2024

Express Scripts Canada
Drug Trend Report

EXPRESS SCRIPTS®

Foreword

The drug benefits landscape in Canada is evolving – shaped by political changes, clinical breakthroughs, and optimizing benefits for a workforce with changing priorities. Express Scripts Canada uses data insights to drive solutions that focus on what matters most to those we serve.

Foreword

In this year's report we shift to highlight the impact of chronic disease. One in three members claimed a drug for one of cardiovascular disease, diabetes and/or obesity. The prevalence of all three conditions — named cardiodiabesity - amongst members is staggering.

Cardiodiabesity and disease progression are costly — to both a member's quality of life and the overall treatment costs. The overall drug spend per member with diabetes continues to increase year over year. Over time, these members are more likely to take additional medications for diabetes as well as medications for related complications, such as nerve pain and eye diseases.

Overall, the relative spend per member increased by 5.2% in 2023 with a decrease in the proportion of members making a claim. This continues the upward trend in spend seen in 2022. We also expect this to continue, as pipeline drugs have the potential to drive drug plan expenditures.

In 2023, we noted trends that will likely increase in the coming years: prescribing of newly marketed high-cost drugs, utilization of advanced technology for diabetes management (including flash glucose monitoring), increased use of ADHD medications, and growing use of biosimilars.

Federal health care policies will continue to bring change to our business. The Pharmacare Act announced in 2024 aims to provide coverage for contraception and select diabetes medications and supplies. The implications on private payers will become clearer following negotiations with individual jurisdictions throughout the year.

At Express Scripts Canada, we continue to provide drug plan solutions to address the shifting drug landscape and focus on opportunities to deliver the best care to Canadians. Together, we will ensure long-term plan sustainability while also addressing the need for inclusive drug benefits.

Mike Roszak
President

1 Drug Trend and Utilization

OVERALL DRUG TREND

Express Scripts Canada tracked trend from a different perspective this year to account for the vast changes in spend, claim and claimant data in 2023. Given these substantial changes, year over year trend could not be reported and compared with the same member base as in 2022. As such, trends outlined in this report have been calculated on a relative instead of absolute basis in 2023. We have confirmed that the large change in absolute data did not have any significant impacts on the underlying trends presented in this report.

Relative Spend per plan member ($)	2022	2023
	$591	$622

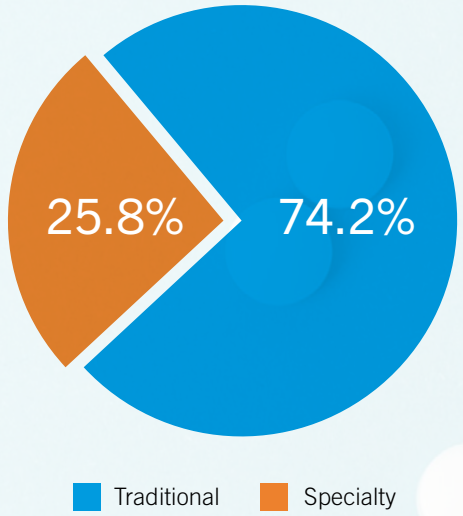
Overall trend (% change) **+5.2%**

Drug Trend and Utilization

TRADITIONAL *VS.* SPECIALTY DRUG TREND

The year over year trend could not be reported with the same member base as in previous years and thus, differs from previous drug trend reports. Based on this, the data needed to be presented in a different way from previous years. In the last 2 years, the proportion of traditional spend continued to hover around 74% to 75%, while specialty spend was estimated around 25% to 26% of overall spend.

Traditional and Specialty Spend 2023



Traditional *vs.* Specialty Drug Trend

Drug type	Estimated annual spend per claimant		2022	2023	Trend*
Traditional drugs	< $10,000	% Spend	74.6%	74.2%	↓ -0.5%
		% Claims	99.4%	99.3%	↓ -0.1%
		% Members with Traditional claim	66.3%	64.6%	↓ -2.6%
Specialty drugs	≥ $10,000	% Spend	25.4%	25.8%	↑ +1.4%
		% Claims	0.6%	0.7%	↑ +16.7%
		% Members with Specialty claim	0.77%	0.76%	↓ -1.3%

*To adjust for the large influx of data, reported trend calculations in 2023 were different than in previous years, using relative rather than absolute changes observed year over year.

There was a 2.6% reduction (not shown in table) in overall members making any drug claim. In addition, the percentage of members with a traditional drug claim dropped to 64.6% in 2023 – a 2.6% decrease compared to 2022. Finally, the percentage of members with a specialty drug claim also decreased slightly to 0.76%.

Drug Trend and Utilization

Top 10 Drugs (by overall spend)

Rank by overall spend	2022		2023	
	Drugs: Chemical name (BRAND)	**Therapeutic class**	**Drugs:** Chemical name (BRAND)	**Therapeutic class**
1	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes
2	Adalimumab* (HUMIRA®)	Inflammatory Conditions	Adalimumab* (HUMIRA®)	Inflammatory Conditions
3	Infliximab* (REMICADE®)	Inflammatory Conditions	Infliximab* (REMICADE®)	Inflammatory Conditions
4	Ustekinumab (STELARA®)	Inflammatory Conditions	Ustekinumab (STELARA®)	Inflammatory Conditions
5	Lisdexamfetamine (VYVANSE®)	ADHD	Lisdexamfetamine (VYVANSE®)	ADHD
6	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies
7	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis
8	Empagliflozin (JARDIANCE®)	Diabetes	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD
9	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis	Empagliflozin (JARDIANCE®)	Diabetes
10	Budesonide-Formoterol (SYMBICORT®)	Asthma/COPD	Dupilumab (DUPIXENT®)	Skin Conditions

*Biosimilar(s) or generic(s) available

The top five drugs ranked by overall spend remained unchanged in 2023. These drugs continue to drive the spend in their respective therapeutic classes: semaglutide in Diabetes, adalimumab, infliximab and ustekinumab in Inflammatory Conditions and lisdexamfetamine in ADHD.

Flash Glucose Sensors (FREESTYLE LIBRE®) moved up from 7th to 6th place, due to a 12% increase in claimants and 13.3% increase in the number of claims. Popularity of this alternative to traditional blood glucose monitoring continues to grow. A newer version of the FREESTYLE LIBRE® is expected in the coming year, with the smallest sensor available in the market that allows for continuous glucose monitoring, this could further expand its patient base. Coverage for continuous glucose monitoring (CGM) devices will remain a point of discussion in the coming years. These CGM devices have previously been covered under extended health care benefits, however, with technology that blurs the line between flash and continuous blood glucose monitoring, classification could be reconsidered.

Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®) moved up from 9th to 7th place, due to a 19.7% increase in claimants. In 2023, the expanded indication, to include children as young as 2 years of age, increased the eligible patient population and could have accounted for a portion of the increase in claimants. Patients also switched from the other Cystic Fibrosis medications to this newer option. The high cost of this medication will likely keep this drug in the top 10 list.

Dupilumab (DUPIXENT®) moved into 10th place, with a 49.6% increase in claimants and a 26.9% increase in spend. Previously approved for atopic dermatitis and severe asthma, this drug continued to accumulate new indications. In 2023, it was approved for the treatment of prurigo nodularis and eosinophilic esophagitis while also receiving an expanded indication for atopic dermatitis for patients as young as 6 months of age.

Budesonide-Formoterol (SYMBICORT®) moved out of the top 10, due to a 5.5% decrease in claimants and a 1.1% decrease in claims. This is likely stabilization after considerable increases in claimants and claims in 2022. Since its approved use as an “as needed” inhaler for relief of acute attacks, patients may have not needed regular fills of this drug.

Drug Trend and Utilization

Top 10 Specialty Drugs (by overall spend)

Rank by overall spend	2022		2023	
	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	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis
5	Dupilumab (DUPIXENT®)	Skin Conditions	Dupilumab (DUPIXENT®)	Skin Conditions
6	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease
7	Ocrelizumab (OCREVUS®)	Multiple Sclerosis	Risankizumab (SKYRIZI®)	Inflammatory Conditions
8	Omalizumab (XOLAIR®)	Asthma/COPD	Ocrelizumab (OCREVUS®)	Multiple Sclerosis
9	Golimumab (SIMPONI®)	Inflammatory Conditions	Omalizumab (XOLAIR®)	Asthma/COPD
10	Etanercept* (ENBREL®)	Inflammatory Conditions	Golimumab (SIMPONI®)	Inflammatory Conditions

*Biosimilar(s) available

More than half of the Top 10 Specialty Drugs are used for the treatment of Inflammatory Conditions such as rheumatoid arthritis, Crohn's disease and psoriasis.

Adalimumab (HUMIRA®), infliximab (REMICADE®) and ustekinumab (STELARA®) retained their top rank positions in 2023, which together accounted for 6.9% of overall spend in 2023. Adalimumab and infliximab spend decreased due to biosimilar availability and adoption of biosimilar transitioning policies. Ustekinumab (STELARA®) biosimilars have been approved by Health Canada and were marketed in early 2024. We can anticipate that these biosimilars will be added into biosimilar transition initiatives and will lower spend on this popular therapy.

Risankizumab (SKYRIZI®) moved into the top 10 specialty drugs in 7th place, in part due to a 67.6% increase in claimants. This drug was approved for new indications in late 2022 for Crohn's disease and psoriatic arthritis, which expanded the eligible patient population. There are currently no biosimilars available for this molecule.

Outside of the top 10, other Specialty drugs that showed notable increases in spend in 2023:

- Bimekizumab (BIMZELX®), which was approved in 2022, showed substantial uptake in 2023 (+300% in spend). This molecule was shown to be more efficacious than adalimumab, secukinumab and ustekinumab for the treatment of psoriasis. In clinical trials, more patients treated with bimekizumab achieved complete clearance of psoriasis compared to these other drugs.
- Ofatumumab (KESIMPTA®) for multiple sclerosis had a 100% increase in spend. Clinical trial data published in 2023 showed that this treatment had sustained efficacy over the course of five years. This long-term data may help support its use. This drug can also be self-administered which may be favoured by patients.

Drug Trend and Utilization

Top 10 Traditional Drugs (by overall spend)

Rank by overall spend	2022		2023	
	Drugs: Chemical name (BRAND)	**Therapeutic class**	**Drugs:** Chemical name (BRAND)	**Therapeutic class**
1	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes
2	Lisdexamfetamine (VYVANSE®)	ADHD	Lisdexamfetamine (VYVANSE®)	ADHD
3	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies
4	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic Supplies	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD
5	Empagliflozin (JARDIANCE®)	Diabetes	Empagliflozin (JARDIANCE®)	Diabetes
6	Budesonide-Formoterol (SYMBICORT®)	Asthma/COPD	Rosuvastatin* (CRESTOR®)	High Cholesterol
7	Rosuvastatin* (CRESTOR®)	High Cholesterol	Budesonide-Formoterol (SYMBICORT®)	Asthma/COPD
8	Sitagliptin-Metformin (JANUMET®)	Diabetes	Escitalopram* (CIPRALEX®)	Depression
9	Escitalopram* (CIPRALEX®)	Depression	Blood Glucose Test Strips (various brands)	Diabetic Supplies
10	Blood Glucose Test Strips (various brands)	Diabetic Supplies	Onabotulinumtoxin-A (BOTOX®, XEOMIN®)	Muscle Relaxant

*Generic(s) available

Semaglutide (OZEMPIC®, RYBELSUS®) for the treatment of type 2 diabetes continued to be the top drug by overall spend in 2023. OZEMPIC® was plagued by several periods of shortages in 2023. The newest drug in this class, tirzepatide (MOUNJARO®) was available in the last quarter of the year. However, this latter product was only available as single-use vials, which was an inconvenient dosage form for patients. The single-use pens will be marketed in 2024. MOUNJARO® will be followed closely in upcoming years as trials showed efficacy to exceed that of OZEMPIC® and thus, prescribers may favour this agent within the class.

See our section on CARDIODIABESITY

Rosuvastatin (CRESTOR®) moved up from 7th to 6th place, with a 3.6% increase in claimants and a 2.8% increase in claims. This is a genericized product that retained its position due to the steady growth in number of claimants while maintaining relatively low cost. The average annual spend per claimant is about $90.

