2023 DRUG TREND REPORT

EXPRESS SCRIPTS CANADA

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FOREWORD

Looking at the 2022 pharmacy landscape in Canada, it's a fair statement that the pharmacy benefit management landscape continues to experience turbulence, and is adapting in real time to the changing healthcare needs of Canadians.

The concept of health equity is an aspiration that all Canadians have the same opportunity to achieve positive health outcomes regardless of their social, economic, gender identity, demographic, or geographic background. Despite recognition by the World Health Organization and the Canadian Medical Association that obesity is a chronic disease, 65% of Plan Members do not have prescription drug coverage for obesity medications.

We must continue to address the social and economic factors that can negatively impact an individual's access to treatment.

We've also noted significant interest from organizations developing their Diversity, Equity and Inclusion (DEI) programs in the workplace. Employers are striving to provide more inclusive benefits to remain competitive, and ensure

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they are taking care of all employees equally. The goal is to have positive returns in engagement, attraction, retention and overall business performance.

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In 2022, we noted increases in the number of claimants for medications used for depression and attention deficit hyperactivity disorder (ADHD), and we continue to see an increased focus on mental health services.

The trends in medication use described in the report require effective drug plan management tools. These include opportunities for prior authorization, step therapy, and potentially Product Listing Agreements (PLAs). These strategies are intended to ensure long-term plan sustainability and appropriate utilization of effective medications.

ESC continues to follow and respond to trends in real-time, offering our clients solutions and approaches to deliver the best care to Canadians. New treatments in the development pipeline may offer new or alternative treatment options but with high price tags.

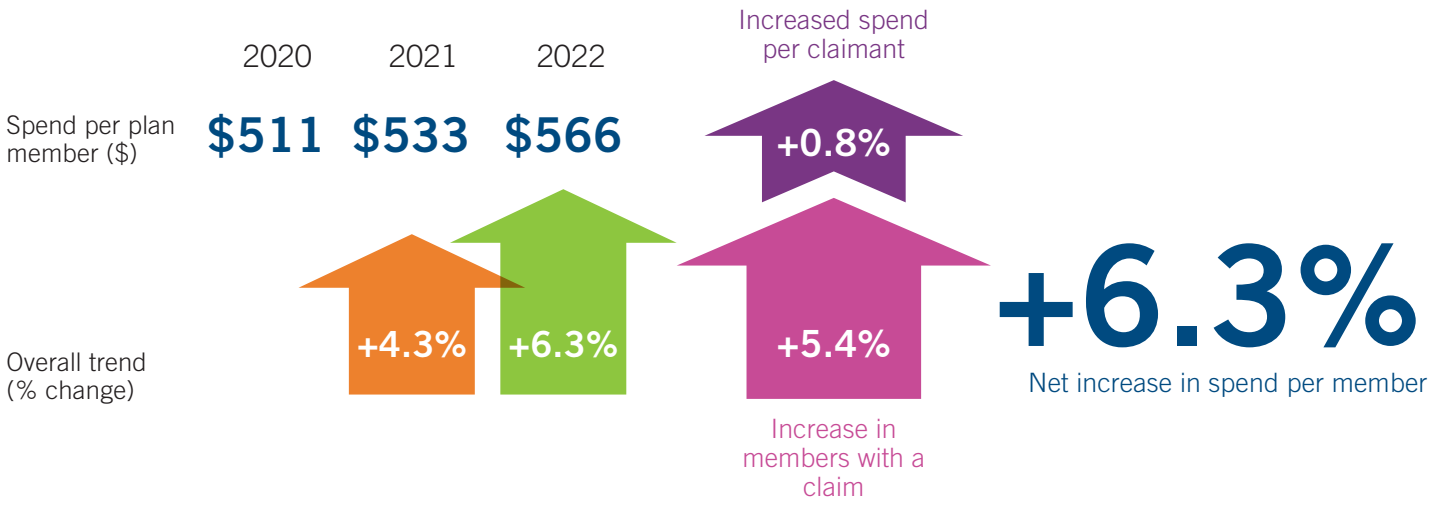
At Express Scripts Canada, we are dedicated to supporting our clients, introducing new programs and innovative solutions to address affordability as well as control plan costs.

Dr. Dorian Lo
President

DRUG TREND AND UTILIZATION

Overall Drug Trend

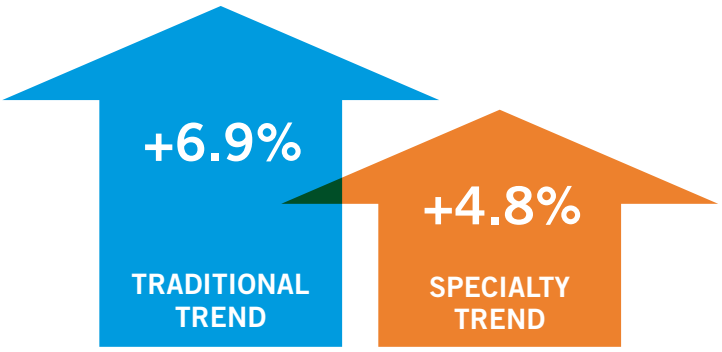
The overall drug trend, which is the annual drug spend per plan member, increased by 6.3%, driven primarily by a 5.4% increase in plan members who made a claim. At the same time, the spend per claimant grew by 0.8%.

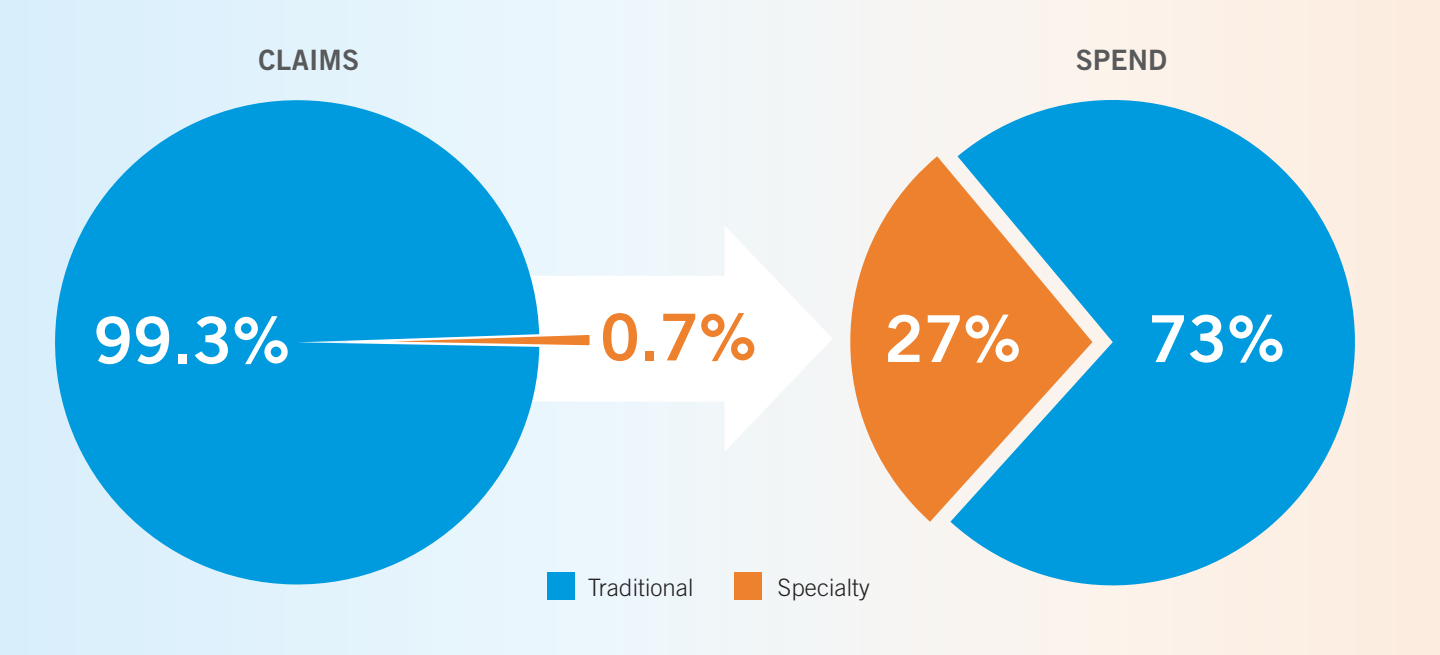


DRUG TREND AND UTILIZATION

Traditional *vs.* Specialty Drug Trend

2022	Estimated annual spend per claimant	% Spend	% Claims	Trend
Traditional Drugs	< $10,000	73%	99.3%	+6.9%
Specialty Drugs	≥ $10,000	27%	0.7%	+4.8%





Traditional Drug Trend

The spend per plan member for traditional drugs increased by 6.9% in 2022.

The proportion of plan members making a claim increased by 5.4%, and the spend per claim increased by 3.0%.

A key driver was the 10% increase in the spend per claim for diabetes medications. *See Diabetes section for more details.*

Specialty Drug Trend

In 2022, specialty drugs represented 27% of overall spend and 0.7% of claims.

Spend per plan member for specialty drugs increased by 4.8%. Utilization, the proportion of plan members making a specialty claim, increased by 5.4%.

Traditional Drug Trend cont'd

Top 10 Traditional Drugs (by overall spend)

Rank by overall spend	2021		2022	
	Drugs: Chemical name (BRAND)	**Therapeutic class**	**Drugs:** Chemical name (BRAND)	**Therapeutic class**
1	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes
2	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies	Lisdexamfetamine (VYVANSE®)	ADHD
3	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD
4	Lisdexamfetamine (VYVANSE®)	ADHD	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies
5	Empagliflozin (JARDIANCE®)	Diabetes	Empagliflozin (JARDIANCE®)	Diabetes
6	Sitagliptin-metformin (JANUMET®)	Diabetes	Budesonide-formoterol (SYMBICORT®)	Asthma/COPD
7	Rosuvastatin* (CRESTOR®)	High Cholesterol	Rosuvastatin* (CRESTOR®)	High Cholesterol
8	Blood glucose test strips	Diabetic Supplies	Sitagliptin-metformin (JANUMET®)	Diabetes
9	Budesonide-formoterol (SYMBICORT®)	Asthma/COPD	Escitalopram* (CIPRALEX®)	Depression
10	Esomeprazole* (NEXIUM®)	Ulcer/Reflux	Blood glucose test strips	Diabetic Supplies

*Generic(s) available

Semaglutide (OZEMPIC®, RYBELSUS®) for the treatment of type 2 diabetes was the top drug by overall spend again in 2022. *See Diabetes section for additional information.*

Lisdexamfetamime (VYVANSE®) moved up from 4th to 2nd place in 2022, likely because it is one of the last drugs in the Attention Deficit Hyperactivity Disorder (ADHD) class without generic alternatives. *See Top Therapeutic Classes section for more details.*

Budesonide-formoterol (SYMBICORT®) for the treatment of asthma and chronic obstructive pulmonary disease (COPD) moved from 9th to 6th place, which could be due to its new indication as rescue inhaler in addition to a maintenance therapy, and its higher cost compared to the most common rescue inhaler salbutamol (Ventolin® and its generic alternatives). *See Top Therapeutic Classes section for more details.*

Specialty Drug Trend cont'd

Top 10 Specialty Drugs (by overall spend)

Rank by overall spend	2021		2022	
	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	Dupilumab (DUPIXENT®)	Skin Conditions	Ivacaftor, tezacaftor and elexacaftor (TRIKAFTA®)	Cystic Fibrosis
5	Omalizumab (XOLAIR®)	Asthma/COPD	Dupilumab (DUPIXENT®)	Skin Conditions
6	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease
7	Etanercept* (ENBREL®)	Inflammatory Conditions	Ocrelizumab (OCREVUS®)	Multiple Sclerosis
8	Golimumab (SIMPONI®)	Inflammatory Conditions	Omalizumab (XOLAIR®)	Asthma/COPD
9	Ocrelizumab (OCREVUS®)	Multiple Sclerosis	Golimumab (SIMPONI®)	Inflammatory Conditions
10	Secukinumab (COSENTYX®)	Inflammatory Conditions	Etanercept* (ENBREL®)	Inflammatory Conditions

*Biosimilar(s) available

More than half of the Top 10 Specialty Drugs are used to treat inflammatory conditions such as rheumatoid arthritis and psoriasis.

