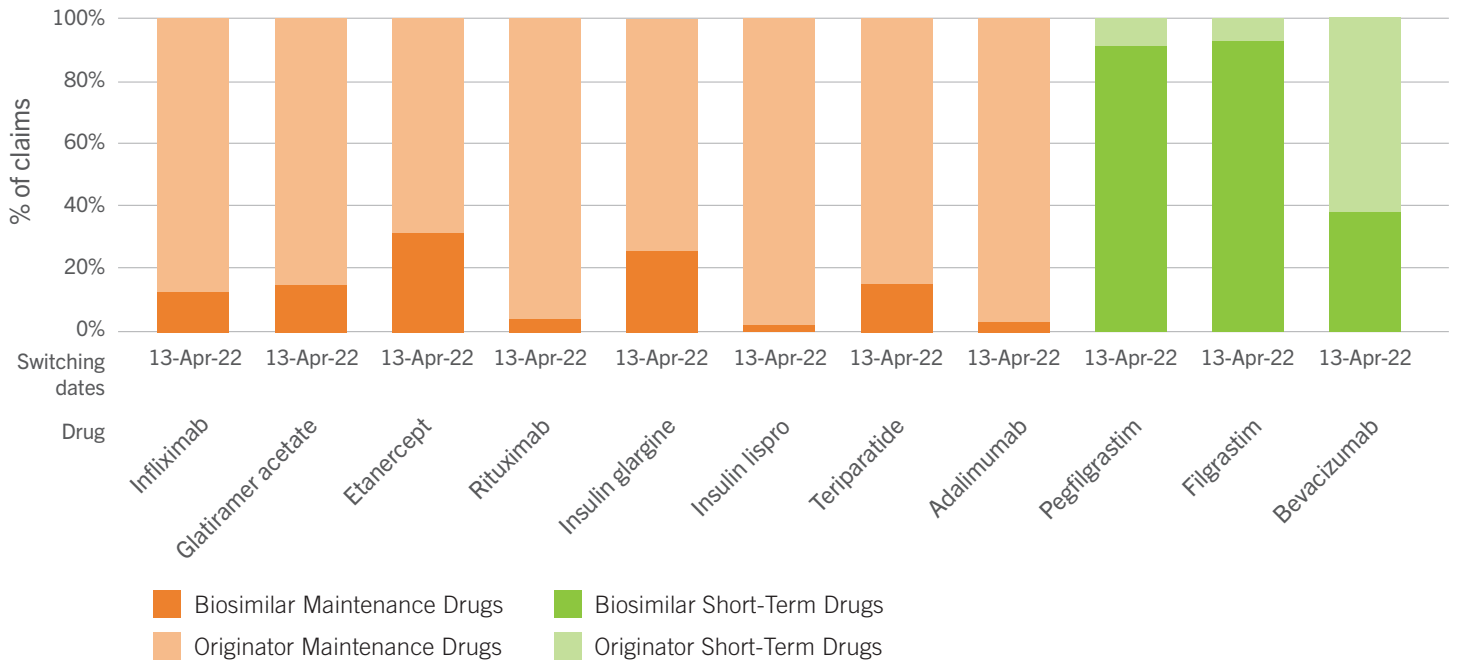
Biosimilars cont'd

Quebec

Quebec's biosimilar initiative was announced in 2021 with a transition deadline of April 13, 2022. Insulin aspart was added later with a July 2022 transition deadline. Quebec private biosimilar claims paralleled Alberta with short-term drugs showing a higher biosimilar uptake.

What to watch for in 2022: There is a potential for impact on private claims if payors choose to implement similar biosimilar switching policies or physicians' biosimilar prescribing behaviour extends to patients. Private payor biosimilar claims for these drugs will likely grow as the provincial transition deadline nears.

Quebec – Biosimilar claims penetration in 2021



Biosimilars cont'd

Impact of provincial switch programs on private claims:

Province with a biosimilar switch program:

- BC, a pharmacare province, had the highest private drug plan biosimilar penetration rate
- Non-pharmacare provinces (AB, NB, QC)
  - Private plans in Alberta had the highest biosimilar penetration rate among the non-pharmacare provinces because the province launched their biosimilar switch policy first.
  - New Brunswick's transition period ended in November 2021, so the private drug plan biosimilar penetration has grown.
  - Quebec's provincial biosimilar program was only announced in 2021, with an April 2022 transition period end date, so the impact on private drug plan claims remains to be realized.

Provinces without a biosimilar switch program:

- Ontario has an approximately 15% biosimilar penetration rate.

If the Ontario government were to implement a biosimilar switch program, we would expect the impact on private claims to be closer to that of Alberta versus British Columbia.

Province	Pharmacare province	Existing provincial biosimilar switch program	Observations
BC	✔	✔	Private payors followed biosimilar switch deadlines
AB	✖	✔	Non-pharmacare; spillover may occur
NB	✖	✔	Non-pharmacare; spillover may occur
QC	✖	✔	RAMQ to delist originator biologics. Private payors may similarly de-list and spillover effect may occur
ON	✖	✖	No public biosimilar switching policy currently in effect