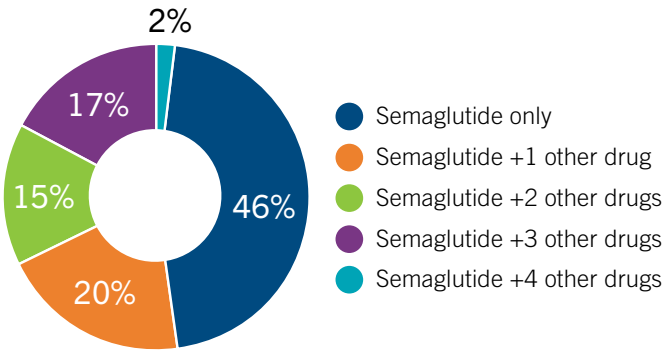
Escitalopram (CIPRALEX®) moved up from 9th to 8th place, in part due to Sitagliptin-Metformin (JANUMET®) moving out of the top 10 traditional drugs. JANUMET® fell out of the top 10 this year due to the availability of marketed generics. This popular drug was the first available in its subclass and therefore, became the most popular. The availability of lower-cost generics significantly impacted spend.

Onabotulinumtoxin-A (BOTOX®) moved into the top 10 this year. This drug has multiple indications including cervical dystonia and chronic migraine prevention. Access to this therapy is generally granted through prior authorization programs to ensure claims are not paid for cosmetic purposes.

Drug Trend and Utilization

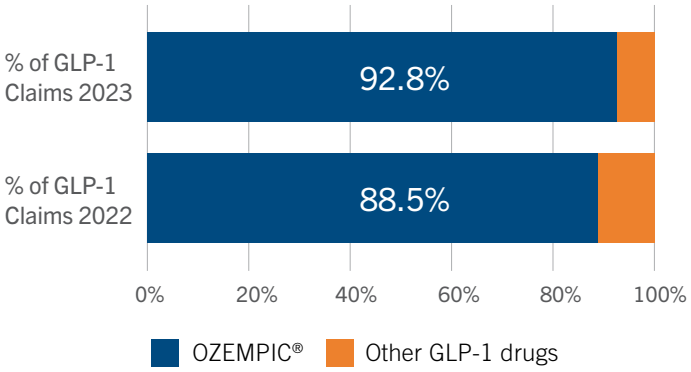
DIABETES

Percentage of semaglutide claimants and number of other diabetes drugs claimed in 2023



Analysis of semaglutide (OZEMPIC® and RYBELSUS®) claims identified that 46% of patients claimed semaglutide as their only diabetes drug treatment, which was up from 31% in 2022. Semaglutide is approved to be used alone when first-line drugs are not tolerated. However, treatment guidelines for diabetes recommend cumulative therapy with multiple agents. This emphasizes the importance of Prior Authorization programs, which consider appropriate first-line diabetes treatments prior to using semaglutide.

Proportion of GLP-1 claims - 2022 vs. 2023

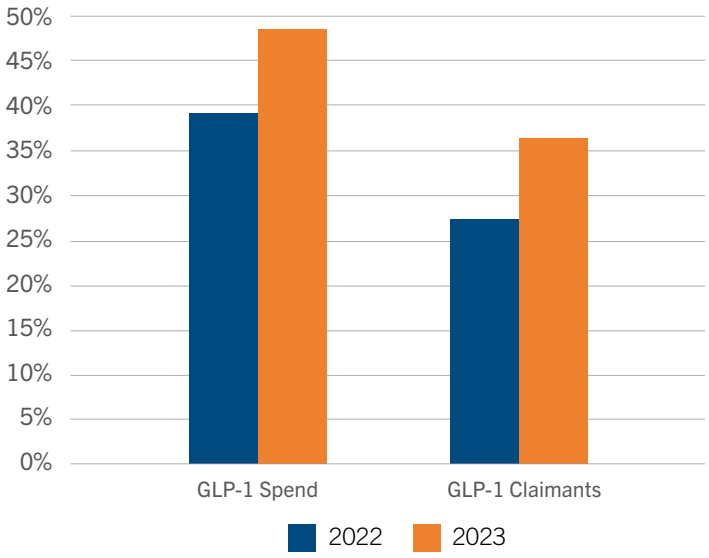


When we assessed the GLP-1 agonist drugs, OZEMPIC® claims continued to make up the majority of claims. We even saw an increase in OZEMPIC® claims despite product shortages throughout 2023 and there was no significant shift towards other GLP-1 agents. OZEMPIC® continued to show an increase in the proportion of claims. Claims for the oral formulation of semaglutide (RYBELSUS®) dropped slightly from 3.2% to 3.0%. Similarly, liraglutide (VICTOZA®) and dulaglutide (TRULICITY®) saw small decreases in the proportion of claims.

OZEMPIC® and other GLP-1 drugs are associated with adverse effects which may not be tolerated by all patients. Doses are started low and titrated up slowly to minimize the side effects such as nausea, which is the most commonly reported side effect among patients. Our 2023 data demonstrated that 43% of new OZEMPIC® claimants (not shown in graphs) were non-adherent to therapy. These patients had not claimed a refill for the drug for over 120 days.

GLP-1 Agonist drugs

Percentage of GLP-1 spend and claimants in diabetes class - 2022 vs. 2023



When we focused on all GLP-1 agonist drug data, there was a 9% increase in claimants between 2022 and 2023. At the same time, spend increased by 10%. This whole sub-class of diabetes drugs provides the additional benefit of weight loss as a common effect.

Drug Trend and Utilization

TOP THERAPEUTIC CLASSES

Express Scripts Canada tracked trend from a different perspective this year to account for the vast changes in spend, claim and claimant data in 2023. That being said, the top four therapeutic classes in terms of spend remain unchanged in 2023 compared to 2022.

Cardiovascular Disease and Ulcer/Reflux have fallen out of the Top 10, while Diabetic Supplies and High Cholesterol filled spots 9 and 10 respectively. The Cancer class rose from 6th to 5th place and the Attention Deficit Hyperactivity Disorder (ADHD) class also jumped one place from 7th to 6th.

Several categories of the top classes were related to our focus topic of cardiodiabesity: high cholesterol, diabetes, diabetic supplies, and high blood pressure.

Top 10 Therapeutic Classes (by overall spend)

Rank 2023	Rank 2022	Change	Therapeutic class	% of overall spend 2023	% of overall spend 2022	% of overall claims 2023	% of overall claims 2022	Relative Trend	
								% of overall spend	% of overall claims
1	1	–	Inflammatory Conditions	12.1%	12.6%	0.4%	0.4%	-3.5%	+7.6%
2	2	–	Diabetes	11.8%	11.6%	7.1%	6.5%	+1.2%	+8.5%
3	3	–	Asthma/COPD	5.0%	5.2%	3.9%	4.1%	-5.4%	-4.9%
4	4	–	Depression	4.6%	5.0%	8.9%	9.2%	-7.1%	-4.1%
5	6	+1	Cancer	4.5%	4.3%	0.6%	0.6%	+4.0%	-0.1%
6	7	+1	ADHD	4.2%	3.8%	2.7%	2.4%	+9.6%	+11.2%
7	5	-2	High Blood Pressure	4.1%	4.4%	13.3%	13.6%	-6.5%	-2.5%
8	8	–	Skin Conditions	3.5%	3.1%	2.9%	2.7%	+11.3%	+5.7%
9	14	+5	Diabetic Supplies	2.8%	2.5%	1.4%	1.3%	+12.5%	+3.6%
10	11	+1	High Cholesterol	2.7%	2.7%	7.0%	7.0%	-0.8%	+0.1%

ADHD: Attention deficit hyperactivity disorder; COPD: chronic obstructive pulmonary disease

#1 Inflammatory Conditions:

Spend in the Inflammatory Conditions class decreased by 3.5% overall but remains the top class. The top three drugs by overall spend continue to be adalimumab, infliximab and ustekinumab.

Spend on adalimumab (HUMIRA®) decreased by 13.3%, whereas infliximab (REMICADE®) spend decreased by 9.2%. These decreases can be attributed to the use of lower-priced biosimilars and adoption of biosimilar transition policies. In contrast, ustekinumab (STELARA®) spend increased by 1.5%, in part due to a 2.5% increase in claimants. Biosimilars for ustekinumab were approved by Health Canada in late 2023 and have been marketed in early 2024.

The two drugs which saw the highest growth in this class were risankizumab (SKYRIZI®) and upadacitinib (RINVOQ®). Although both drugs did not contribute significantly to the overall spend, the 60% and 49% respective increases in spend were the most significant for this class. These advanced therapies have followed the trend of others as new trials continued for additional uses after initial market release. SKYRIZI® received new indication approvals for Crohn's disease and psoriatic arthritis in late 2022 while RINVOQ® received new indications for both ulcerative colitis and Crohn's disease in 2023.

Drug Trend and Utilization

#2: Diabetes and #9: Diabetic Supplies

The number of claimants for Diabetes medications increased by 10%, which increased spend by 1.2%. The prevalence of diabetes continues to increase year over year nationally and thus, spend and claimant numbers were expected to rise.

As in previous years, semaglutide (OZEMPIC®, RYBELSUS®) remained the top drug in overall spend in 2023; the number of claimants increased by 50% and overall spend increased by 30.6%. Payers continue to monitor for appropriate use of semaglutide and other GLP-1 agonists in this class.

Another notable molecule in this class was empagliflozin (JARDIANCE®) for which overall spend increased by 5.6%, in part due to an 8% increase in claimants.

Additionally, spend on common insulin products fell between 5-10% as less costly biosimilar products were introduced for insulin glargine, lispro, and aspart in recent years.

New to the top 10 therapeutic classes, Diabetic Supplies, which accounted for 2.8% of overall spend in 2023. The Diabetic Supplies class jumped significantly over the past six years and was up from 17th place in 2018 to 9th place in 2023. While measures were adopted to limit blood glucose test strips coverage, the availability of flash glucose sensors caused spend in this class to significantly increase.

Flash glucose sensors were responsible for a 24% increase in diabetic supplies spend and 12% increase in claimants while the reductions in spend and claimants for blood glucose test strips were 11% and 7%, respectively. Comparing the cost of the newer technology: the annual spend per claimant for flash glucose sensors was about $1,200 while test strips was about $190.

See our section on CARDIODIABESITY

#3: Asthma/COPD

The number of claimants for Asthma/COPD treatments decreased by 8.9%, which decreased overall spend by 5.4%. However, this therapeutic class still remained in the top 3.

As the top drug in this class, budesonide-formoterol (SYMBICORT®) overall spend decreased by 4%, driven in part by a 5.5% decrease in claimants. Salbutamol (VENTOLIN® and its generic alternatives) had a 9.9% decrease in claimants, which decreased overall spend by 10.8%. Previous year data (2022) saw significant increases in the temporary use of these inhalers, which was not as apparent in 2023.

Mepolizumab (NUCALA®) and omalizumab (XOLAIR®) were the biologics in this class with the highest spend. NUCALA® overall spend increased by 13.1% while XOLAIR® overall spend decreased by 4.8%. There are biosimilars under development for NUCALA® which may reduce spend in this category once approved.

Drug Trend and Utilization

#4: Depression

The number of claimants for depression treatments decreased by 4.6%, which led to a 4.1% decrease in claims and 7.1% decrease in spend. The majority of antidepressants have multiple generic alternatives. Selective serotonin reuptake inhibitors (SSRIs) continue to drive the spend in this class making up over 40% of spend for the Depression category. Most therapies in this class saw a decrease in spend, except for agents such as esketamine and bupropion.

#5: Cancer

In 2023, Cancer drug spend increased by 4% which only boosted its ranking by one place. A number of oral targeted therapies are in the top spend including ibrutinib, palbociclib, ribociclib, and olaparib. Some provincial oncology programs do not cover oral drugs and thus, the costs of these medications impacted private plans.

The prevalence of breast cancer continues to drive spend in the cancer therapeutic class. One of the therapies with the highest growth in claimants was abemaciclib (VERZENIO®), which was originally approved for use in advanced and metastatic breast cancer and received Health Canada approval for early breast cancer in 2022.

#6: ADHD

The number of claimants for ADHD treatments increased by 12.7%, which increased claims by 11.2% and spend by 9.6%. The two ADHD drugs which have continued to be prominent in the top 10 drug list over the years were lisdexamfetamine and methylphenidate. Although new claimants were mostly adults in this class, the most prevalent patients are still those under the age of 18.

Lisdexamfetamine (VYVANSE®), had a 25% increase in claimants, which led to a 24.7% increase in claim volume and a 22.3% increase in spend. VYVANSE® remains one of the last branded products in the class with generic alternatives anticipated to be marketed this year. With many generic options, methylphenidate (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®) overall spend increased by 1.9%, in part due to a 5% increase in claimants and a 3.8% increase in claims.