- Adalimumab (HUMIRA® and its biosimilars) continues to be the top drug by spend; however, this may change due to biosimilar availability and provincial biosimilar transitioning policies.
- Spend on etanercept (ENBREL® and its biosimilars) dropped from 7th to 10th place, likely due to provincial biosimilar transitioning policies and increased efficacy of alternative agents.

In 2022, overall spend on cystic fibrosis (CF) drugs increased by 58%, driven by a 26.7% increase in new claimants - notably higher than expected annual growth.

Top Therapeutic Classes in 2022

The top nine 2022 therapeutic classes remained unchanged from 2021; however, spend on multiple sclerosis dropped from 10th to 12th place, and cardiovascular disease rose from 12th to 10th place. Asthma/COPD had a significant increase in claim volume in 2022, which led to an increase in spend.

Top 10 Therapeutic Classes (by overall spend)

Rank by % of overall spend			Therapeutic class	% of overall spend	Trend	
2022	2021	Change			Spend	Volume of claims
1	1	–	Inflammatory Conditions	**12.7%**	1.2%	2.5%
2	2	–	Diabetes	**11.7%**	17.9%	7.1%
3	3	–	Depression	**5.4%**	5.7%	2.1%
4	4	–	Asthma/COPD	**5.3%**	13.0%	22.3%
5	5	–	High Blood Pressure	**4.4%**	-1.6%	-0.3%
6	6	–	Cancer	**4.4%**	-1.4%	-0.3%
7	7	–	Attention Deficit Hyperactivity Disorder	**3.8%**	15.7%	12.4%
8	8	–	Skin Conditions	**3.1%**	4.7%	-0.5%
9	9	–	Ulcer/Reflux	**2.8%**	-3.6%	-0.7%
10	12	▲ 2	Cardiovascular Disease	**2.8%**	2.0%	0.9%

THERAPEUTIC CLASS HIGHLIGHTS

#1: Inflammatory conditions

The spend for inflammatory conditions increased slightly by 1.2%.

The top three drugs in terms of overall spend remained adalimumab (HUMIRA® and its biosimilars), infliximab (REMICADE® and its biosimilars) and ustekinumab (STELARA®).

- Adalimumab (HUMIRA® and its biosimilars) overall spend decreased by 11.8% due to increased availability of biosimilars and growth in provincial biosimilar transitioning policies. *See Biosimilars section for more details.*
- Infliximab (REMICADE® and its biosimilars) spend remained relatively stable in 2022.
- Ustekinumab (STELARA®) had an increase in spend by 10.9% and claimants by 5.1%.

Although upadacitinib (RINVOQ®) did not contribute significantly to overall spend, the growth in the number of claimants was the most significant for this class. It was first marketed in 2020 and treats similar conditions to the top three drugs, however it is an oral medication, which may be more convenient because it does not require injection or infusion.

Top Therapeutic Classes in 2022 cont'd

THERAPEUTIC CLASS HIGHLIGHTS

#2: Diabetes

The number of claimants using drugs to treat diabetes increased by 7.7%, which was expected due to the rising prevalence of type 2 diabetes.

Overall spend in this class increased by 17.9%, driven in part by a 10.0% increase in spend per claim. This was expected and will continue to grow due to the increased price of new drugs and treatment guidelines that recommend add-on therapy.

The spend for semaglutide, for the treatment of type 2 diabetes, was the highest again in 2022 with a 66% increase in claimants. The dual action of blood glucose control and moderate weight loss provides benefit to patients living with diabetes.

Semaglutide has been approved in Canada in several formats and dosages:

1. Marketed as OZEMPIC® and RYBELSUS® to treat patients living with type 2 diabetes.
2. Expected to be launched in Canada as WEGOVY® for weight management.

Diabetic supplies were not included in this class and remained in 14th place.

See *Diabetes* section for more details.

#3: Depression

The number of claimants for depression treatments increased by 1.8%, which led to a 2.1% increase in claim volume, which is similar to 2021 growth.

Spend per claim increased by 3.5%, contributing to the 5.7% increase in overall spend.

SPRAVATO® (esketamine) is a relatively new medication related to the anesthetic ketamine that has been approved for treatment-resistant depression and administered as a nasal spray. The annual cost of this treatment is significantly higher (up to $42,000 annually) compared to oral antidepressants ($360-$1,800 annually) and is additive to existing antidepressant therapy. This treatment would be appropriate for prior authorization to ensure patients have tried lower cost, well-established therapies first.

Top Therapeutic Classes in 2022 cont'd

#4: Asthma/COPD

2022 Asthma/COPD claims increased by 22.3% driven by a 47% increase in claimants. While spend per claim decreased by 7.6%, overall spend increased by 13% due to growth in number of claimants.

SYMBICORT® (budesonide-formoterol) continued to increase its number of claimants; likely tied to the new indication as rescue inhaler in addition to its use as a maintenance therapy. It has a higher spend per claim compared to salbutamol (VENTOLIN® and its generic alternatives) the most common rescue inhaler.

The claim volume increase in this class was driven by salbutamol (VENTOLIN® and its generic alternatives) with a 49% increase in claimants and 28.1% growth in drug spend.

- This drug is most commonly prescribed for wheezing and/or shortness of breath for patients with asthma and COPD.
- In 2022, new claimants for this low-cost medication (with a $28 annual average spend per claimant) made up about 66% of claimants and of those, 39% did not claim any other asthma or COPD drug. This suggests that some new claimants may have been prescribed these for treatment of respiratory infections.

Triple ingredient combination inhalers like TRELEGY® (fluticasone-umeclidinium-vilanterol) and BREZTRI® (budesonide-formoterol-glycopyrronium) continued to see an increase in claim volume and claimants. These products may reduce the number of different inhalers a patient must use for maintenance therapy in COPD. The cost of the triple combination inhalers is slightly less expensive than the cost of multiple individual inhalers to achieve the same combination.

Biologics for the treatment of asthma contributed significantly to the overall spend in this category.

- NUCALA® (mepolizumab) had the biggest increase in claimants of all the biologic treatments in this category. It was approved for two new indications in 2021: nasal polyps and asthma in children as young as 6 years of age, which may have contributed to claimant growth.
- Some of the injectable biologic treatments have received additional indications to treat various severe asthma subtypes and may expand further to the treatment of COPD, which may increase the eligible patient population and, consequently, the spend in this category.

Top Therapeutic Classes in 2022 cont'd

#5: Attention Deficit Hyperactivity Disorder (ADHD)

The number of claimants increased 16.4%, which led to a 12.4% increase in claim volume. The overall spend increased by 15.7% and spend per claim grew by 2.9%.

VYVANSE® (lisdexamfetamine) had the largest increase in claimants at 25%, leading to a 25% increase in spend. It is one of the few drugs in this class without generics.

Despite the availability of generics, this category continues to grow. In 2022, the greatest growth in claim volume was for claimants 25 to 34 years of age.

See Top Traditional Drugs section for more information.

#6: Cancer

In 2022 cancer drug spend dropped by 1.4% and the number of claimants reduced by 0.4%.

The majority of 2022 claimants filled prescriptions for lower-cost cancer drugs (less than $200/year), such as letrozole (FEMARA® and its generic alternatives) and tamoxifen (NOLVADEX® and its generic alternatives).

The top cancer drugs by spend in 2022 were all oral treatments; palbociclib (IBRANCE®), ibrutinib (IMBRUVICA®) and lenalidomide (REVLIMID® and its generic alternatives), respectively. As predicted last year, the availability of lenalidomide generics in 2022 provided more than a 50% reduction in spend for that drug. Because of the different provincial cancer drug funding mechanisms, the impact on private plans would vary by region.

Comorbidities

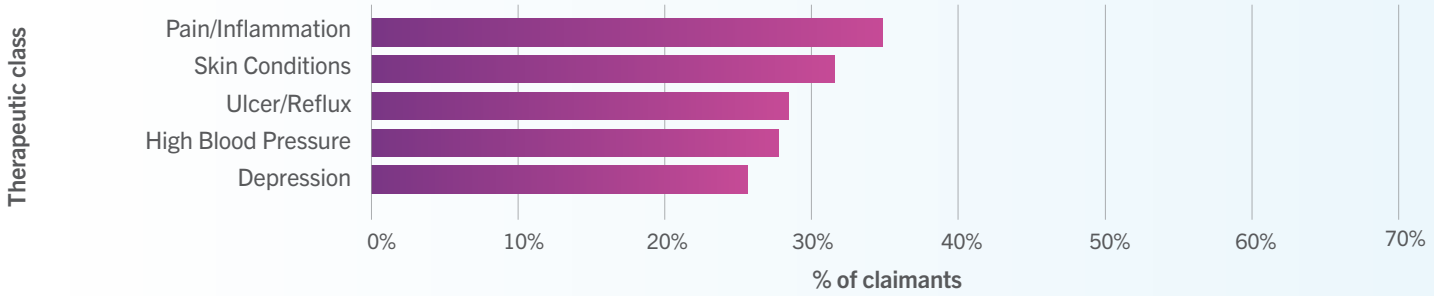
A comorbidity is the presence of two or more medical conditions in a patient at the same time. Comorbidities increase treatment complexity as patients must manage several medical conditions at once. They may be seeing a variety of physicians and taking multiple medications. Drug spend associated with patients with comorbidities is higher, and adherence decreases as the number of medications increases.

Inflammatory Conditions

Inflammatory conditions includes diseases such as rheumatoid arthritis, Crohn's disease, ulcerative colitis and psoriasis. The most common comorbidity for patients with inflammatory conditions was pain and inflammation; medications in this class are often used to manage the symptoms of rheumatoid arthritis.

Claims for drugs to treat skin conditions had the second-highest correlation for this therapeutic class. Medications in the skin conditions class include various topical treatments, which are used by patients with psoriasis.

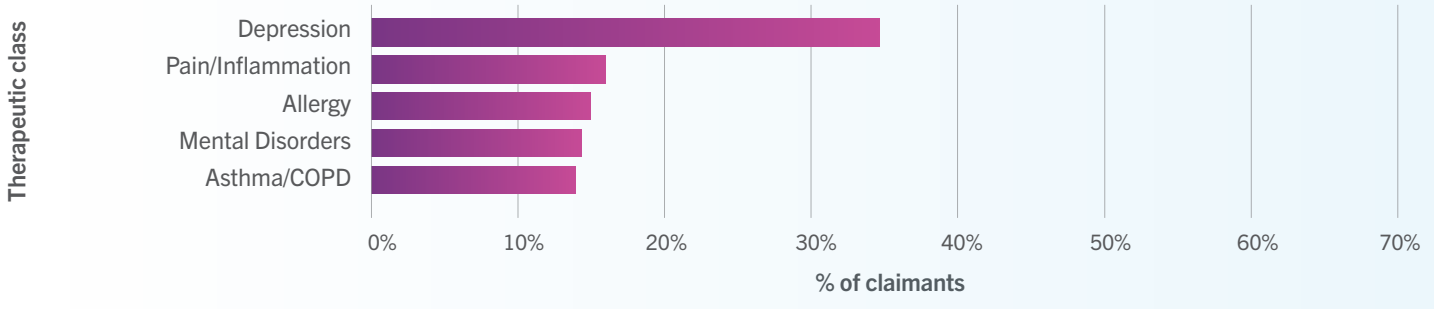
Percentage of claimants with inflammatory conditions who also had claims for drug(s) to treat other conditions



Attention Deficit Hyperactivity Disorder (ADHD)

The ADHD class was among the highest growing therapeutic classes in 2022 and the most common comorbidity was depression. The second-highest correlated condition was pain and inflammation, followed by allergy and mental disorders.

Percentage of claimants with ADHD who also had claims for drug(s) to treat other conditions



Comorbidities cont'd

Diabetes

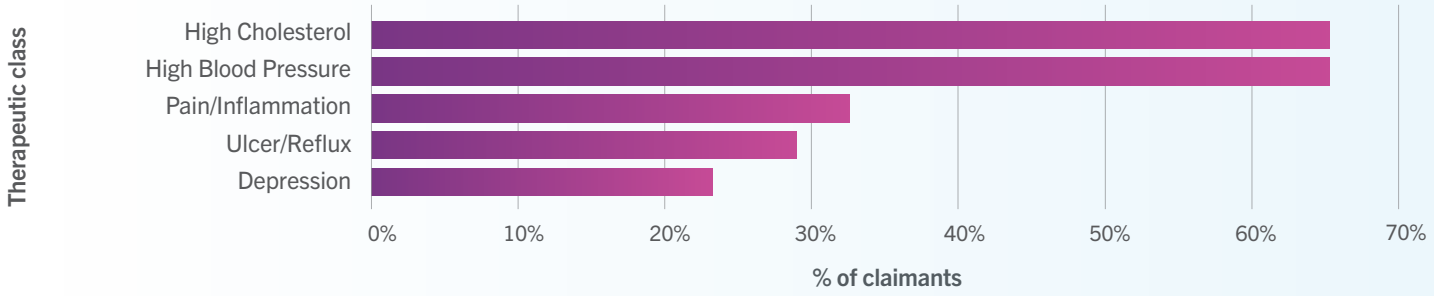
Diabetes is one of the most prevalent conditions in Canada and its incidence is expected to continue to rise. Over time, diabetes can damage the heart, blood vessels, eyes, kidneys, and nerves.