Biosimilar penetration as percentage of claims in 2021

Chemical Name	BC	AB	NB	QC	ON
Adalimumab	27%	3%	1%	3%	3%
Bevacizumab	50%	0%	0%	38%	55%
Etanercept	84%	51%	18%	32%	26%
Filgrastim	93%	94%	95%	92%	90%
Glatiramer acetate	35%	39%	0%	15%	12%
Infliximab	89%	27%	6%	12%	9%
Insulin glargine	90%	37%	29%	26%	7%
Pegfilgrastim	89%	88%	89%	91%	98%
Rituximab	92%	55%	0%	4%	26%
Somatropin	44%	18%	11%	27%	11%
Teriparatide	6%	7%	Insufficient Claims	16%	18%
Trastuzumab	Insufficient Claims	Insufficient Claims	Insufficient Claims	Insufficient Claims	63%
Total	71%	30%	14%	21%	15%

Biosimilars cont'd

Although biosimilars for adalimumab (HUMIRA®) were approved by Health Canada in 2018, most were not available in Canada until 2021, and the biosimilar transition period ends in 2022 for many provincial biosimilar switch programs. Adalimumab (HUMIRA®) was the top drug based on overall spend for private plans in 2020 and 2021, and provincial biosimilar switching programs may generate savings.

Plan Adoption

The question of drug plan sustainability continues to be a major preoccupation for the industry. Cost containment plan design strategies have increased over the past several years. However, there is room for the industry to improve adoption rates. Here is a glimpse into the adoption of a few options that plan sponsors may want to consider.

Generic Substitution: Generic substitution helps manage plan costs by reimbursing the cost of a drug up to the price of the lowest-priced alternative medication. When a drug has an interchangeable generic and generic substitution applies, the ingredient cost is reduced to the lower-cost alternative (generic) drug. The national adoption rate for this program is 84%, with Alberta, New Brunswick, Nova Scotia and PEI coming in at over 90%.

Co-insurance: On average, seven out of 10 claims are subject to a co-insurance – with the majority of co-insurance set at 80%. Co-insurance is defined as the percentage of eligible expenses above the deductible that is eligible for reimbursement under the plan. Co-insurance requires the employee to pay a percentage of the expense, and motivates the plan members to be more active stakeholders in their healthcare decisions. Unlike deductibles, co-insurance keeps pace with inflation and should help discourage excessive utilization.

Dispensing Fee Caps: Approximately 33% of our drug claims are subjected to a dispensing fee cap. The highest prevalence of dispense fee caps is in Ontario, with just shy of 50% of our plans being affected. Dispensing fee caps help control costs, keep premiums manageable and encourage members to become more active stakeholders in their healthcare decisions to reduce their out-of-pocket expenses.

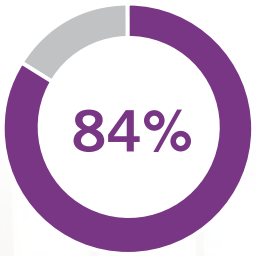
Plan Adoption cont'd

Annual Plan Maximums: 14% of our drug claims are subject to annual maximums and 72% of claims have a limit of less than $10,000. Annual maximums are placed to limit the plan sponsor's liability, and potentially shift the expense to government-funded plans, if they are available.

Lifetime Maximums: 6% of our drug claims are subject to lifetime maximums. 50% of all claims with lifetime maximums are subject to limits of less than $250,000.

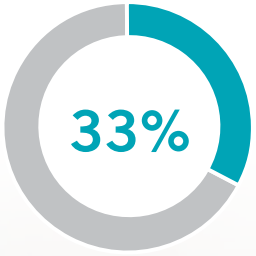
The highest adoption rates are in BC, where 17% of plans are subject to this limit. Low adoption rates could be indicative that plans are favouring other cost-containment programs.

These types of maximums are sometimes perceived to penalize plan members who are the sickest and most in need of medications. The result may be that these members skip essential medications to ensure they have access to higher-cost drugs.

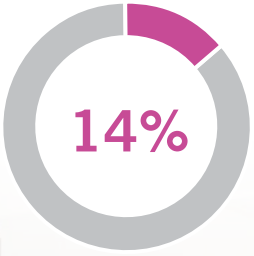


Generic substitution

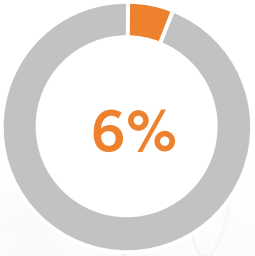
Co-insurance



Dispensing fee caps



Annual maximums



Lifetime maximums

Glossary

Biosimilar: A biological product developed such that there are no clinically meaningful differences between the biological product and the reference (originator) product in terms of safety, purity and potency.

Claimant: Any one individual for whom a claim is reimbursed. This may be the primary cardholder or any one of the primary cardholder's dependants.

Member: A unique individual who is eligible for prescription drug coverage through a healthcare benefit plan.

Originator: A first-to-market biologic drug made from or that contains components of living organisms. Also known as an "innovator biologic."

Specialty drug: A drug that has an estimated cost of $10,000 and over per claimant per year and is typically used to treat chronic, complex conditions. Specialty medications include injectable and non-injectable drugs that have one or more of the following qualities: frequent dosing adjustments and intensive clinical monitoring, intensive patient training and compliance assistance, limited distribution, and/or the requirement for specialized handling or administration.

Spend: Eligible claim cost, including the ingredient cost, markup and dispensing fee.

Therapeutic class: A grouping of medications defined by their most common indication (the disease that the drug is most commonly used to treat).

Traditional drug: A drug that has an estimated cost less than $10,000 per claimant per year. They are easy to self-administer medications that require less intensive clinical monitoring, such as those used to treat diabetes and high blood pressure.

Trend: The rate of change in total spend per member, including members who did not make a drug claim. Overall trend is impacted by both how many members make a drug claim and the eligible costs per claim.

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