#10 High Cholesterol

High Cholesterol has not been part of the Top 10 classes for the past six years. Over 40% of Canadian adults have high cholesterol. This condition is also highly prevalent in patients with obesity and diabetes, and increases the risk of developing cardiovascular disease.

See our section on **CARDIODIABESITY**

The popularity of the higher-cost proprotein convertase subtilisin/kexin type 9 (PCSK-9) therapies has moved this class into the Top 10. Comparatively, the average annual cost of a PCSK-9 drug is 30 times that of a statin. Inclisiran (LEQVIO®) was a new entrant in this class in 2023 and had significant uptake by claimants. Other PCSK-9 inhibitors, alirocumab (PRALUENT®) and evolocumab (REPATHA®), also demonstrated double-digit growth in spend (22% and 18% respectively) and increases in claimants. This occurred as the spend and claimant number for statins remained relatively unchanged.

CARDIODIABESITY

'Cardio-dia-besity' is a term that captures the complex interrelationship between cardiovascular disease, diabetes, obesity, and metabolic syndrome. Metabolic syndrome is a cluster of health conditions including high blood pressure, impaired blood sugar levels, and large waist circumference that underlie cardiodiabesity. In 2023, about one in three individuals in the Express Scripts Canada database submitted a claim for at least one drug used to treat cardiovascular disease, diabetes and/or obesity.

COMORBIDITY

Comorbidity refers to the simultaneous presence of two or more diseases or medical conditions in a patient. Analysis of the comorbidity data for cardiovascular disease, diabetes, and obesity drugs provided interesting insights about the profile of each cohort of claimants.

Diabetes

Diabetes has been the second highest therapeutic class by spend for the last six years. The increase in the number of claimants each year represented an uptrend for diabetes prevalence. Adding to the complexity of the disease, patients with diabetes are at a greater risk of cardiovascular morbidity due to the progressive damage to the heart, nerves, eyes, and kidneys. We examined the data to look for correlations between the drugs used to treat these complications in diabetes claimants. These drugs were categorized by the following classes:

- **Cardiovascular Disease:** drugs used for high blood pressure, high cholesterol, arrhythmia and anticoagulation
- **Neuropathy:** includes anticonvulsants which may be used for neuropathic pain. These drugs have multiple indications and therefore, data for neuropathy may be overestimated.
- **Obesity:** drugs indicated for weight loss (XENICAL®, CONTRAVE®, and SAXENDA®)
- **Eye Disease:** VEGF inhibitors indicated for the treatment of eye diseases associated with diabetes. These drugs also have other uses and thus, this data may also be overestimated.

Among claimants with diabetes, a high proportion of them (81.9%) submitted a claim for cardiovascular drugs in 2023. This value has been relatively consistent from 2018 to 2023, where on average 81.2% of claimants with diabetes also submitted a claim for cardiovascular drugs. It is expected that most patients with type 2 diabetes are prescribed high blood pressure and/or high cholesterol drugs to reduce their cardiovascular risk, which aligns with clinical practice guideline recommendations for diabetes.

The 2023 data also revealed that diabetic neuropathy (i.e., nerve damage) has likely developed in 11.2% of these diabetes drug claimants. The proportion of diabetes drug claimants claiming for neuropathic drugs gradually increased from 9.9% in 2018. With a much smaller correlation, claims for drugs used for the treatment of diabetic macular edema and macular degeneration make up less than 1% of diabetes claimants and represented patients with more advanced disease. This value has increased by 0.2% from 2018. Lastly, only a small portion of diabetes claimants had an obesity drug, which may be due to either the lack of drug coverage, or that patients may already be on a diabetes drug with inherent weight loss benefit.

Cardiovascular Disease and Obesity

Of the claimants with cardiovascular disease in 2023, about 26% were also using a diabetic drug. Similar to the claimants with diabetes, the proportion of patients has been quite consistent from 2018 to 2023. To further demonstrate the interconnection of cardiovascular disease, diabetes, and obesity, in members who claimed a drug for obesity, 41.5% claimed a drug for cardiovascular disease in 2023.

Drug Trend and Utilization

Notably, obesity is one of the few chronic conditions for which drugs are not readily covered by drug plans. In contrast, most drugs for diabetes and cardiovascular disease are widely covered. This was evident in 2023, where obesity drugs accounted for less than 0.5% of claimants and overall spend with the minority of plan members having coverage. Also, plan policies often impose maximum limits on obesity drugs, which do not adequately cover the cost for long-term treatment and effectively restrict overall access to these drugs.

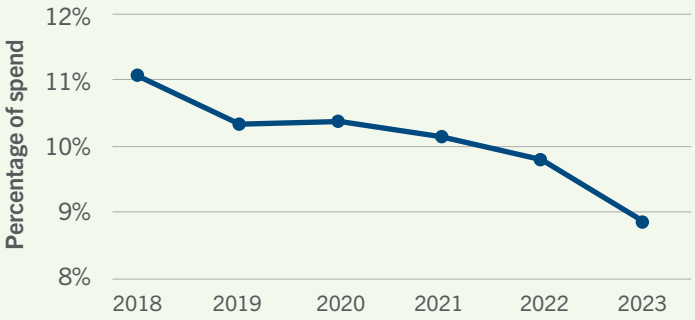
Impact of Cardiodiabesity on Drug Plans

Patients with cardiodiabesity have overlapping risk factors. People with obesity are at a higher risk of developing diabetes and cardiovascular disease, and those with diabetes are more likely to develop cardiovascular complications. Increased prevalence of any of these conditions have financial impact associated with drug treatments and other medical interventions related to these conditions.

CARDIOVASCULAR DISEASE

Cardiovascular disease continues to be the second leading cause of death in Canada.[1] Recent statistics from 2021 estimated that around 2.4 million Canadians were diagnosed with heart disease.[2] Cardiovascular Disease claimants represent about 27.7% of all claimants in 2023 and these drugs represented 8.9% of overall spend in 2023. The percentage of spend on cardiovascular drugs has decreased over the last 6 years as seen in the graph below. The loss of patent and genericization of drugs in this class have reduced impact to overall spend over time.

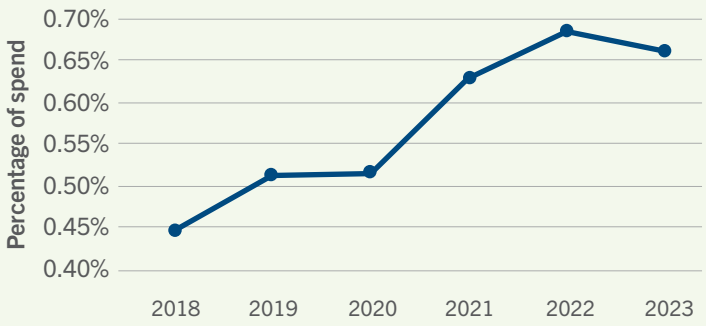
Percentage of overall spend on Cardiovascular drugs



OBESITY

Not surprisingly, obesity drug claimants represented less than 0.5% of all claimants for the last 6 years and impact to overall spend has been minimal. Due to limitations in coverage for obesity drugs, patients living with obesity are likely underreported in our data compared to Canadian estimates, where around 8.7 million Canadians were classified as obese in 2022, which increased from around 7.3 million in 2018.[3]

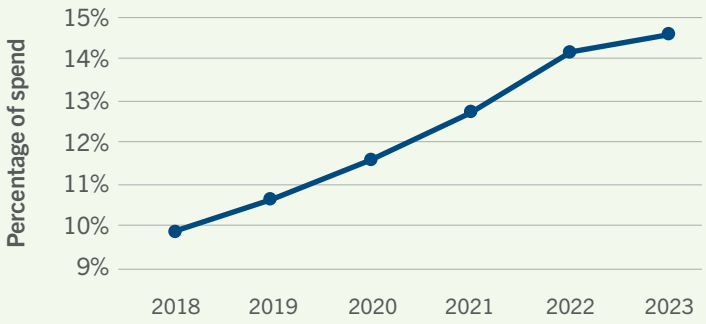
Percentage of overall spend on Obesity drugs



DIABETES AND DIABETIC SUPPLIES

The drivers of diabetes drug spend are the increasing costs of newer drugs and the cumulative approach of add-on treatments. Shown in the graph below, overall spend on diabetes drugs and diabetic supplies has increased over time from 9.9% in 2018 to 14.6% in 2023.

Percentage of overall spend on Diabetes drugs and Diabetic Supplies

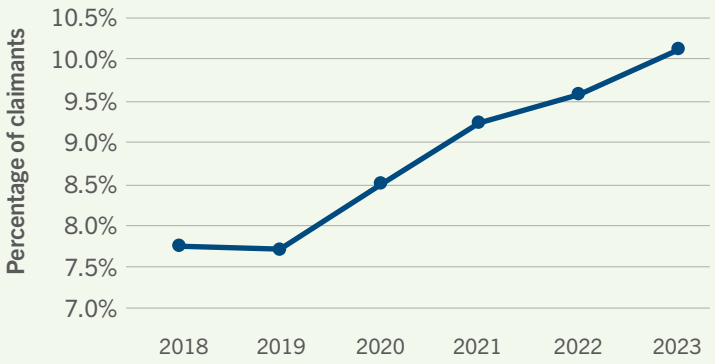


[1] Leading causes of death, total population, by age group (statcan.gc.ca)
[2] Cardiac care | CIHI
[3] Statistics Canada. Table 13-10-0096-01 Health characteristics, annual estimates

Drug Trend and Utilization

Another driver of diabetes drug spend is increasing prevalence. The graph at right shows the proportion of diabetes claimants has increased over the last 6 years making up 10.1% of all claimants by 2023. The actual prevalence of diabetes cannot be represented since the graph on the right only considers members who have claimed diabetes drugs. Pre-diabetic members or members not on diabetes medications would not be captured. Recent data from Diabetes Canada estimated that there was approximately 11.9 million Canadians living with diabetes (diagnosed and undiagnosed) or prediabetes in 2023[4].

Percentage of overall claimants for Diabetes drugs

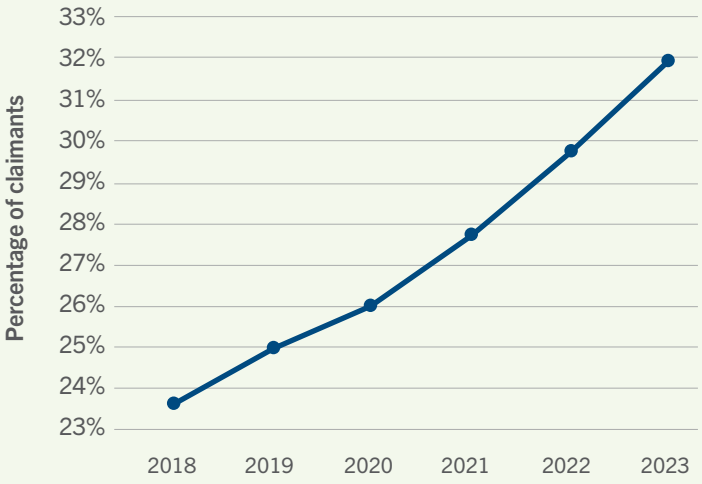


DISEASE PROGRESSION

Disease progression was observed by following a group of patients on one class of medication and following them for 6 years. After 6 years, we saw that each patient group showed possible development of comorbid conditions based on their drug claims.

CARDIOVASCULAR DRUG CLAIMANTS

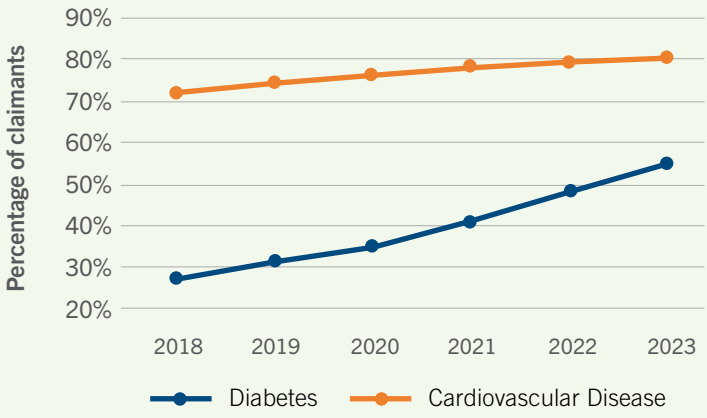
Percentage of Cardiovascular drug claimants taking Diabetes drugs



Our analysis identified that there was a consistent increase in the proportion of cardiovascular drug claimants who also had claims for diabetes drugs each year, demonstrating an 8.3% increase from 2018 to 2023.