Claims analysis showed a high correlation between diabetes, elevated cholesterol, and high blood pressure. Since increased blood pressure and cholesterol levels are risk factors for cardiovascular disease, clinical guidelines recommend that both these conditions be treated to reduce the risk of a patient with diabetes having a stroke or heart attack.

Benefit management strategies can support plan members living with diabetes and related comorbidities through chronic disease management and wellness programs.

See Top Therapeutic Classes and Diabetes sections for more details.

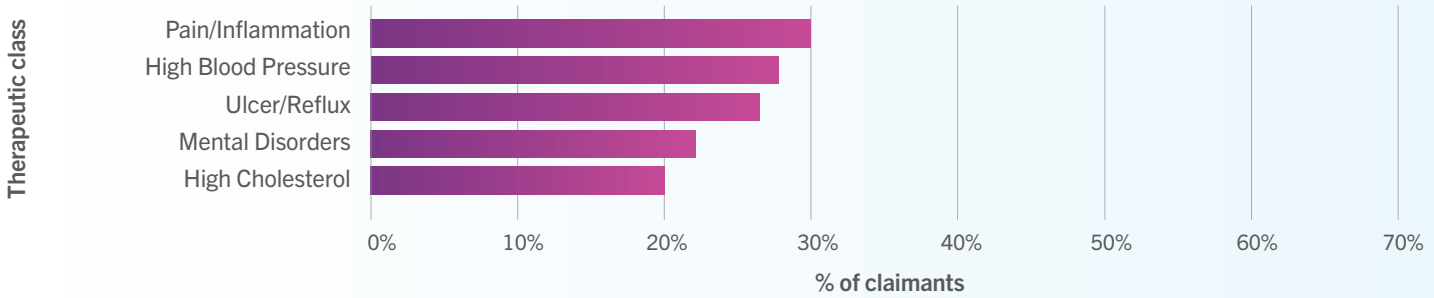
Percentage of claimants with diabetes who also had claims for drug(s) to treat other condition



Depression

Depression is a complex illness and commonly observed to coexist with anxiety in medical literature. There was a 22% correlation between depression and the mental disorders class. This class contains benzodiazepines, which are commonly used to manage symptoms of anxiety. Also, there is an established correlation between depression and pain, which was apparent for 30% of claimants.

Percentage of claimants with depression who also had claims for drug(s) to treat other conditions

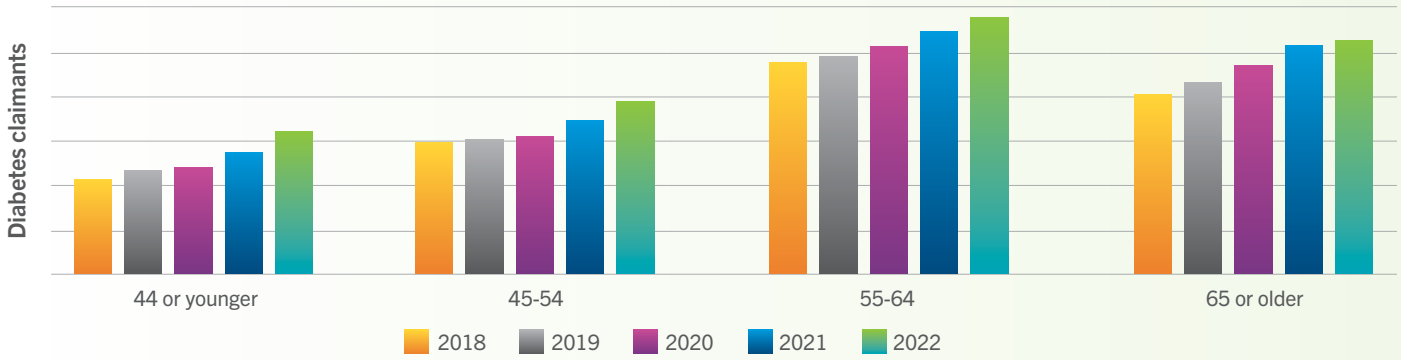


Diabetes

In 2022, there were more than 5.7 million Canadians living with diagnosed type 1 or 2 diabetes[1] compared to 1.3 million in 2000/2001[2] and this number is expected to grow.

Analysis of Express Scripts Canada claims data reflects a similar pattern with the number of claimants growing year over year in every age group.

Diabetes claimants by age group – 2018 to 2022

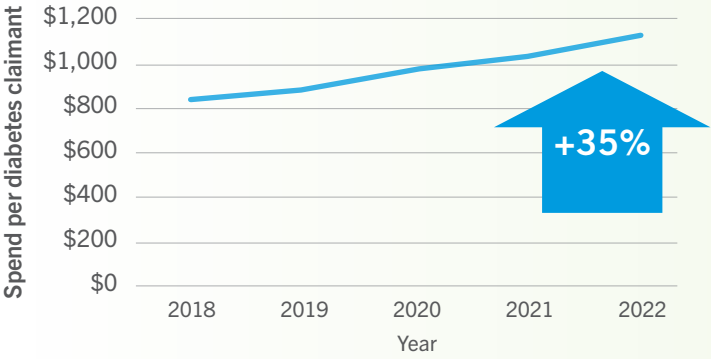


[1] https://www.diabetes.ca/media-room/press-releases/diabetes-rates-continue-to-climb-in-canada
[2] https://www.canada.ca/en/public-health/services/publications/diseases-conditions/diabetes-canada-review-2021.html

Diabetes cont'd

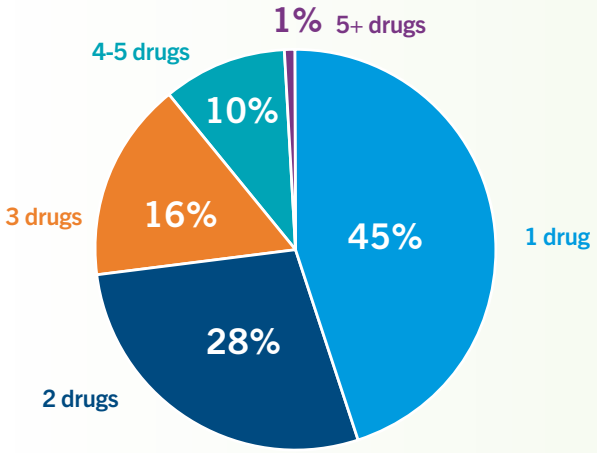
Over the last five years, diabetes drug spend per claimant has continued to grow with a 35% increase between 2018 and 2022.

Diabetes drug spend per claimant over time – 2018 to 2022



Diabetes therapies launched in recent years have gained popularity and have higher annual costs. Furthermore, new diabetes treatments are generally cumulative. Most patients with diabetes will start on one medication and clinical guidelines recommend that therapies with different mechanisms of action to be added to achieve treatment goals. This would result in patients taking multiple drugs and analysis showed that 55% of claimants are taking two or more diabetes medications.

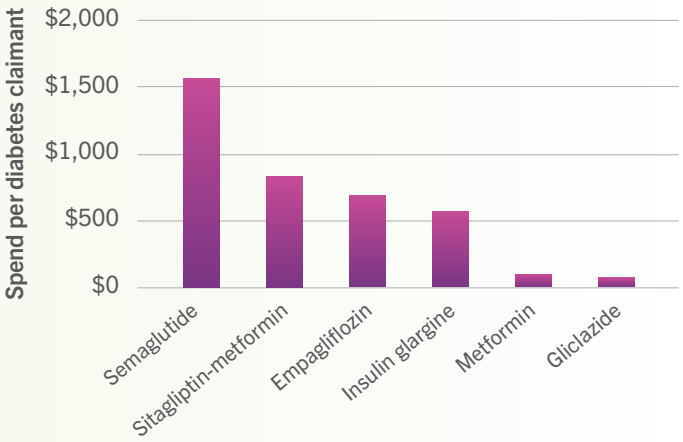
Percentage of claimants with single or multiple diabetes drugs claimed in 2022



Diabetes Drugs

Semaglutide generated the highest drug spend per claimant in 2022 and was the primary cost driver for the diabetes therapeutic class. The annual drug spend per claimant was significantly higher for semaglutide (approx. $1,500) compared to metformin (approx. $100), which has generic options available. For sitagliptin-metformin (JANUMET®), the average drug spend per claimant is expected to decrease in 2023 because generics were marketed in late 2022.

Average spend per claimant by diabetes drug in 2022



Drug	Brand Name(s)	Generics available in 2022
Semaglutide	OZEMPIC®, RYBELSUS®	No
Sitagliptin-metformin	JANUMET®	Yes (end of 2022)
Empagliflozin	JARDIANCE®	No
Insulin glargine	LANTUS®	Yes - Biosimilar
Metformin	GLUCOPHAGE®	Yes
Gliclazide	DIAMICRON®	Yes

Diabetes cont'd

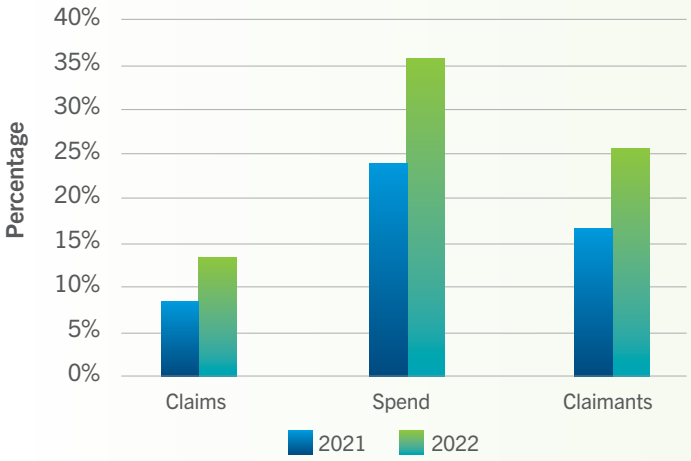
Focus on Semaglutide

Semaglutide is currently marketed as OZEMPIC® (injectable) and RYBELSUS® (oral) in Canada for the treatment of diabetes however, the majority (96%) of 2022 claims were for OZEMPIC®. Semaglutide is expected to be launched in Canada as WEGOVY® for weight loss.

Spend on semaglutide represented approximately 36% of the total 2022 spend on diabetes medications and increased 12% over 2021.

Semaglutide may be popular due to its convenience (once weekly administration for OZEMPIC®) while providing effective control of A1C and positive impact on weight loss.

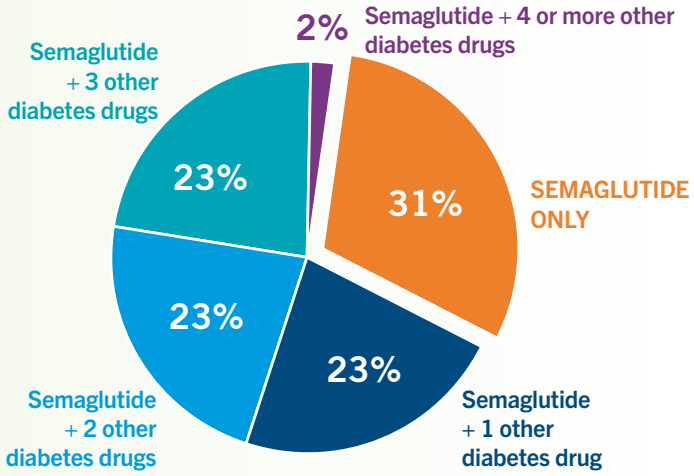
Percentage of semaglutide claims, spend and claimants in diabetes class - 2021 vs. 2022



The number of semaglutide claimants increased by 66% in 2022. Further analysis showed that 31% of these patients claimed semaglutide as their only diabetes drug treatment, which was up from 20% in 2021. Although this drug has been approved to be used alone when first-line drugs are not tolerated, generally, treatment guidelines for diabetes recommend cumulative therapy and therefore, treatment with only semaglutide is not typical.

This highlights the importance of effective plan management strategies such as Step Therapy or Prior Authorization programs, which consider appropriate first-line diabetes treatments prior to using semaglutide.

Percentage of semaglutide claimants and number of other diabetes drugs used in 2022



Obesity

Obesity is a complex chronic disease where the accumulation of excessive fat negatively impacts well-being and increases the risk of developing other medical complications.[3]

About 1 in 4 Canadian adults are currently living with obesity.[4] The Canadian Medical Association recognized obesity as a chronic disease in 2015,[5] and the World Health Organization identified obesity as a global health problem as far back as 1997.[6]

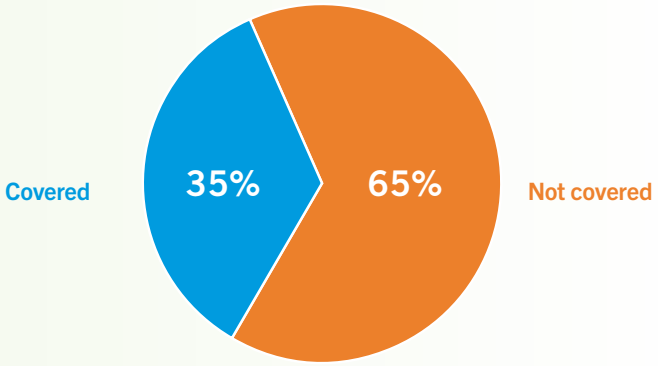
Misconceptions and misinformation are among the reasons why obesity is still not recognized widely as a chronic disease. Many do not understand that obesity is caused by a combination of biological, behavioural, environmental and psychological factors. Unfortunately, this disease is commonly viewed as a lifestyle choice or a risk factor for other diseases. Individuals, who are overweight or obese are often stigmatized as people choosing to lead unhealthy lifestyles, or lack the willpower to make healthy changes.

Many drug plans consider obesity as a lifestyle choice and exclude coverage for weight loss drugs. Consequently, plan members living with obesity do not have access to effective medications that can help them address this serious condition.

Weight Loss Drug Coverage

65% of plan members do not have coverage for weight loss drugs and the majority of those with coverage are limited to a maximum.

Percentage of plan members with coverage for weight loss drugs



[3] https://www.canada.ca/en/health-canada/services/healthy-living/your-health/lifestyles/obesity.html
[4] https://health-infobase.canada.ca/datalab/canadian-risk-factor-atlas-obesity-blog.html?=undefined&wbdisable=true
[5] https://www.cma.ca/obesity-canada
[6] https://www.worldobesity.org/what-we-do/our-policy-priorities/obesity-as-a-disease

Obesity cont'd

Weight Loss Drug Trends

Weight loss drugs accounted for less than 1% of overall spend and less than 1% of overall claimants in 2022.

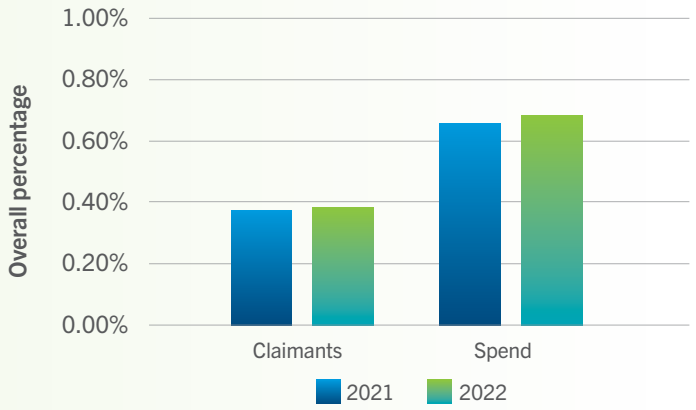
In 2022, weight loss drug spend increased by 9.9% and claimants increased by 7.5%.

- The key driver was an increase in liraglutide (SAXENDA®) claimants, which accounted for 77% of total weight loss drug spend in 2022.
- Bupropion/naltrexone (CONTRAVE®) also had an increase in claimants, which impacted its claim volume and spend.
- Claimant volume for orlistat (XENICAL®) decreased in 2022, which in turn reduced claim volume and spend. Orlistat accounts for only 3% of weight loss drug spend, likely due to its unpleasant gastrointestinal adverse effects.

What to Watch

A new weight loss drug, semaglutide (WEGOVY®), was expected to be launched in Canada in 2022, however, it has yet to be marketed. The launch in the United States generated high demand leading to medication shortages. Semaglutide is currently marketed as OZEMPIC® and RYBELSUS® in Canada for diabetes treatment.

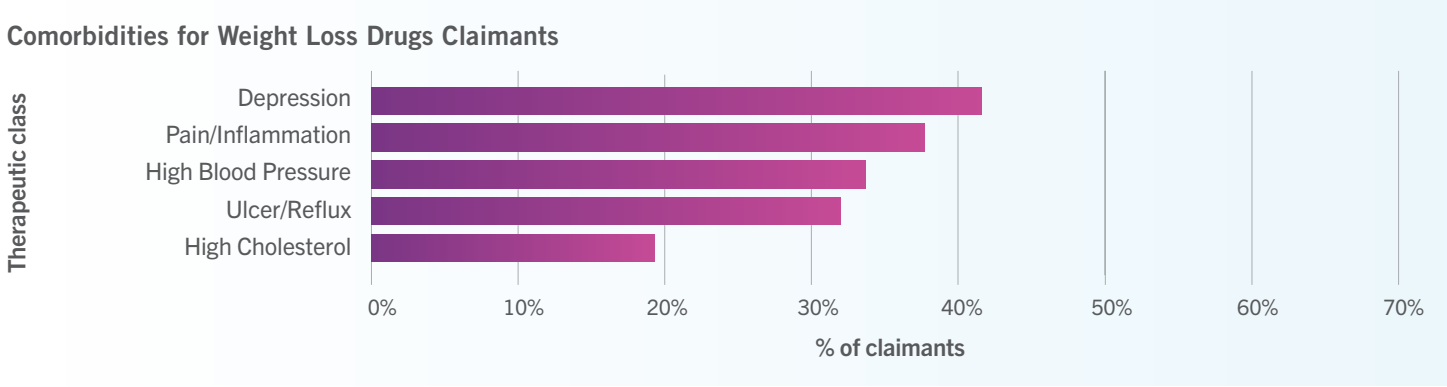
Overall percentage of claimants and spend for Weight Loss Drugs 2021 vs. 2022



Obesity cont'd

Comorbidities for Weight Loss Drugs Claimants

Obesity is a complex chronic disease, which increases the risk of developing other medical conditions[6]. Obesity and increased central fat are associated with type 2 diabetes, hypertension, heart disease and other chronic conditions. Evidence has shown that modest weight loss can improve these conditions[7].



Although the data is limited due to the small percentage of plan members with coverage for weight loss drugs, claims analysis showed:

A large subset of claimants for weight loss drugs also claimed antidepressant drugs, which aligns with the established correlation between obesity and depression.

The third most common comorbidity was high blood pressure, which aligns with the epidemiological association between increased adiposity and the development of hypertension.

Obesity is a risk factor for gastrointestinal-related disease, including gastroesophageal reflux disease, and explains the common use of ulcer and reflux treatments in 32% of claimants.

Obesity is associated with changes in lipid metabolism, including elevated cholesterol and triglycerides, as well as a reduction in HDL (high-density lipoprotein) cholesterol. This may explain why 19% of claimants for weight loss drugs also claimed high cholesterol medications.

[6] https://www.worldobesity.org/what-we-do/our-policy-priorities/obesity-as-a-disease
[7] https://pubmed.ncbi.nlm.nih.gov/28455679/

PHARMACY LANDSCAPE

Biosimilars

Biosimilars have been the focus of benefit management strategies for the past few years. Public programs in various provinces have led the way with some carriers and plan sponsors following suit. Biosimilar transition or switching policies implemented by provincial drug programs may impact private drug claims depending on the province, drug and plan design.

In addition to British Columbia, Alberta, Northwest Territories, Quebec, New Brunswick and Nova Scotia, the Ontario and Saskatchewan provincial drug programs announced biosimilar transition policies that will be implemented in 2023.

2023 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

Biosimilar policies for new and existing patients

Biosimilar policies may be different for new patients, who are starting on a drug, versus existing patients, who have been on the medication for a long time. A policy may require new patients to start on a biosimilar, however, to generate more significant savings, the policy must address existing patients already taking a biologic for a chronic condition; thus, a biosimilar transition or switching policy may be required.

Short-term vs long-term biosimilars

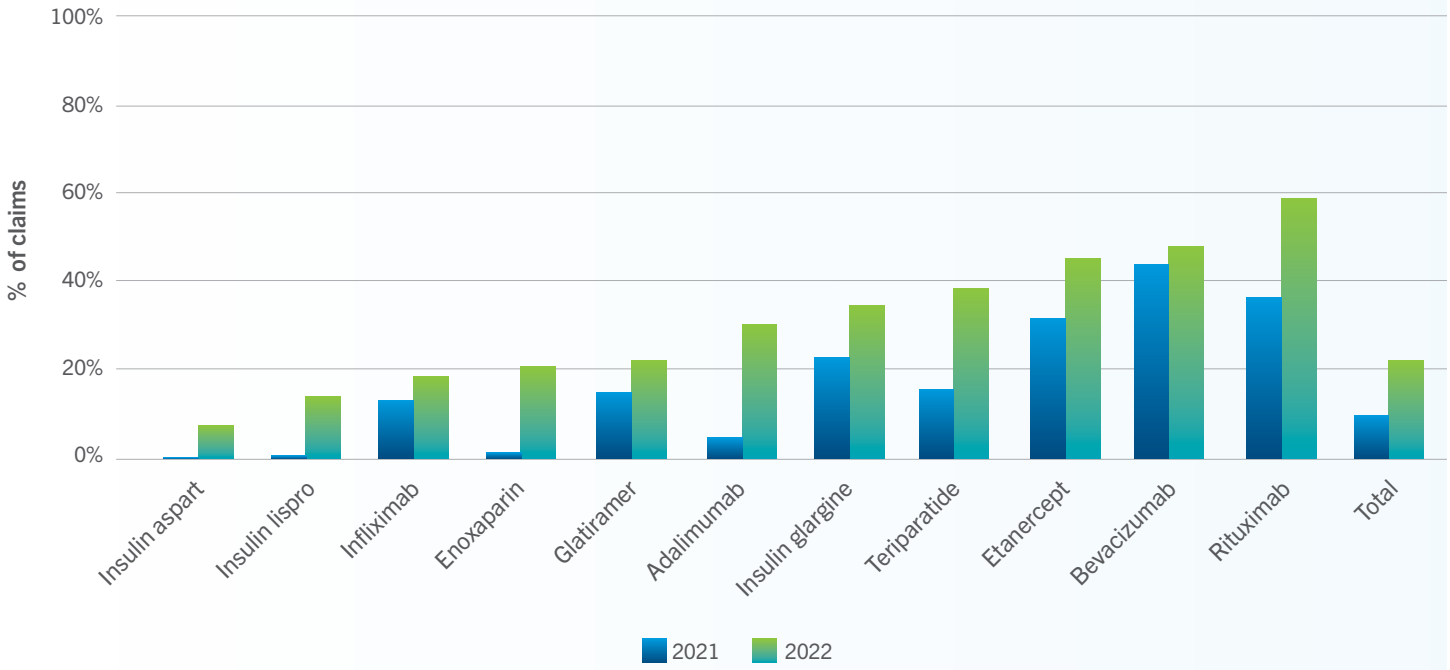
Claims for acute or short-term conditions showed a much higher biosimilar uptake, due to the greater influx of new patients and payers' biosimilar-first policy. Claims for maintenance or long-term use biologic drugs have not generated similar biosimilar penetration since there are fewer new patients than existing ones. Existing claimants made up the bulk of the originator claims for maintenance treatments, and increased biosimilar penetration is possible if patients are switched to biosimilars through targeted benefit plan designs.

Medications that are primarily used for short-term or acute treatments have achieved close to 100% biosimilar penetration. For that reason, medications such as pegfilgrastim and filgrastim, used in supportive cancer care were excluded from this analysis.