OBESITY DRUG CLAIMANTS

Percentage of Obesity drug claimants taking Diabetes and Cardiovascular drugs



A similar year-over-year increase was observed in the proportion of obesity drug claimants, who also claimed cardiovascular drugs from 2018 to 2023, having a total increase of 8.6%. Meanwhile, the data showed a more dramatic increase of 27.3% in obesity drug claimants who also had claims for diabetes drugs in the last 6 years. Although the data presented here are correlational and limited to a 6-year horizon, they are consistent with the interrelationship observed in literature between cardiovascular disease, diabetes, and obesity.

[4] Diabetes in Canada National Backgrounder 2023

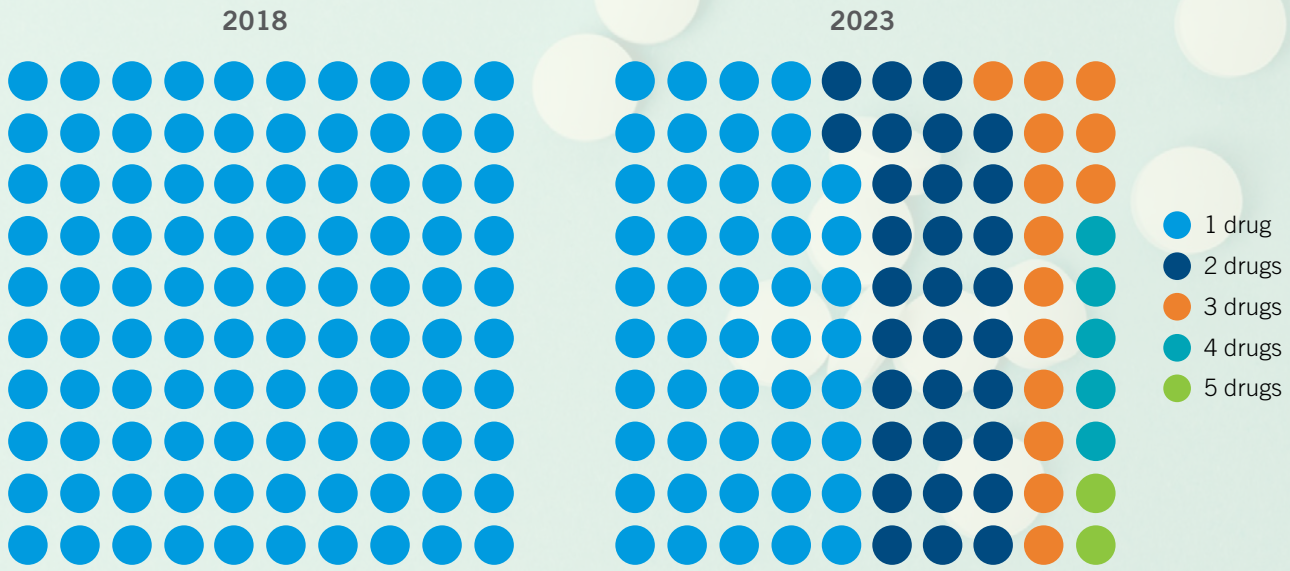
Drug Trend and Utilization

DIABETES DRUG CLAIMANTS

Progression of diabetes can also be observed by examining the cumulative number of add-on treatment and the need for other drugs to manage the complications of diabetes over time.

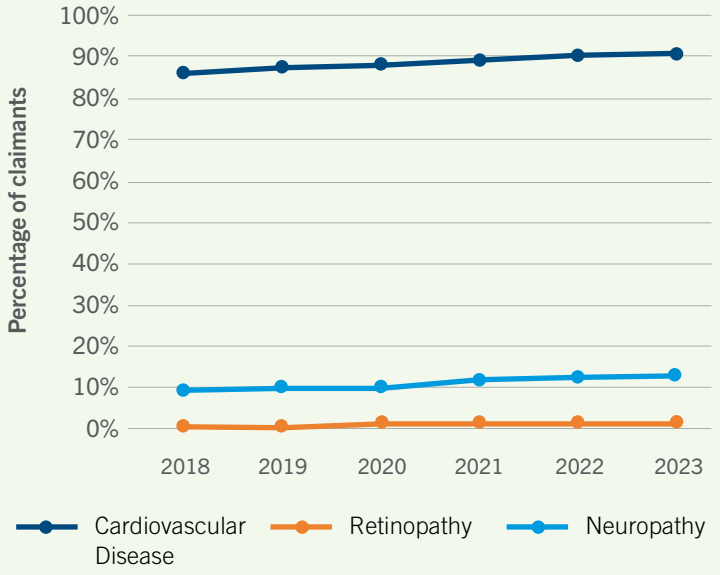
Based on the figure below, by the end of 2023, 48% of the 2018 diabetes drug claimants were still on one drug, while the rest (52%) were on more than one diabetes drug. This would suggest worsening and progression of disease as these claimants required additional diabetes drugs.

Proportion of claimants on one diabetes drug in 2018 over 6 years



Furthermore, in the same cohort of diabetes drug claimants, there was a continued year-over-year increase in claims for drugs used in cardiovascular disease, neuropathic pain, and retinopathy drugs. This trend is consistent with the progressive nature of diabetes which predisposes patients to develop cardiovascular-related complications later in their diagnosis such as nerve damage (diabetic neuropathy) and eye damage (retinopathy). Although the graph on the right showed small increases in the percentage of claimants requiring additional drugs to treat complications (cardiovascular disease, retinopathy and neuropathy), it is suggestive of diabetes progression of disease from 2018 to 2023.

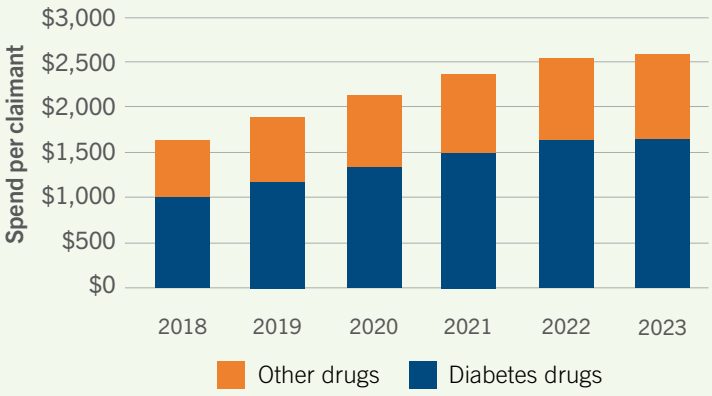
Percentage of Diabetes drug claimants taking cardiovascular, retinopathy and neuropathy drugs



Drug Trend and Utilization

Adding the cost of diabetes drugs to other drugs used to treat complications gives more insight into the overall drug cost associated with a claimants with diabetes. The graph below shows the increase in overall diabetes drug spend from about $1,650 to $2,600 annually. Diabetes drugs (in blue) remained the driver of this increase in spend relative to other drugs to treat cardiovascular, neuropathy and retinopathy complications (in orange).

Average spend for the 2018 diabetes drug claimants from 2018 to 2023



Cardiodiabesity is on the rise. The number of different drugs a claimant takes can increase over time, which can be attributed to disease worsening and the development of other medical conditions. Drug management of cardiodiabesity involves a multi-pronged approach, which focuses on interventions for weight management alongside cardiovascular and diabetes treatments. Newer drugs in the market (see *Drug Pipeline* section) have the potential to address each aspect of cardiodiabesity and provide long-term health outcomes from cardiovascular complications. Appropriate drug category management is required to ensure members have access to appropriate therapies for these chronic diseases. This includes re-considering coverage for therapies to treat obesity and potential plan management strategies for diabetes drugs including Step Therapy and Prior Authorization.

2 Pharmacy Landscape

BIOSIMILARS

2023 HIGHLIGHTS

- Ontario's biosimilar transition period concluded at the end of December 2023
- Yukon's first transition phase was completed in October 2023, with a second transition phase extending until May 2024
- Newfoundland and Labrador and Prince Edward Island announced initiatives that will be completed in 2024
- HUMALOG® was added back to biosimilar programs in British Columbia and Saskatchewan after shortage of the biosimilar was resolved
- Health Canada confirmed insulin pump compatibility with HUMALOG® biosimilar
- Availability of biosimilar for popular LUCENTIS® therapy for eye diseases becomes the newest target for provincial programs

Pharmacy Landscape

Biosimilar quick reference chart

Chemical name	Corresponding originator
Adalimumab	HUMIRA®
Bevacizumab	AVASTIN®
Enoxaparin	LOVENOX®
Etanercept	ENBREL®
Glatiramer	COPAXONE®
Infliximab	REMICADE®

Chemical name	Corresponding originator
Insulin aspart	NOVORAPID®
Insulin glargine	LANTUS®
Insulin lispro	HUMALOG®
Ranibizumab	LUCENTIS®
Rituximab	RITUXAN®
Teriparatide	FORTEO®

National biosimilar penetration rate

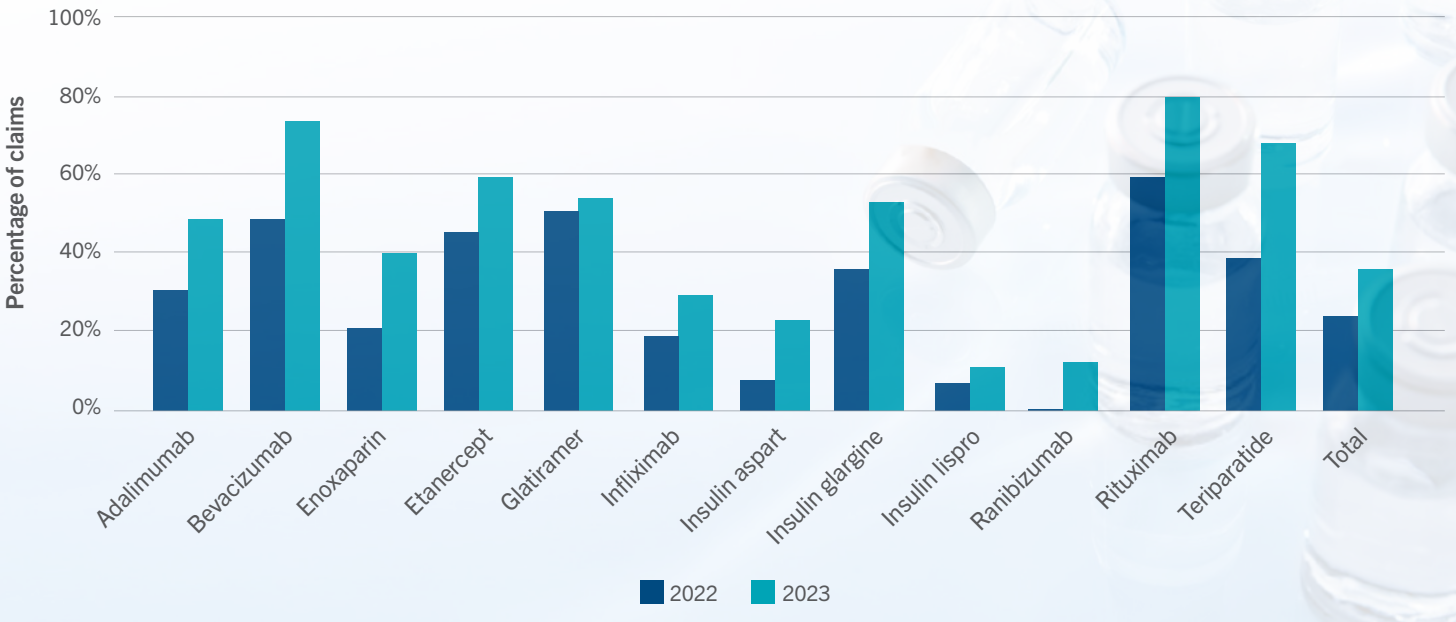
The national biosimilar penetration rate is calculated by comparing the percentage of biosimilar claims for specific drugs in each year. The overall biosimilar penetration rates increased from 23.5% to 35.8% in 2023.

Similar to 2022, rituximab and bevacizumab have the highest biosimilar penetration rates overall, likely due to short-term use for oncology indications. Rituximab is used to treat both inflammatory conditions and cancer while bevacizumab is primarily used to treat cancer. As cancer treatments, these drugs are generally used for shorter durations than other biologics which may be used long-term to treat inflammatory conditions.