Biosimilar penetration rates may also be higher for some cancer treatments due to shorter treatment durations and ongoing influx of new patients, who may start treatment on a biosimilar (example: bevacizumab).

Biosimilars cont'd

National biosimilar penetration rate – % of claims in 2021 and 2022



Biosimilar quick reference chart

Chemical name	Corresponding originator
Adalimumab	HUMIRA®
Bevacizumab	AVASTIN®
Enoxaparin	LOVENOX®
Etanercept	ENBREL®
Glatiramer	COPAXONE®
Infliximab	REMICADE®
Insulin aspart	NOVORAPID®
Insulin glargine	LANTUS®
Insulin lispro	HUMALOG®
Rituximab	RITUXAN®
Teriparatide	FORTEO®
Trastuzumab	HERCEPTIN®

The national biosimilar penetration rate shows the percentage of biosimilar claims for specific medications in each year.

Bevacizumab and rituximab have the highest biosimilar penetration rates overall.

- Bevacizumab is used to treat cancer, which could result in greater number of new claimants with shorter treatment times.
- Rituximab is used to treat both inflammatory conditions and cancer. Therefore, when used as a cancer treatment there may be a greater number of new patients on shorter treatments compared to other biologics that only treat inflammatory conditions.

Adalimumab biosimilars were marketed in early 2022, and generated very quick biosimilar penetration, likely due to the lower cost and provincial biosimilar transition policies. This had a direct effect on the reduction in spend for the inflammatory conditions therapeutic class.

Biosimilars cont'd

Insulin biosimilars are less costly than other biosimilars but have larger claimant pool. Biosimilars for insulin glargine have been available the longest and demonstrated the highest penetration rate amongst insulins. The rapid-acting insulin options (insulin aspart and insulin lispro) saw some increased biosimilar penetration with some provincial policies ending in 2022.

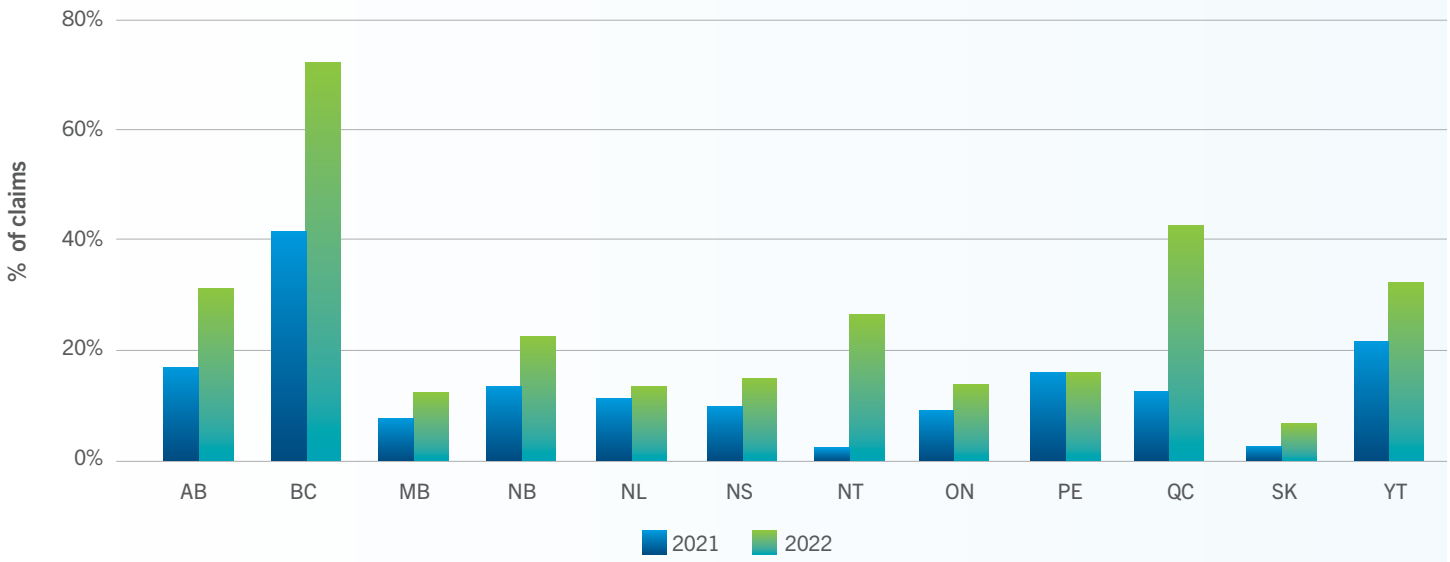
The provincial biosimilar penetration rates vary depending on the implementation of private plan biosimilar policies, the drugs included, and how the provincial programs integrate with private plans.

British Columbia has the highest biosimilar penetration rate because it was the first province to adopt a biosimilar transition policy. In addition, it is considered a pharmacare province where integration between public and private plans is quite common.

Quebec's biosimilar penetration increased significantly due to the provincial biosimilar transition policy that was finalized in April 2022.

Alberta and New Brunswick had relatively smaller increases in biosimilar penetration. Although these provinces introduced biosimilar transition policies, their provincial programs do not typically provide coverage for individuals with private plans, which leads to less integration.

Provincial biosimilar penetration rate - % of claims in 2021 and 2022



Biosimilars cont'd

Impact of provincial biosimilar policies on private drug claims

Private plans may benefit from provincial biosimilar policies due to the spillover effect. 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 biosimilar policy exists.

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 payers develop adjudication protocols to integrate the programs and policies to reduce overall costs by shifting claims, where possible, from private to public.

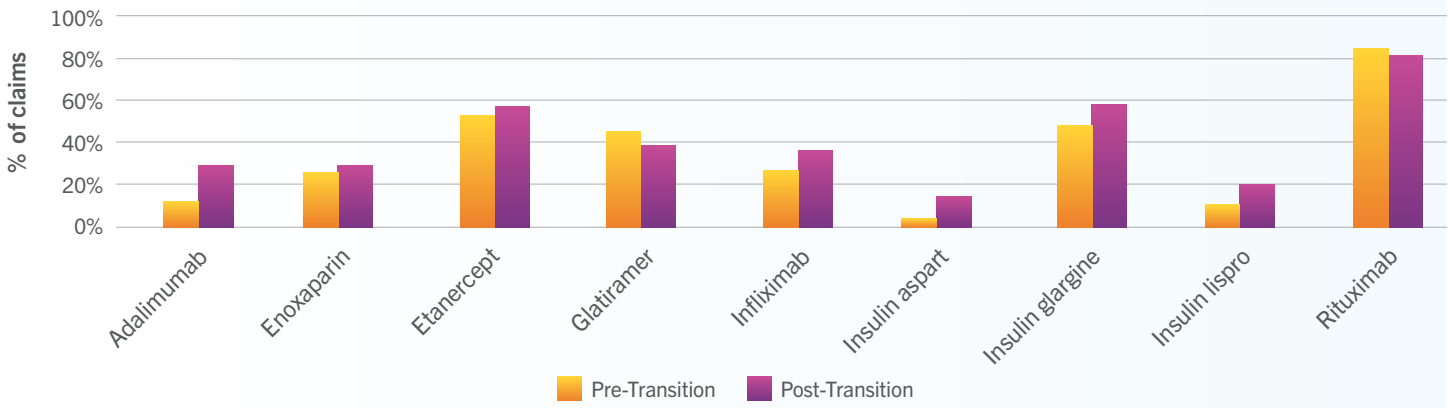
Biosimilar penetration rate - Percentage of claims in 2022

Chemical Name	BC	QC	AB	NB	ON	SK
Adalimumab	95%	52%	24%	7%	15%	13%
Bevacizumab	Insufficient Claims	58%	Insufficient Claims	Insufficient Claims	51%	Insufficient Claims
Enoxaparin sodium	40%	42%	28%	24%	6%	19%
Etanercept	86%	71%	56%	22%	33%	23%
Glatiramer acetate	41%	33%	41%	Insufficient Claims	14%	0%
Infliximab	83%	26%	33%	8%	12%	4%
Insulin aspart	36%	20%	11%	2%	1%	0%
Insulin glargine	92%	60%	55%	48%	14%	10%
Insulin lispro	48%	40%	17%	11%	3%	1%
Rituximab	100%	65%	83%	Insufficient Claims	48%	Insufficient Claims
Teriparatide	13%	52%	Insufficient Claims	Insufficient Claims	37%	Insufficient Claims
TOTAL	71%	40%	30%	21%	9%	7%

Biosimilars cont'd

Alberta

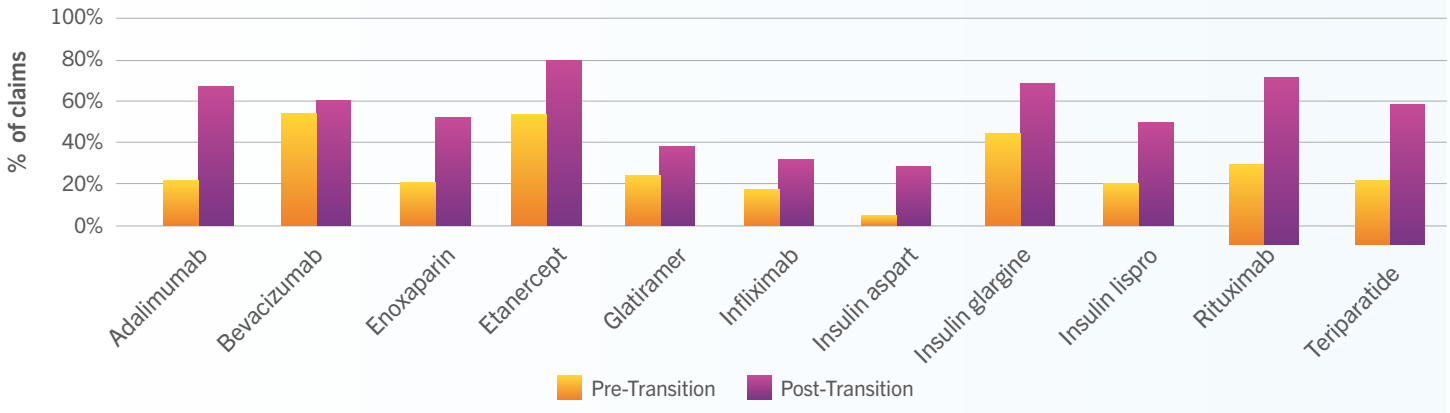
Alberta biosimilar penetration rate - % of claims before and after transition deadline of May 1, 2022



Alberta's biosimilar transition policy was phased, starting in 2021 and wrapped up in 2022. The bulk of the transitions were completed in 2021 and therefore, there were only slight increases in biosimilar penetration in 2022. In addition, Alberta is considered a non-pharmacare province where the public biosimilar programs are less likely to impact private drug plan claims.

Quebec

Quebec biosimilar penetration rate - % of claims before and after transition deadline of April 13, 2022

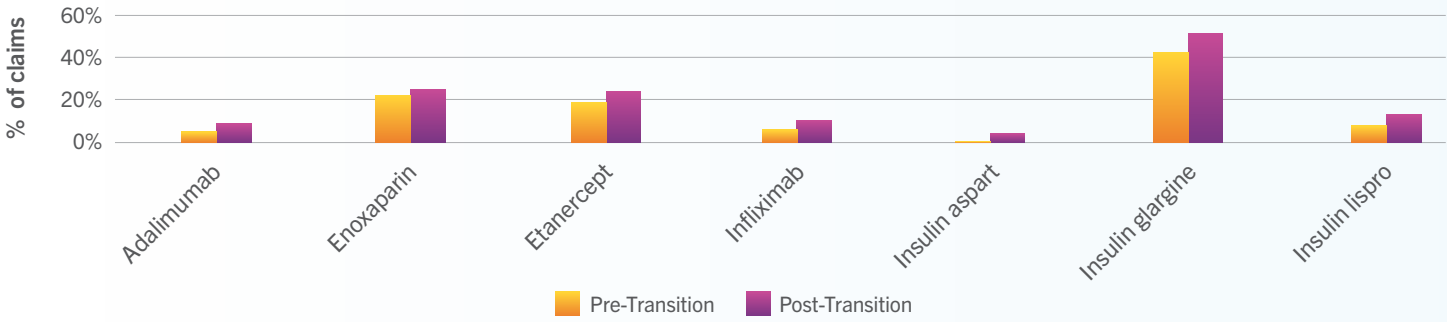


The Quebec biosimilar transition policy implementation was finalized on April 13, 2022. The biosimilar penetration rate increased across all drugs. Notably, the penetration rate was higher for insulins and popular biologics for inflammatory conditions. Adalimumab generated significant biosimilar penetration, despite biosimilars only being marketed in 2022.

Biosimilars cont'd

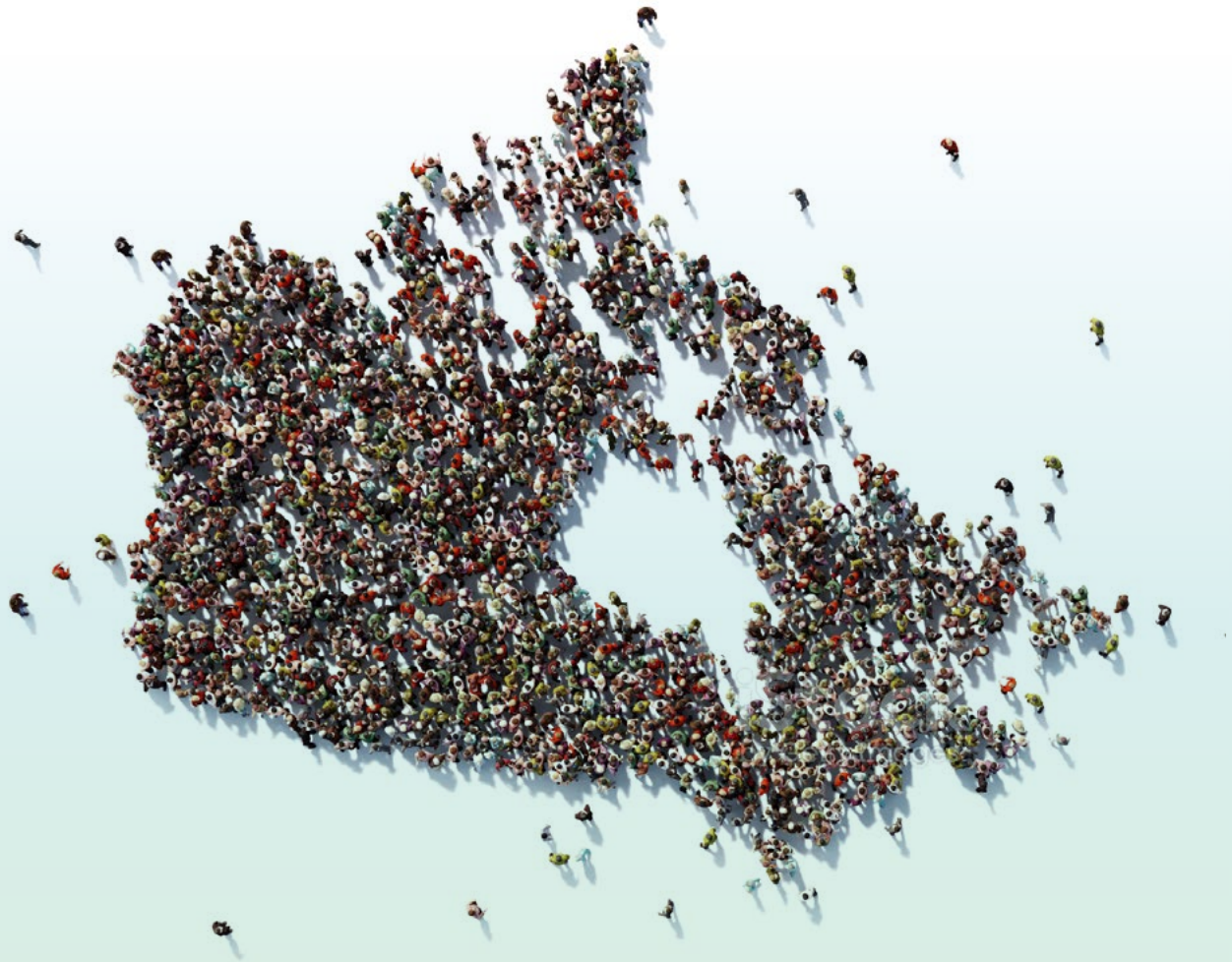
New Brunswick

New Brunswick biosimilar penetration rate - % of claims before and after transition deadline of May 31, 2022



The New Brunswick biosimilar transition policy implementation was completed on May 31, 2022. Insulin glargine had the highest biosimilar penetration rate in the province.

New Brunswick is considered a non-pharmacare province where the public biosimilar policies are less likely to impact private drug plan claims.



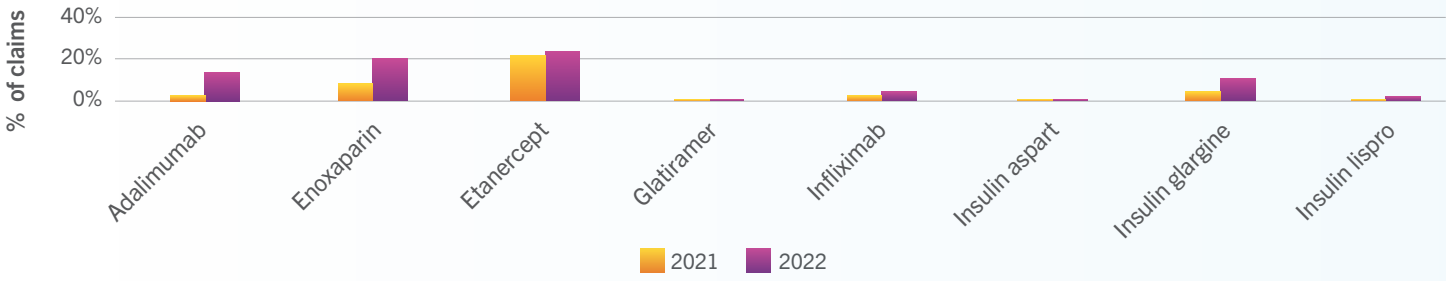
Biosimilars cont'd

WHAT TO WATCH FOR IN 2023

In 2022, the Ontario and Saskatchewan provincial drug programs announced biosimilar transition policies that will be implemented in 2023. Recently, the Yukon government announced their biosimilar transitioning plan.

Saskatchewan

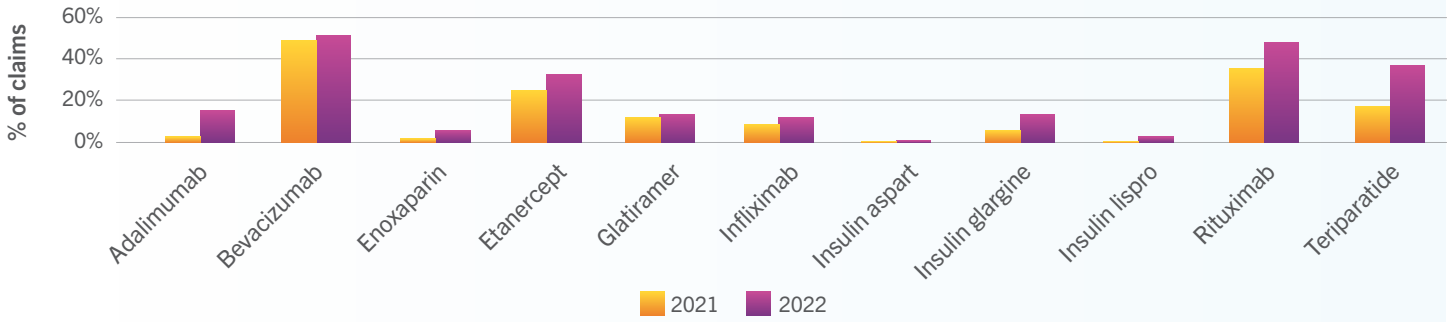
Saskatchewan biosimilar penetration rate - % of claims in 2021 and 2022



Saskatchewan is considered a pharmacare province, therefore their biosimilar policy will likely provide greater biosimilar uptake on private plans, as observed in B.C. Biosimilar penetration is currently quite low.

Ontario

Ontario biosimilar penetration rate - % of claims in 2021 and 2022



Ontario announced their biosimilar transition policy in 2022, which was implemented in March and ends in December of 2023. There was very little difference between 2022 and 2021 biosimilar penetration rates. Ontario is considered a non-pharmacare province where the public biosimilar policies are less likely to impact private drug plan claims.

Yukon Territory

The Yukon government announced a biosimilar switching initiative targeting insulin glargine and adalimumab in late March. The transition will occur from April to October 2023 and will affect individuals who are enrolled in the Yukon's Pharmacare or Chronic Disease and Disability Benefits programs.

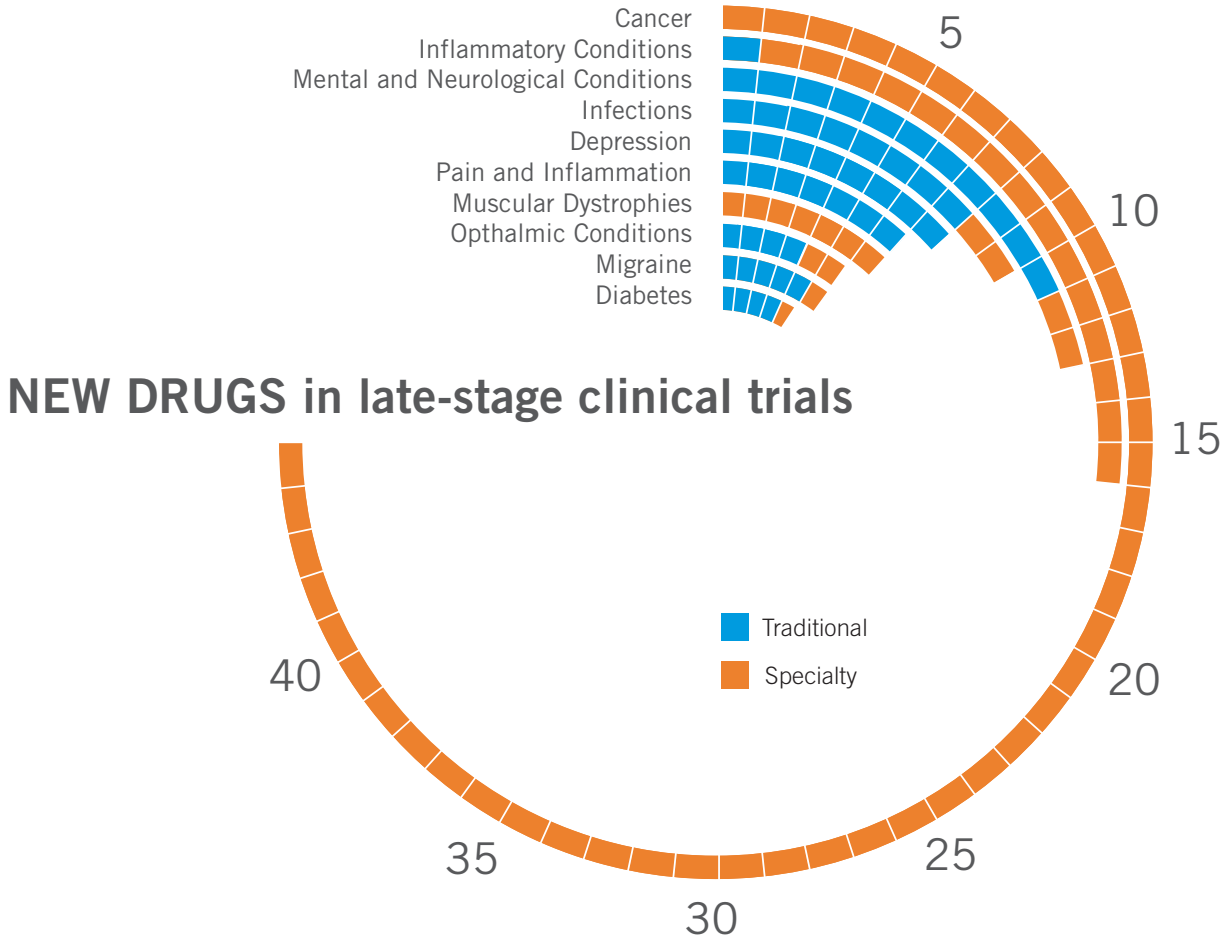
Drug Pipeline

PIPELINE DRUGS AND NEW INDICATIONS

New drugs and new indications in the pipeline may bring improved health outcomes, treat previously untreatable conditions, or offer alternative therapies for those that have exhausted all existing options. However, they may also have a financial impact on private drug plans.