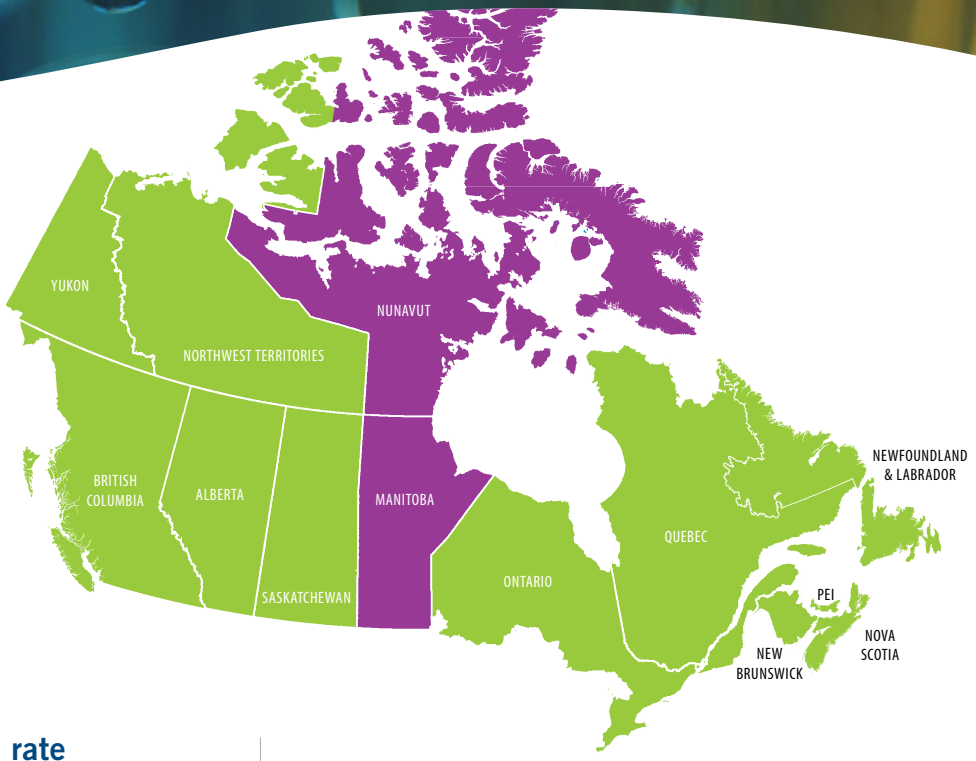
Use of teriparatide biosimilars increased by approximately 28% and was only included in the Quebec biosimilar initiative. Teriparatide (FORTEO®) is a treatment used for osteoporosis with a maximum duration of treatment of two years.

The insulin lispro biosimilar continued to have the lowest penetration rate amongst the molecules with biosimilars available. This is likely due to a short supply of the biosimilar that occurred in 2023 which delayed the transition policies targeting this molecule.

National biosimilar penetration rate – Percentage of claims in 2022 and 2023



Pharmacy Landscape



2023 Provincial Biosimilar Policies

- Biosimilar First
- Biosimilar First + Biosimilar transitioning or switching

Provincial biosimilar penetration rate

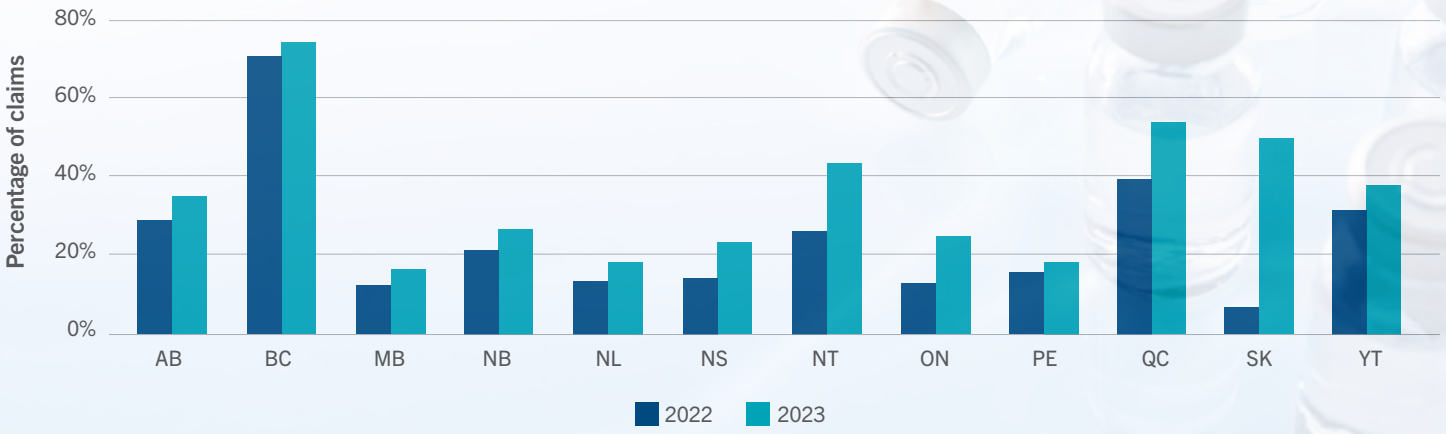
The provincial biosimilar penetration rates vary depending on the uptake of biosimilar programs, the targeted drugs, and if there is integration between private and public plans.

British Columbia continued to have the highest biosimilar penetration rate because it was the first province to adopt a biosimilar transition policy. Also, this jurisdiction is considered a pharmacare province, where integration between public and private plans is common and thus, prescribers are more likely to switch private plan patients to a biosimilar.

Saskatchewan's biosimilar penetration rate increased significantly as a result of the provincial biosimilar transition initiative announced in October 2022. The transition phase for most drugs was concluded in April 2023. Saskatchewan is also considered a pharmacare province and therefore, provincial integration contributed to the high biosimilar use.

Manitoba had the lowest biosimilar penetration rate of all provinces. It is one of the last jurisdictions to continue with a biosimilar-first policy and has not moved forward with a transitioning policy.

Provincial biosimilar penetration rate – Percentage of claims in 2022 and 2023



Pharmacy Landscape

Provincial biosimilar penetration rate - Percentage of claims in 2023

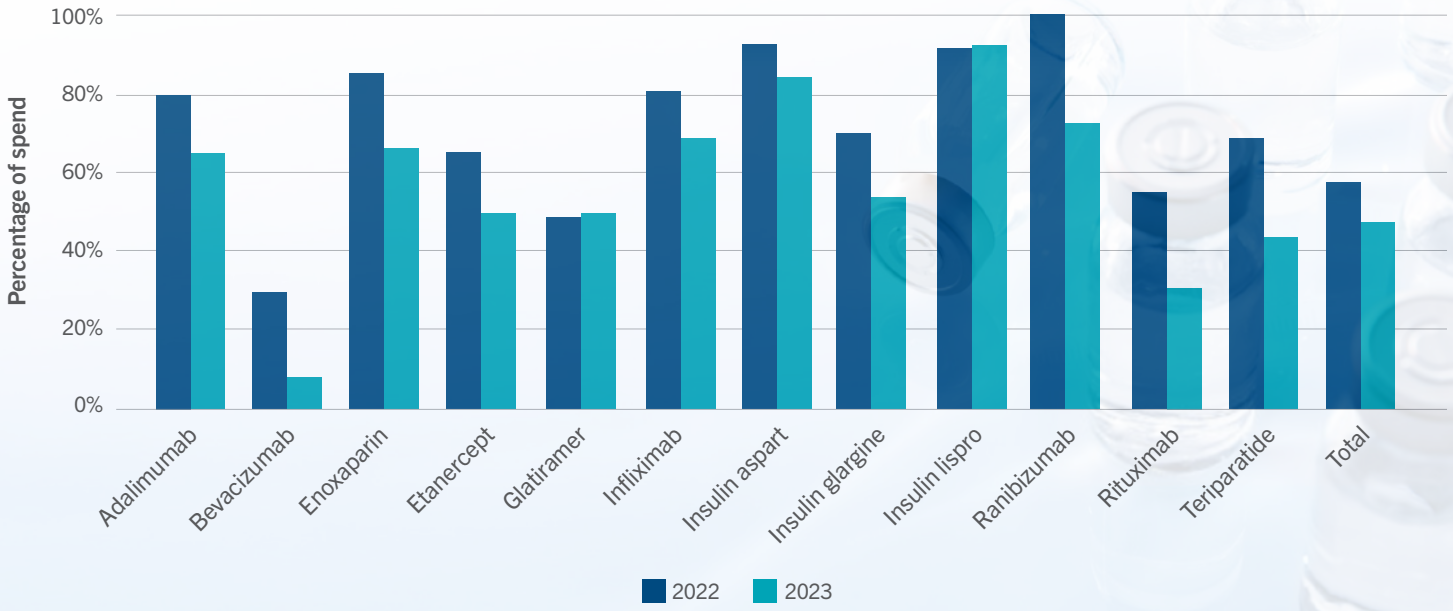
Chemical Name	AB	BC	NB	NS	ON	PE	QC	SK	YT
Adalimumab	38%	88%	17%	21%	34%	16%	74%	81%	62%
Bevacizumab	96%	78%	Insufficient Claims	Insufficient Claims	73%	Insufficient Claims	82%	Insufficient Claims	Insufficient Claims
Enoxaparin	47%	68%	41%	56%	17%	56%	72%	74%	50%
Etanercept	61%	87%	38%	27%	47%	30%	84%	87%	100%
Glatiramer	66%	77%	16%	Insufficient Claims	34%	Insufficient Claims	77%	67%	Insufficient Claims
Infliximab	42%	90%	12%	8%	16%	2%	44%	82%	Insufficient Claims
Insulin aspart	21%	48%	7%	13%	16%	11%	37%	49%	Insufficient Claims
Insulin glargine	62%	88%	56%	53%	31%	65%	73%	73%	61%
Insulin lispro	9%	51%	7%	3%	3%	Insufficient Claims	36%	4%	3%
Ranibizumab	Insufficient Claims	Insufficient Claims	12%	Insufficient Claims	8%	Insufficient Claims	72%	Insufficient Claims	Insufficient Claims
Rituximab	87%	99%	87%	66%	69%	Insufficient Claims	83%	91%	33%
Teriparatide	57%	67%	100%	100%	66%	Insufficient Claims	72%	Insufficient Claims	Insufficient Claims
TOTAL	35%	74%	27%	24%	25%	19%	54%	49%	38%

Pharmacy Landscape

Percentage of spend on originator biologics

While the overall biosimilar penetration rate increased from 23.5% to 35.8% in 2023 (see section *National biosimilar penetration rate*), the percentage of overall spend on originator biologics decreased from 57% to 47%. In the future, spend on originator biologics is expected to decrease further, as biosimilar alternatives become more readily available.

Percentage of spend on originators in 2022 and 2023



Impact of provincial biosimilar policies

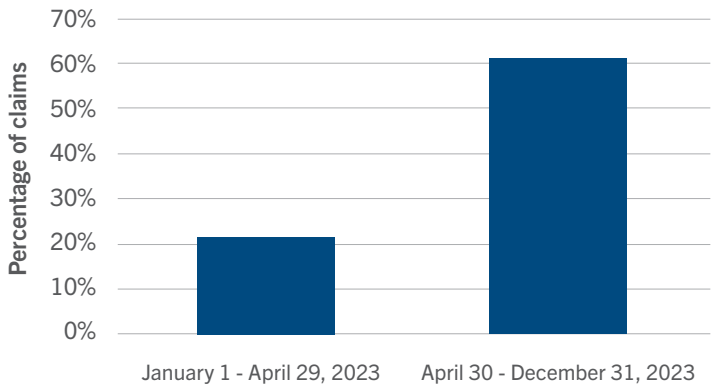
As in most biosimilar transitions, Saskatchewan delisted several originator biologics from the public formulary. Saskatchewan is considered a pharmacare province and therefore the biosimilar transition policy provided relatively high biosimilar uptake for private drug plans.

The province also extended the transition time for insulin lispro (ADMELOG®) as the supply of the biosimilar was unstable throughout 2023. The supply has now stabilized and the transition phase ended on March 31, 2024.

BIOSIMILAR PENETRATION RATE IN SASKATCHEWAN

As expected, the biosimilar penetration rate increased after the deadline was reached in Saskatchewan.