Pipeline drugs

Specialty drugs for cancer continue to dominate the new drug development pipeline followed by inflammatory conditions. These are generally medications with high annual costs due to specialized treatment.



Drug Pipeline cont'd

Some categories that have a notable pipeline are highlighted below.

CANCER

Bispecific antibodies are artificial proteins that have promising applications in the field of cancer immunotherapy due to their ability to target multiple disease-specific signalling pathways. The research is currently in late-stage clinical trials primarily in hematology and could potentially have a high impact on drug spend.

Initial therapies in this class have been intravenous formulations, whereas some of the new treatments in the pipeline are subcutaneous such as mosunetuzumab, a bispecific antibody for lymphoma. This could shift the place of administration to home or outpatient care and reduce time spent at treatment centres.

Selective estrogen receptor degraders (SERDs) are used in hormone receptor positive metastatic breast cancer. Fulvestrant is the only SERD currently available in Canada and is administered by intramuscular injection.

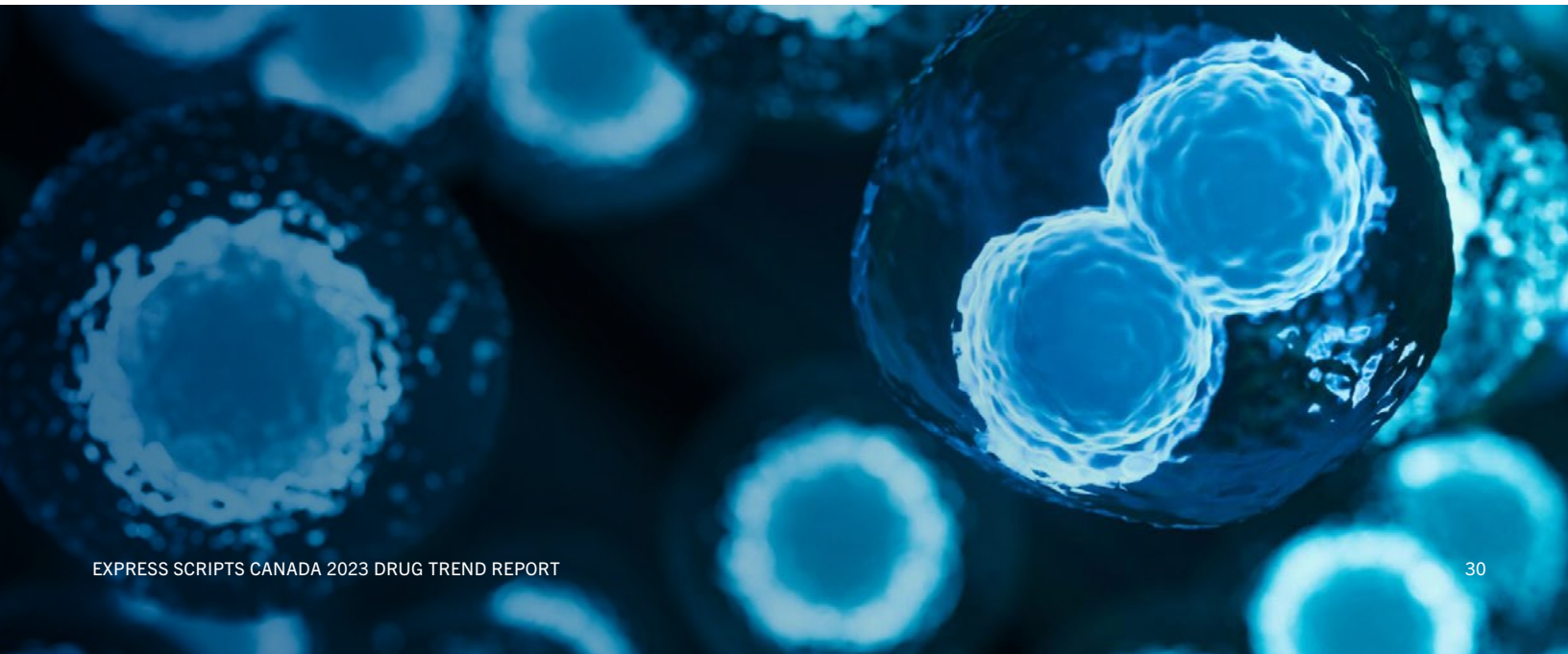
There are several new oral SERDs in the pipeline such as giredestrant and amcenestrant. Another drug, elacestrant, was granted priority review by the FDA in August 2022, because it has the potential to provide significant improvements over current standard of care.

The introduction of oral therapies in this class could shift treatment from hospital to home administration, which could impact private payers in some provinces, where cancer agencies don't fund oral treatments.

Gene Therapies. Most existing gene therapies modify a patient's own cells (autologous) and transplant them back to the patient, which must be done in hospital.

However, there are new "off-the-shelf" gene therapies which use cells from healthy donors (allogeneic) to treat multiple patients. EBVALLO® (tabelecleucel) received its first approval in Europe in December 2022 as the first allogeneic cell-based gene therapy.

Advancements in cell-based technology may help address time-to-treatment, preparation, and administration challenges associated with these therapies that could potentially shift the administration to non-hospital settings, such as infusion centres. Hospital treatments are traditionally publicly funded, however, if they move outside of hospital settings the cost could shift to private plans.



Drug Pipeline cont'd

MIGRAINE

New oral anti-calcitonin gene-related peptide (CGRP) antagonists are on the radar due to the high utilization observed with the existing injectable treatments for migraine prevention.

New options designated as both acute and preventative may offer an alternative for individuals who are averse to the injectable CGRP agents. QULIPTA® (atogepant) is an oral treatment for migraine prevention, while UBRELVY® (ubrogepant) was a recently approved for acute treatment. UBRELVY® represents an alternative to triptans for acute treatment but costs 25-50% more.

Zavegepant nasal spray and rimegepant oral tablets are two other CGRP antagonists approved by the FDA. The introduction of these new options could result in a potential increase in claim spend, and drug plan management strategies will be required to ensure appropriate stepwise approach for reimbursement of these new treatments.

MENTAL AND NEUROLOGIC CONDITIONS

Alzheimer's Disease

Aducanumab, an anti-amyloid beta therapy, was approved by the FDA in June 2021 after much controversy; and was subsequently submitted to Health Canada for review. The submission was withdrawn by the manufacturer prior to receiving any decision for market authorization.

Lecanemab had positive clinical trial results, compared to what had been observed with aducanumab. Lecanemab was approved by the FDA in January 2023; with the annual cost estimated to be USD $26,000; which is significantly higher than conventional oral Alzheimer's Disease therapies currently available in Canada. There is no submission to Health Canada at this time.

Drug Pipeline cont'd

New Indications

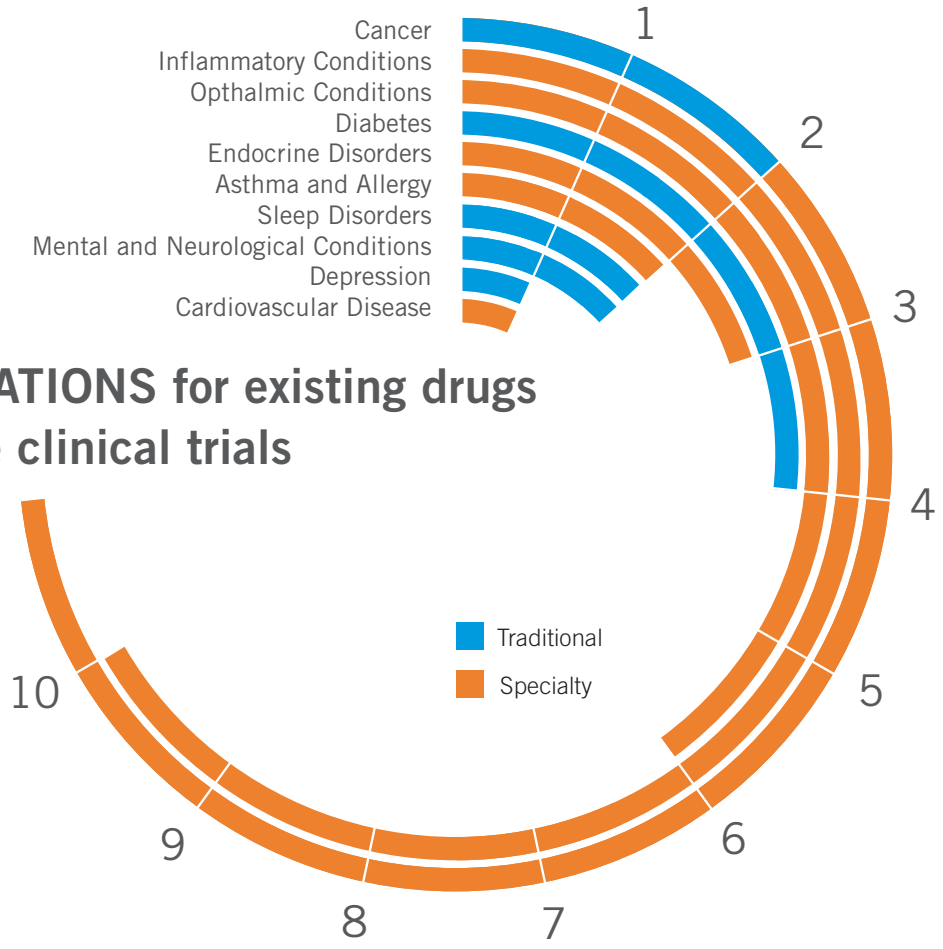
New indications refer to new conditions that can be treated by an existing marketed drug. The new drug indication will have to go through clinical trials and regulatory approval. The categories with the highest number of new drug indications under review are cancer and inflammatory conditions.

Cancer therapies have evolved to treat multiple tumour sites based on a common genetic marker. Therefore, a single drug may receive new indications for multiple tumour locations as scientific research and clinical trials evolve. Likewise, treatments for inflammatory conditions with a common disease pathway may be effective for multiple related conditions.

In the Ophthalmic category, new extended dosage regimen of injectable Vascular Endothelial Growth Factor (VEGF) inhibitors like aflibercept are being reviewed, which could potentially improve adherence.

Currently approved for asthma, NUCALA® (mepolizumab) is being investigated for its potential effectiveness in chronic obstructive pulmonary disease (COPD) with an eosinophilic phenotype. Typically, COPD would be managed using traditional inhalers, which are less costly.

Stay up to date by reading Express Scripts Canada Drug Pipeline Report: https://www.express-scripts.ca/ideas-and-insights/drug-pipeline-reports



NEW INDICATIONS for existing drugs in late-stage clinical trials

Legislative Updates

1. Scope of Practice Changes

The scope of practice for pharmacists and the services they provide continues to evolve in part to reduce the burden on the healthcare system, and address the growing number of Canadians without a family physician. These additional services may facilitate access to care but are unlikely to have a significant impact on private drug claims costs based on the current reimbursement environment.

A pharmacist's scope of practice is regulated provincially and varies across the country[8]. Some examples of expanded scope are assessing patients and prescribing a necessary drug for certain medical conditions, renewing a prescription, adapting a prescription when medication is not optimized, chronic disease management, and ordering lab tests and interpreting their results.

Ontario's pharmacists were authorized to prescribe for 13 minor ailments as of January 1, 2023, which will provide Ontarians with increased access to assessment and treatment for common conditions. The pharmacist's professional fee for the assessment will be funded by the provincial government.

Pharmacists in British Columbia received broadened authority to adapt prescriptions, make therapeutic substitutions, issue emergency supplies and administer prescribed intranasal and injectable medications. The BC College of Pharmacists and the Ministry of Health are working on regulations that would allow pharmacists to prescribe for minor ailments and oral contraception, with a potential spring 2023 implementation.

Dieticians in Quebec were granted the authority to prescribe certain nutritional formulas and enzymes in addition to the ability to adjust patient's insulin and anti-diabetic medications. This may improve access to care but is unlikely to increase claims.

[8] Overview of pharmacy scope of practice across Canada: https://www.pharmacists.ca/advocacy/scope-of-practice/

Legislative Updates cont'd

Quebec's Minister of Health's plan to improve health care and social services over the next three years included an objective to improve healthcare accessibility by allowing pharmacists more autonomy, and increasing the number of services they can offer. In addition, part of a recent agreement between the Quebec Association of Proprietor Pharmacists (AQPP) and Quebec Ministry of Health included an increase in number of clinical services pharmacists can offer.

There are ongoing negotiations to adopt an updated reimbursement model for pharmacists and it is expected to be implemented by April 2024.

Impact to Private Payers

The additional professional services may facilitate easier access to assessment and treatment for common conditions, and alleviate strain on the health care system.

Private plans may see additional drug claims from pharmacist prescribers; due to patients who might have previously avoided seeking care due to backlogs, wait times, or not having a family doctor.

2. Provincial Biosimilars Initiatives

Several lower-cost biosimilar drugs have come to market in recent years for high-cost originator biologics. Several provinces implemented biosimilar switching policies in 2022, and the impact on private plans varies depending on the type of province and program, as well as plan designs.

A. Provincial biosimilar policies implemented in 2022

Alberta, Northwest Territories, New Brunswick and Quebec implemented biosimilar policies in 2022. All are non-pharmacare provinces or territories, so the direct impact on private plans may be minimal.

See Biosimilars section for a review of the impact of provincial policies on private drug plans.

B. Provincial biosimilar policies announced in 2022 with implementation in 2023

Saskatchewan, Nova Scotia and Ontario announced biosimilar policies in 2022 that will be implemented in 2023. Saskatchewan is considered a pharmacare province, therefore their biosimilar policy may have more of an impact on private plans than those in Nova Scotia and Ontario.

3. CADTH Launches Post Market Drug Evaluation Program - Real World Evidence for Decision Making

Canadian Agency for Drugs and Technologies in Health (CADTH) is the organization that reviews drugs and makes reimbursement recommendations to Canada's federal, provincial, and territorial public drug programs, with the exception of Quebec, to guide their drug reimbursement decisions.

They announced a new post-market drug evaluation program to provide government decision-makers with information and advice regarding the safety, effectiveness, and appropriate use of drugs already in use in Canadian healthcare systems.

Legislative Updates cont'd

Although there is no direct impact to private plans, the data published may become useful to private payers who are similarly conducting ongoing drug reviews to ensure access to the most cost-effective therapies. The data could influence drug coverage decisions for private payers, especially for drugs for rare disease where clinical trials are small and usually limited in duration.

4. Pan-Canadian Prescription Drug List

CADTH is continuing work on a potential pan-Canadian prescription drug list, or formulary, which includes consultation periods for stakeholder feedback. It is not clear when and how this formulary may be implemented, and the population it will target, which makes it difficult to assess the potential impact on private drug plans.

5. National Strategy for Drugs for Rare Disease

In March 2023, more details were provided as an update to the federal rare disease program. The announcement clarified that up to $1.4 billion will be made available to provinces and territories through bilateral agreements to improve access to new and emerging drugs.

Funding will support enhanced access to existing drugs, early diagnosis, and screening for rare diseases. There is also funding specifically identified to support eligible First Nations and Inuit patients.

As well, allotments for CADTH and the Canadian Institute for Health Information (CIHI), Canadian Institutes for Health Research will focus on research and data collection.

What to Watch

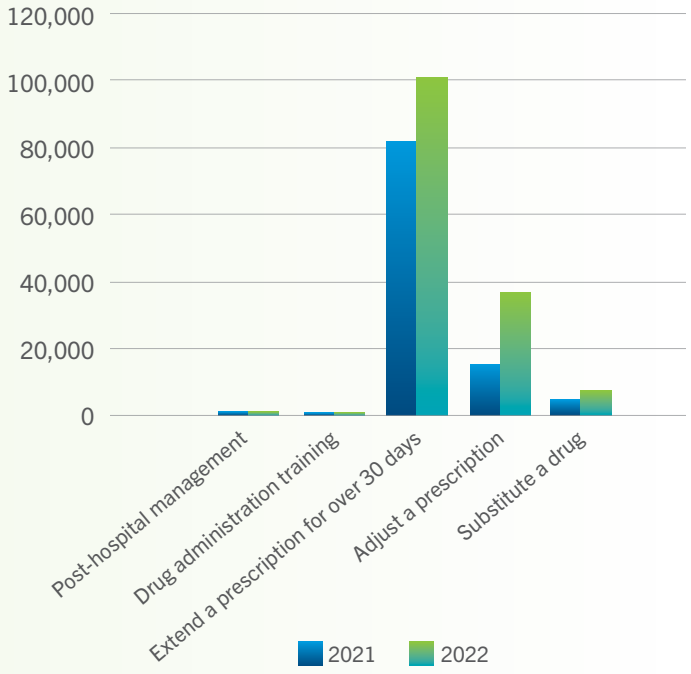
Although drugs or rare disease generally have high annual costs, they can be life-altering for impacted patients. The impact of this program on medication access and private plan costs will be dependent on the program scope.

6. Quebec Clinical Services

There was an increase in the provision of clinical services in 2022. The service of extending a prescription for over 30 days continued to be the most widely used clinical service for private plans. This was followed by adjusting a prescription and then substituting a drug.

The service of adjusting a medication includes modifying a prescription to ensure patient safety or efficacy of treatment or stopping a therapy. Substitution of a drug incorporates replacement of a drug due to a backorder or discontinued medication in addition to safety or administration concerns.

Quebec clinical services reimbursed by private drug plans – 2021 vs. 2022



PLAN ADOPTION

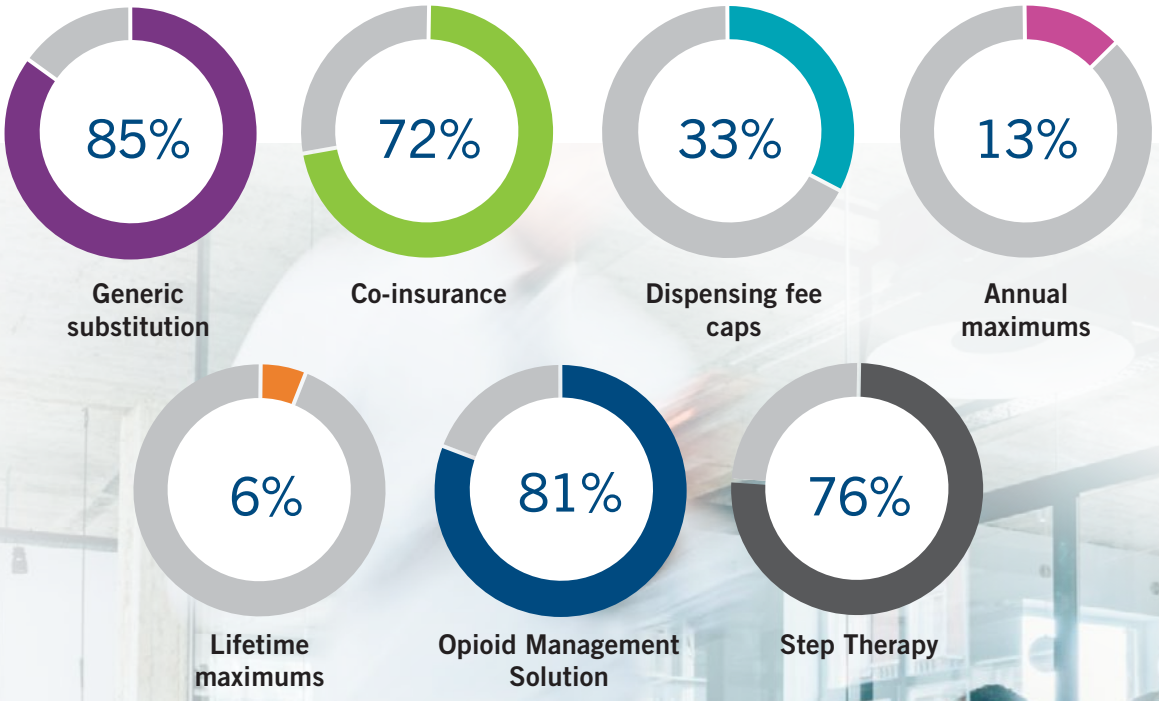
Drug plan management options

As in previous years, drug benefit plans continue to face cost pressures as utilization increases and as more expensive medications come to market, including those that treat common conditions like diabetes, migraine and asthma. Express Scripts Canada offers various drug plan management options that balance the need to lower spend and keep medications available for plan members.

Analysis of the percentage of claims processed in 2022 showed that overall uptake of drug plan management options remained stable compared to 2021.

Below, we take a look at traditional drug plan management options as well newer ones as the drug landscape continues to shift. These options help address the rising cost of drugs while balancing an optimal plan member experience.

Uptake of drug plan management options



Drug plan management options cont'd

Generic Substitution helps manage plan costs for drugs that have interchangeable generic alternatives available. With this plan design, if a brand drug is claimed and has a generic available, the claim's ingredient cost will be reimbursed up to the lower-cost alternative generic medication. The 2022 national uptake showed that 85% of claims had a generic drug plan.

Co-insurance is the percentage of eligible expenses (after the deductible has been paid) that will be reimbursed by the plan. The balance is paid by the plan member, and their financial accountability for a portion of the claim encourages them to play an active role in managing their health and seek out cost effective drugs or pharmacies. In 2022, 72% of claims were subject to a plan that included co-insurance and the most common reimbursement percentage was 80%.

Dispensing Fee Caps Express Scripts Canada manages drug costs, such as drug price, markup and dispensing fees through the usual and customary amounts allowed for drug claims. Some plans choose to add a dispensing fee cap to further manage costs. This is a maximum amount that the drug plan will reimburse towards the dispensing fee. If the member chooses a pharmacy that charges more than the capped amount, they will have to pay the difference. Dispensing fee caps encourage plan members to seek lower cost pharmacies, which helps manage one component of overall drug costs.

In 2022, 33% of claims were subject to a plan with a dispensing fee cap. The majority of those claims (62%) had a plan with a dispensing fee cap between $7.01 and $15.00.

Annual Maximums limits the amount that a plan will pay for drugs for a member each year. In 2022, 13% of claims were subject to a plan that included an annual maximum and 71% of those had an annual limit below $10,000.

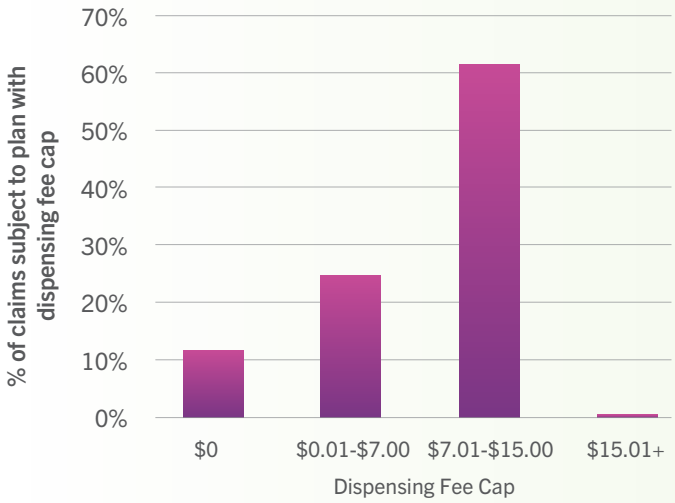
Lifetime Maximums limit the amount that a plan will pay for drugs over a member's lifetime. In 2022, 6% of claims were subject to a plan that included a lifetime maximum, and of those, 51% had lifetime limits below $250,000.

Express Scripts Canada's **Opioid Management Solution (OMS)** offers a robust, clinically sound approach that is focused on driving change, promoting early interventions and safer use of opioids. OMS is designed to address potential dispensing safety gaps and support pharmacists in the dispensing process. The program helps clients and their members by minimizing early opioid exposure and opioid adjacent therapy exposure, and by identifying high opioid dosages and potential duplication of therapies. In 2022, 81% of claims were subject to a plan that included Opioid Management Solution as a drug plan management option.

Step Therapy is used to ensure members try first-line lower cost, clinically effective drugs before stepping up to higher-cost second line treatment options. This approach ensures plan members get the safest, most effective drug treatments – while insurers, plan sponsors and plan members manage their costs. In 2022, 76% of claims were subject to a plan that included Step Therapy as a drug plan management option.

This is list is not meant to be exhaustive, but it demonstrates that there is still room to adopt basic drug plan management options that can yield significant savings to both the plan sponsor and plan member.

Summary of dispensing fee capped amounts



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 amount, 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 spend per claim.

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