Biosimilar Penetration Rate in Saskatchewan – Percentage of claims before and after transition deadline of April 30, 2023

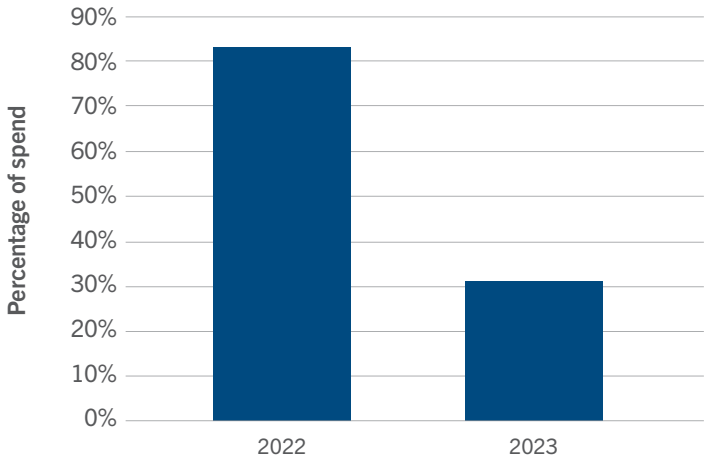


Pharmacy Landscape

PERCENTAGE OF SPEND ON ORIGINATORS IN SASKATCHEWAN

The highest reduction in percentage of spend on originators was observed in Saskatchewan (from 83% to 31%) - the pharmacare province that had the highest increase in biosimilar penetration rate in 2023.

Percentage of spend on originators in Saskatchewan – 2022 and 2023



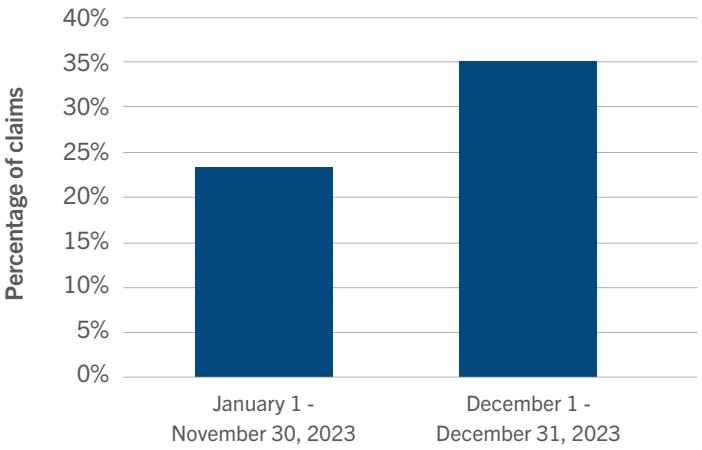
Ontario announced their biosimilar transition policy, which provided nine months for Ontario Drug Benefit (ODB) recipients to transition to biosimilars for glatiramer, etanercept, insulin lispro, adalimumab, insulin glargine, insulin aspart, infliximab, rituximab and ranibizumab. The transition period ended in late December 2023.

This milestone was long anticipated and we might see an impact on private plans in 2024.

BIOSIMILAR PENETRATION RATE IN ONTARIO

As expected, the biosimilar penetration rate increased after the deadline was reached in Ontario.

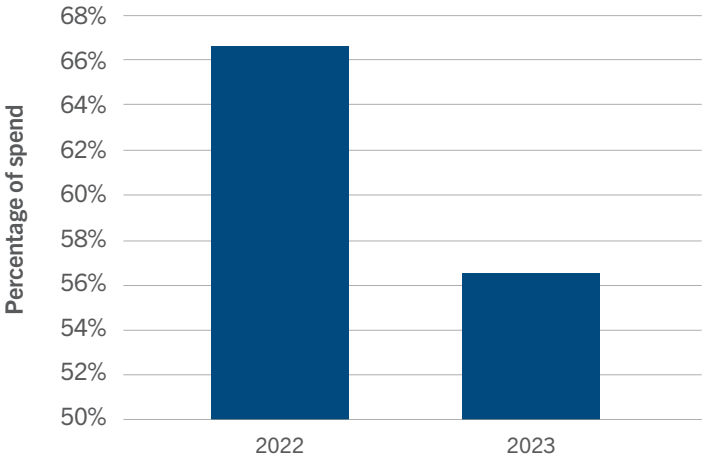
Biosimilar Penetration Rate in Ontario – Percentage of claims before and after December 1, 2023



PERCENTAGE OF SPEND ON ORIGINATORS IN ONTARIO

Spend on originators in Ontario decreased from 67% to 56%, mainly due to increased biosimilar penetration rate in 2023.

Percentage of spend on originators in Ontario – 2022 and 2023



Pharmacy Landscape

PROVINCIAL BIOSIMILAR PROGRAMS CONTINUED TO ADD MORE DRUGS IN 2023

The following provinces have transition phases that will extend into 2024. The impact of these transitions phase will be seen in the upcoming year.

Province	Drug	Coverage End Date
British Columbia	HUMALOG®	May 30, 2024
	NOVORAPID®	November 30, 2024
New Brunswick	NOVORAPID®	July 31, 2024
	LUCENTIS®	February 28, 2024
Newfoundland & Labrador	NOVORAPID® HUMALOG® LANTUS® HUMIRA® ENBREL® REMICADE® COPAXONE® RITUXAN® LOVENOX®	March 31, 2024
	LUCENTIS®	December 1, 2024
Prince Edward Island	NOVORAPID® HUMALOG® LANTUS®	June 30, 2024
	HUMIRA® ENBREL® REMICADE® COPAXONE® RITUXAN®	September 30, 2024
Quebec	LUCENTIS®	May 22, 2024
Yukon	NOVORAPID® HUMALOG® ENBREL® COPAXONE® RITUXAN® LOVENOX®	May 8, 2024

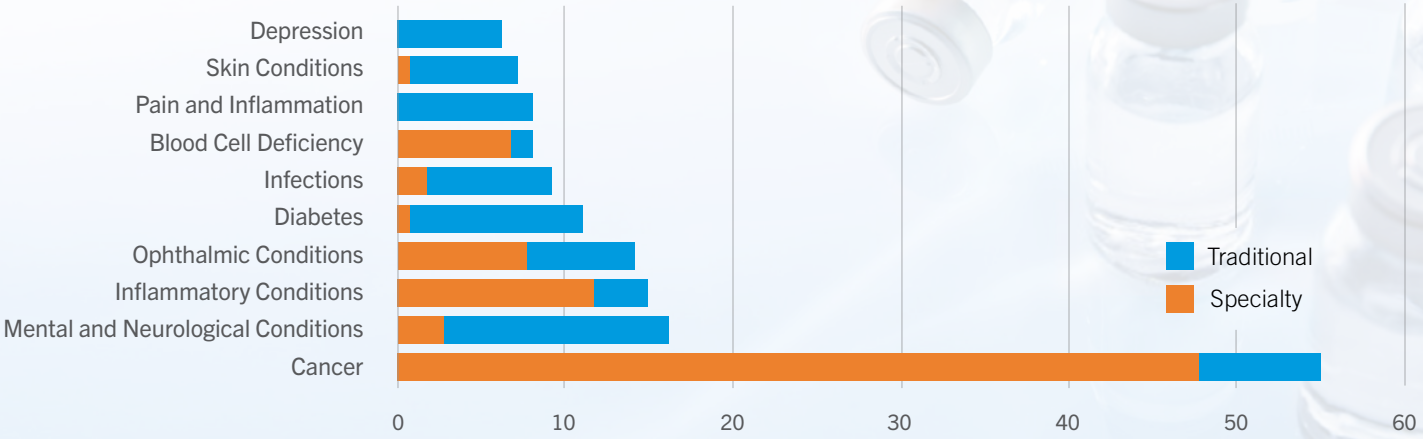
DRUG PIPELINE

New therapies are the focus of ongoing research to identify new ways of treating both common and rare diseases. These therapies attempt to provide better health outcomes than existing therapies or offer more convenient routes of administration. Similarly, indications expand the potential market size of a drug. Both new drugs and new indications in the pipeline have the potential to have a significant financial impact on private plans, if approved.

This year, we touch on some therapeutic areas in pipeline development which are commonly excluded from health benefits. Due to clinical advancements and the need for enhanced support to members as part of diversity, equity and inclusion (DEI) initiatives, we have put the spotlight on some drugs within these therapeutic areas. Obesity, alopecia areata and vitiligo may have been considered lifestyle or cosmetic conditions but are now being regarded as chronic medical conditions with substantial health implications and associated comorbidities (e.g., cardiovascular, mental health, and inflammatory conditions).

NEW DRUGS IN LATE-STAGE CLINICAL TRIALS

The focus of drug development continues to be predominately within the specialty drug space for cancer. The graph also shows other top spend categories which will see new treatment options in the years to come.



Cancer: As shown in the graph, the research in cancer treatment continues to dominate the pipeline. Breast cancer is the most common type of cancer in women worldwide. One notable drug is capivasertib, which is a first-in-class oral AKT inhibitor investigated in combination with fulvestrant, for the treatment of HER2-negative, hormone receptor-positive advanced or metastatic breast cancer, in patients who have failed or became resistant to first-line treatment. When this occurs, treatment options are often limited to standard hospital-administered chemotherapy. This drug is also in late-stage trials for triple-negative breast cancer.

Many current 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 under investigation which use cells from healthy donors (allogeneic) to treat multiple patients. Research in this technology may help address treatment challenges associated with current gene therapies and could potentially shift the administration away from hospitals to infusion centres. Hospital treatments are traditionally publicly funded, however, if they move outside of hospital settings, the cost could shift to private plans.

Pharmacy Landscape

Obesity: Obesity and diabetes treatments have drawn a lot of media attention to the drug class called glucagon-like peptide-1 (GLP-1) receptor agonists, such as semaglutide (OZEMPIC® and WEGOVY®) and liraglutide (VICTOZA® and SAXENDA®). These drugs were originally approved for diabetes and later approved for weight loss at higher doses. Although not classified in the graph as new drugs in late-stage clinical trials for obesity, we can likely infer that some new diabetes molecules will undergo trials to seek the obesity or weight loss indication. Heading into later stages of drug development, several obesity therapies will target other mechanisms promoting weight loss and explore new routes of administration.

Related to the interplay of cardiodiabesity, the obesity therapies identified in the pipeline are concurrently undergoing trials for type 2 diabetes and the majority are under study for other comorbid conditions such as metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatohepatitis (MASH).

Table 1: New drugs with multiple indications

Drug Name	Route of Administration	Drug Class	Possible Indications
Orforglipron	Oral	GLP-1 RA, nonpeptide	Obesity T2DM
Retatrutide	Subcutaneous injection	GIP/GLP-1/ Glucagon Receptor Triagonist	Obesity T2DM OSA
Mazdutide	Subcutaneous injection	Dual GLP-1/glucagon receptor agonist	Obesity T2DM MASH/MAFLD
Danuglipron	Oral	GLP-1 RA, nonpeptide	Obesity T2DM MASH Renal failure
Pemvidutide	Subcutaneous infusion	Dual GLP-1/glucagon receptor agonist	Obesity T2DM MASH/MAFLD

Abbreviations: T2DM = Type 2 Diabetes Mellitus, MAFLD = Metabolic dysfunction-associated Fatty Liver Disease, MASH = Metabolic dysfunction-associated Steatohepatitis, OSA = Obstructive Sleep Apnea

Dual agonist obesity drugs in the pipeline are drugs that provide treatment through two mechanisms of action in the body. Some examples are tirzepatide (ZEPBOUND®), which received FDA approval in November 2023, mazdutide and pemvidutide. These three drugs activate GLP-1 receptors but tirzepatide also activates glucose-dependent insulinotropic polypeptide (GIP) receptors while the latter two drugs activate glucagon receptors. Activation of GLP-1 and GIP or glucagon receptors has resulted in greater weight loss with little increases in adverse effects compared to GLP-1 activation alone. Furthermore, activation of all three receptors will be addressed through retatrutide, which is a drug that has initially demonstrated new record weight loss results. Retatrutide is poised to be the most effective obesity medication in the pipeline based on ongoing study results, to date.

Available GLP-1 agonists are large, peptide-based molecules that require subcutaneous administration or the use of complex technologies for oral delivery such as seen with semaglutide tablets. The development of new generation, oral, small molecule GLP-1 agonists may help ease drug shortages, owing to simpler manufacturing processes involved. Two orally administered drugs in the pipeline are orforglipron and danuglipron, which are in phase 3 and phase 2 trials, respectively.

See our section on CARDIODIABESITY

Pharmacy Landscape

Diabetes: As highlighted in Table 1, many of the new molecules mentioned can potentially treat the comorbid conditions of obesity and diabetes. However, drug research is also focussing on providing patient convenience. More dosage forms of existing therapies are under investigation for the treatment of diabetes. An example includes a subcutaneous implant of exenatide, which releases the drug for either 3 or 6 months.

Focussing on the sodium-glucose linked transporter (SGLT) mechanism, sotagliflozin is dual SGLT-1 and SGLT-2 inhibitor recently FDA approved for the treatment of heart failure in patients with or without diabetes. Similar therapies are currently available which target SGLT-2 to prevent the re-absorption of 90% of the body's glucose. However, the blockade of SGLT-1 is new and these agents will block the remaining 10% of glucose.

See our section on CARDIODIABESITY

Pharmacy Landscape

Rare diseases: Pipeline trends in rare disease favour the development of self-administered therapies such as oral and subcutaneous routes. Although these conditions affect a small number of patients, the high drug costs can have a significant financial impact on private payers.

Table 2: New drugs for rare diseases

Drug Name	Route of Administration	Indication	Estimated Average Annual Cost (US$)
Trofinetide	Oral solution	Rett Syndrome	460,000 to 1.1 million[1]
Iptacopan	Oral capsule	Paroxysmal Nocturnal Hemoglobinuria	500,000[2]
Zilucoplan	Subcutaneous	Myasthenia Gravis	400,000
Eplontersen	Subcutaneous	Hereditary transthyretin amyloidosis-associated polyneuropathy	N/A
Metreleptin	Subcutaneous	Lipodystrophy (abnormal fat storage)	1.1 million[3]
Pozelimab	Subcutaneous	CHAPLE disease	2.2 million[4]

[1] based on weight categories ranging from 9 kg to ≥50 kg; [2] based on average 70 kg male; [3] based on average daily dose of 5 mg in the trial; [4] maintenance dosing; based on average 70 kg male

Oral therapies in the rare disease pipeline include trofinetide for the treatment of Rett Syndrome (RTT) and iptacopan for paroxysmal nocturnal hemoglobinuria (PNH). Trofinetide is an oral solution and is the first disease-modifying treatment for RTT, where patients start to suffer from neurological and developmental deterioration as early as 6 months of age. Oral iptacopan is the first oral therapy developed for PNH, where current drug treatments include intravenous eculizumab (SOLIRIS®) and ravulizumab (ULTOMIRIS®) as well as subcutaneous pegcetacoplan (EMPAVELI®). PNH is a rare blood disorder where the immune system attacks the red blood cells. This disease may be categorized under Blood Cell Deficiencies, which has been experiencing a lot of activity in the pipeline compared to previous years.

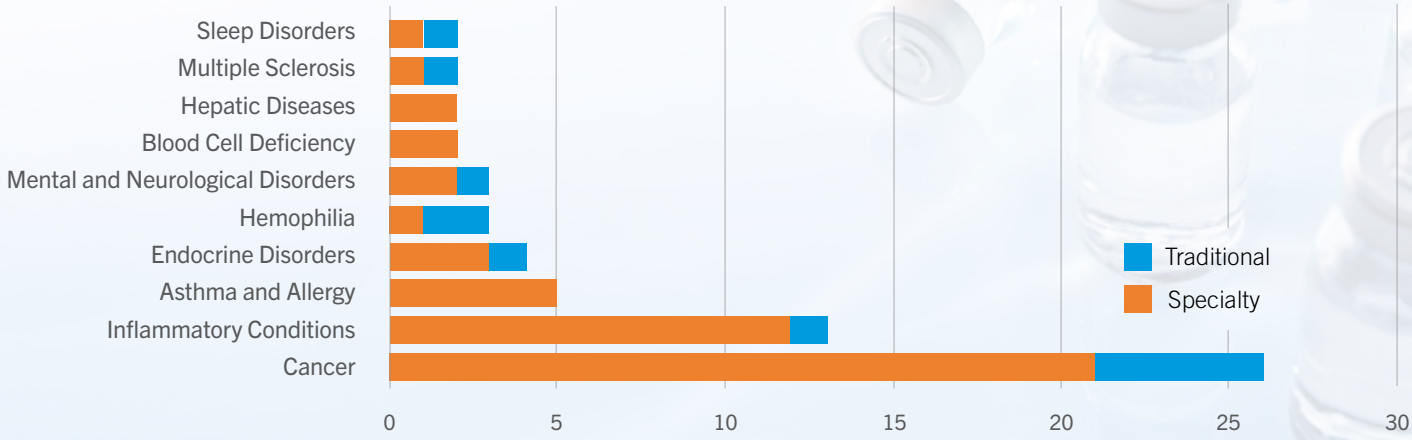
Subcutaneous therapies in the rare disease table, which allow for self-administration, are zilucoplan for the treatment of general myasthenia gravis (gMG), eplontersen for the treatment of nerve disease in patients with hereditary transthyretin amyloidosis (hATTR-PN), metreleptin in lipodystrophy disorders, and pozelimab in CHAPLE disease. These four rare diseases cause destruction of surrounding tissues and organs, which can greatly affect the patient's quality of life and overall survival.

Pharmacy Landscape

NEW INDICATIONS

New indications refer to additional conditions that can be treated by an existing marketed drug. The new indication will proceed through clinical trials and if successful, regulatory approval. The new indications pipeline continues to focus on the areas of cancer and inflammatory conditions. Many inflammatory conditions share a common pathway of disease and therefore one drug may be studied for multiple related conditions. Also, research continues to focus on finding alternative routes of drug delivery, which potentially allows for drug administration to occur away from the hospital setting and to improve convenience.

New indications for existing drugs in late-stage clinical trials



Inflammatory Conditions: Two selective interleukin-23 inhibitors, risankizumab (SKYRIZI®) and guselkumab (TREMFYA®), are in late-stage clinical trials to be used in severe ulcerative colitis. Both of these biologic products were initially approved for the treatment of plaque psoriasis.

Upadacitinib (RINVOQ®), a JAK1 inhibitor, is in late-stage trials for the treatment of vitiligo. RINVOQ® has already been approved for the treatment of rheumatoid arthritis and other inflammatory conditions. Vitiligo is a skin condition, which currently does not have any approved systemic treatment options.

Alopecia areata (AA) is an autoimmune disease that specifically attacks hair follicles and results in either complete or partial hair loss anywhere on the body such as eyebrows, eyelashes, scalp, face, or nose. Alopecia areata is different from androgenetic alopecia, which is hair loss that is not immune-mediated but rather due to hormonal changes (increased androgen levels). Baricitinib (OLUMIANT®) is an oral JAK1/2 inhibitor approved for rheumatoid arthritis that received an additional indication from Health Canada for the treatment of alopecia areata in early 2024. This approval provides an alternative to newly approved ritlecitinib (LIFTULO®) – a new dual JAK3/TEC inhibitor. Of note, RINVOQ® will potentially expand to the AA therapeutic market space awaiting the results of its phase 3 trials. Previously, medications to treat AA would include off-label use of immunosuppressants, topical therapies, and systemic and intradermal injections of corticosteroids.

Asthma and Allergy: Omalizumab (XOLAIR®), which is currently approved for different asthma subtypes, is being investigated for the prevention of severe allergic reactions following accidental exposure to an allergen. Another biologic drug that has been amassing new indications in recent years is dupilumab (DUPIXENT®). This drug is approved for asthma, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis, and prurigo nodularis, but is also under investigation for chronic spontaneous urticaria and COPD. There is currently no biologic drug option for the treatment of COPD.

Pharmacy Landscape

LEGISLATIVE UPDATES

Pharmacist Scope of Practice Updates

Adding minor ailments to the pharmacists' scope of practice is intended to alleviate strain on the province's health care system. Private plans may see additional drug claims from pharmacist prescribers.

Ontario and British Columbia both authorized pharmacists to prescribe treatments for common ailments including urinary tract infections, allergic rhinitis, and acne. The assessment fee in both jurisdictions is funded by the provincial health care system.

Notably in British Columbia, pharmacists were also authorized to prescribe for contraception. Assessments to prescribe contraceptives were the second most common assessment based on data from June to November 2023 published by BC PharmaCare.

New Brunswick and Newfoundland and Labrador also had their list of minor ailments expanded upon in 2023. This allows pharmacists to prescribe for additional range of conditions, further alleviating strain on health care resources. In the same year, Saskatchewan allowed their pharmacists to independently order lab tests to support patient care in the province.

General Updates

British Columbia introduced universal coverage for contraceptives including oral formulations, copper and hormonal IUDs, and emergency oral contraceptives effective April 1, 2023. Universal coverage for contraceptives is also being discussed in other provinces and reflects recognition of improving access to contraception for women. Provincial coverage may shift drug spend from private to public plans.

In Quebec, RAMQ published the new agreement between Association québécoise des pharmaciens propriétaires (AQPP) and the ministère de la Santé et des Services sociaux (MSSS). The agreement is valid until March 31, 2025 and increases the number of clinical services pharmacists are allowed to bill per year. This includes clinical services,

which are fully reimbursed by private payors, such as extension of a prescription and administration of a drug for teaching purposes. There are two new additional clinical services in 2023: Opinion on treatment initiation and Deprescribing, which are reimbursed by the public plan.

AQPP has also been in discussions with the MSSS in the last years to change the remuneration model for pharmacists, which is currently mainly focused on distribution. Considering the changes in the pharmacy practice landscape, AQPP is looking to update the remuneration model to reflect this new reality. Advancements in pharmacy renumeration may transcend other jurisdictions over time.

Provincial Biosimilar Initiatives

Provinces and territories continue to add or expand on existing biosimilar policies with almost all jurisdictions implementing biosimilar transitioning programs by 2023. The impact to private plans varies depending on the province and plan design.

PROVINCIAL BIOSIMILAR POLICY CHANGES IN 2023

Ontario, Prince Edward Island, and Newfoundland and Labrador announced the addition of biosimilar transition strategies in 2023. These provinces have transition dates that stretch into late 2023 or mid-2024. Additionally, these provinces provide limited integration opportunities for private plans and therefore, the direct impact would be minimal.

Many provinces have expanded their biosimilar initiatives to include ranibizumab by announcing the end of coverage for ranibizumab (LUCENTIS®) upon the availability of a biosimilar product.

Popular insulin pumps were also approved by Health Canada to be used with insulin lispro biosimilars in 2023. Many insulin pump users, who were previously excluded from transition policies, were required to transition to a biosimilar in British Columbia and Saskatchewan.

See *Biosimilars* section for additional information.

CADTH

CADTH REAL-WORLD EVIDENCE STRATEGY

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.

The therapeutic areas identified as initial focus areas for the Real-World Evidence strategy are rare diseases (cystic fibrosis and spinal muscular atrophy) and optimal use of drugs for the treatment of plaque psoriasis, multiple myeloma, ulcerative colitis, and dementia. A task force has been established to provide advice on the use of industry-generated real-word data.

These topics are also critical to private payers and the collection of real-world evidence may help support updates to listing decisions on private drug plans.

CADTH PROCESS IMPROVEMENTS

Also announced in 2023 were a series of process changes that aim to improve the reimbursement review process. One of these initiatives is Target Zero campaign which has a goal of zero days between the approval of a drug and the draft recommendation from CADTH. The goal is to increase the number of drugs with a draft recommendation available at approval to facilitate faster access to new drugs for Canadians. These earlier recommendations may help support private payers with listing decisions which historically have been made in advance of publication of CADTH recommendations.

NATIONAL STRATEGY FOR DRUGS FOR RARE DISEASE

In March 2023, the Government of Canada announced funding for the first-ever National Strategy for Drugs for Rare Diseases. The $1.5 billion investment over three years will support initiatives to fund both new and existing drugs for rare diseases. In October, Health Canada announced the members of the Implementation Advisory Group for drugs for rare disease. This group is tasked with creating best practices that will inform the implementation of the overall strategy. The committee includes caregivers, clinicians,

Pharmacy Landscape

representation from the pharmaceutical industry, and researchers. The details of this national strategy have yet to emerge but have a high potential of impacting private payers which may currently fund drugs for rare disease.

CANADIAN DRUG AGENCY (CDA)

In late 2023, the Minister of Health announced the creation of the Canadian Drug Agency, which will formalize CADTH's partnership with the provinces, territories and federal government. The CDA is intended to expand on CADTH's expertise in the pharmaceutical sector and incorporate additional new work streams that focus on pan-Canadian data collection, reducing drug system duplication, and improving the appropriate prescribing and use of medications. It is intended that the government will work with both CADTH and the provinces to develop the CDA. Once it is operational, it will take on a greater role in the drug system. The impact to private payers can be assessed once more details emerge regarding the strategy and objectives of the CDA are published.

PAN-CANADIAN PHARMACEUTICAL ALLIANCE – NEW AGREEMENT

A new 3-year term for pricing of generics was reached between the pCPA and the Canadian Generic Pharmaceutical Association. The new initiative is effective October 1, 2023 for a period of three years. The tiered pricing mechanism remains unchanged. However, there was a change to the pricing of newly launched single source generics, where pricing would be decreased to 55% that of the brand product three months after public funding in that jurisdiction.

NATIONAL PHARMACARE

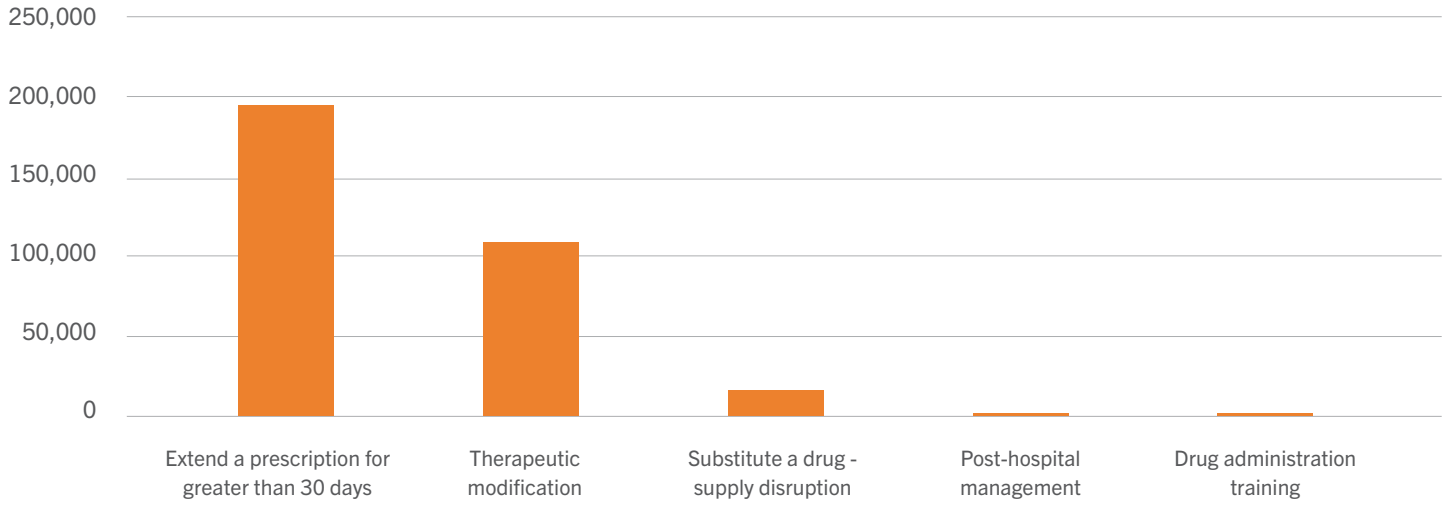
"The Government of Canada announced the first phase of the National Universal Pharmacare on March 1, 2024. The Pharmacare Act (Bill C-64) proposes a list of therapies for diabetes as well as contraceptive medications and devices for negotiation with provinces and territories, with the goal of providing a universal, single-payer coverage for Canadians."

QUEBEC TRENDS

Quebec Clinical Services

The professional 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 prescription 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.

Claims for clinical services in Quebec - 2023



Quebec Overall Trend

There was a 2.7% increase in spend per Quebec claimant between 2022 and 2023. The annual spend per claimant in Quebec exceeds that of claimants in the rest of the country by 41%. Contributing factors to the higher spend per claimant in Quebec include the number of claims and days' supply per claim.

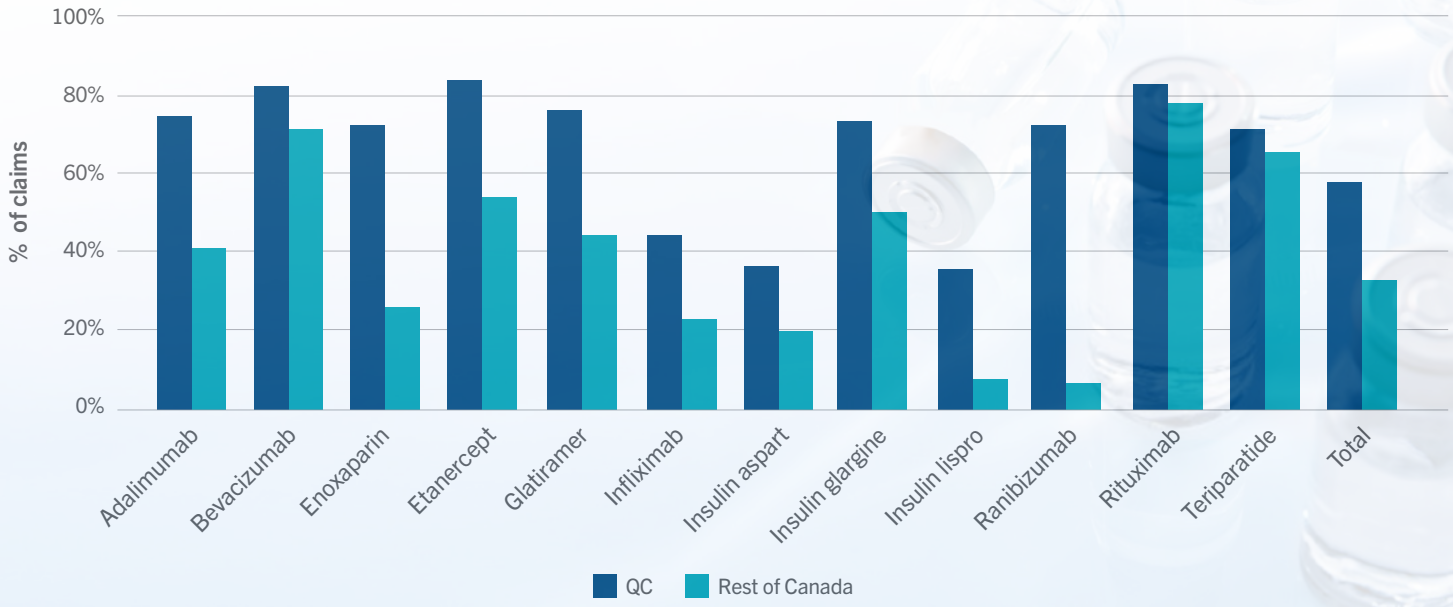
2023	Quebec	Rest of Canada
Average days' supply per claim	28.3	40.7
Number of claims per claimant	18.5	11.6

Pharmacy Landscape

Biosimilar penetration – Quebec vs. rest of Canada

Use of biosimilars is higher in Quebec for all molecules. The difference is most significant for ranibizumab which was added as a RAMQ benefit in 2023; however, the transition period extends into 2024. The use of insulin biosimilars, particularly insulin lispro also exceeds that of rest of Canada by 27.7%.

Biosimilar penetration rate in 2023 - QC vs. Rest of Canada



3 Plan Adoption

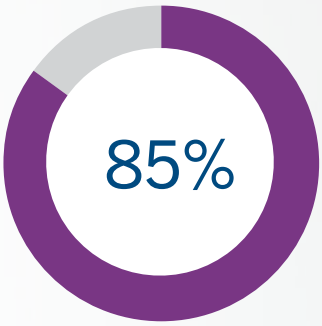
DRUG PLAN MANAGEMENT OPTIONS

Express Scripts Canada offers various drug plan management and clinical programs that balance the need to lower spend yet provide members with access to essential treatments.

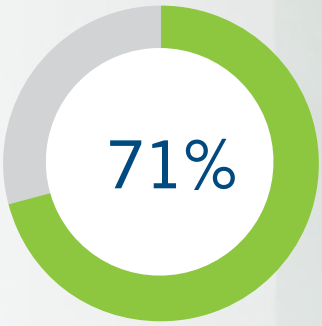
Each year, we analyze the uptake of traditional drug plan management options as well as clinically based programs, like Step Therapy and the Opioid Management Solution. These options support members with optimal therapies while addressing the rising cost of drugs.

Plan Adoption

Uptake of drug plan management options based on analysis of the percentage of claims processed in 2023

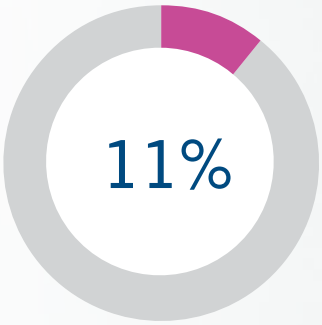


Generic substitution

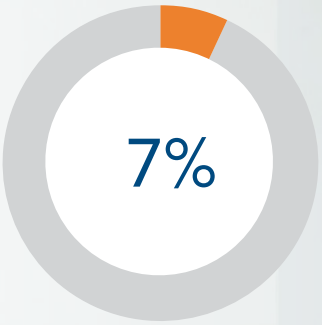


Co-insurance

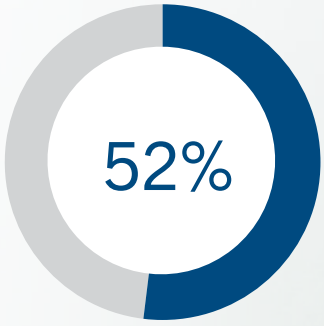
Dispensing Fee Caps



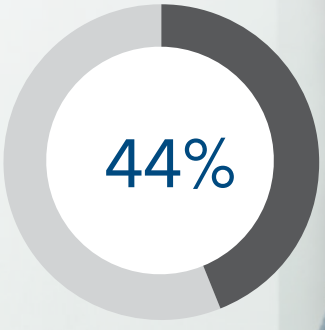
Annual Maximums



Lifetime Maximums



Opioid Management Solution



Step Therapy

Plan Adoption

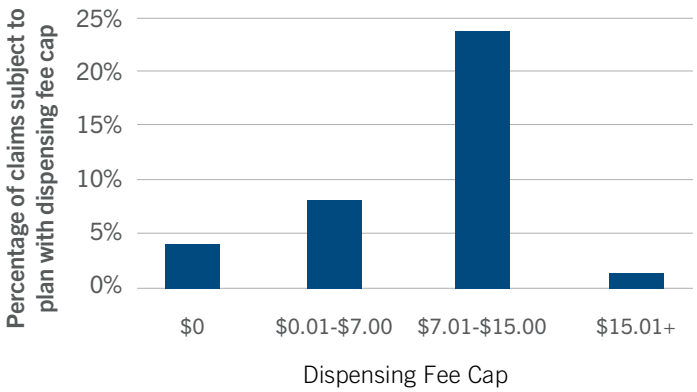
Generic Substitution helps manage plan costs for drugs that have interchangeable generic alternatives available. The claim cost will be reimbursed up to the lower-cost alternative generic medication. The 2023 national uptake showed that 85% of claims had a generic substitution drug plan.

Co-insurance is the percentage of eligible expenses (after any 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. In 2023, 71% of claims were subject to a plan that included co-insurance.

Dispensing Fee Caps. 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 fees more than the capped amount, the member will pay for the difference. Dispensing fee caps encourage plan members to seek pharmacies with lower dispensing fees. Some provinces require pharmacies to post their dispensing fees for the public.

In 2023, 38% of claims were subject to a plan with a dispensing fee cap.

Summary of dispensing fee capped amounts



Annual Maximums limits the amount that a plan will pay for drugs for a member each year. In 2023, 11% of claims were subject to a plan that included an annual maximum.

Lifetime Maximums limit the amount that a plan will pay for drugs over a member's lifetime. In 2023, 7% of claims were subject to a plan that included a lifetime maximum.

Express Scripts Canada's **Opioid Management Solution** (OMS) is intended to promote early interventions and safer use of opioids. The program minimizes early opioid exposure and identifies high opioid dosages as well as potential duplication of therapies. In 2023, 52% of claims were subject to a plan that included Opioid Management Solution.

Step Therapy is used to ensure members try first-line, clinically effective drugs before stepping up to higher-cost second line treatment options. This approach is common for conditions like diabetes where there is a significant cost difference between first and second-line therapies. In 2023, 44% of claims were subject to a plan that included Step Therapy.

Express Scripts Canada offers additional programs and plan features to address both clinical and cost-saving goals. This analysis illustrates that there remains an opportunity to incorporate plan management options that can yield significant savings.

Glossary

Biosimilar: A biological product developed such that there are no clinically meaningful differences between the biological product and the 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.

EXPRESS SCRIPTS®

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