Express Scripts®





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FOREWORD



Canada's drug benefits landscape continues to evolve, driven by legislative changes, introduction of new treatments, and emerging trends. Express Scripts Canada leverages data insights to drive solutions that prioritizes what is most important to those we serve.

FOREWORD

In this year's report, we monitor drug trends and shed a spotlight on two feature topics, Women's Health, and Attention Deficit Hyperactivity Disorder (ADHD). Our Women's health section explores the differences in both health conditions and drug consumption for men and women, while also examining how women are more prone to health conditions that impact their day-to-day life. Due to the rise in ADHD amongst adolescents, and adults, we will share data driven findings that further illustrate this uptake. ADHD can have a great effect on one's quality of life, education, and workplace productivity.

In addition to these topics, we will also be re-exploring Diabetes and Obesity. Through our report, we will explore the trends in the use of GLP-1 agonists in diabetes and obesity, as we could start to see a drive in usage due to the new indications and a shift in the definition of obesity – emphasizing health outcomes and not on achieving an ideal body weight.

Legislative changes such as provincial biosimilar switching influenced drug spend in recent years and thus, as national pharmacare is introduced in 2025, Express Scripts Canada will continue to monitor federal and provincial agreements. Although this latter development does not yet show in our data, we will likely see some impact on 2025 drug claims.

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

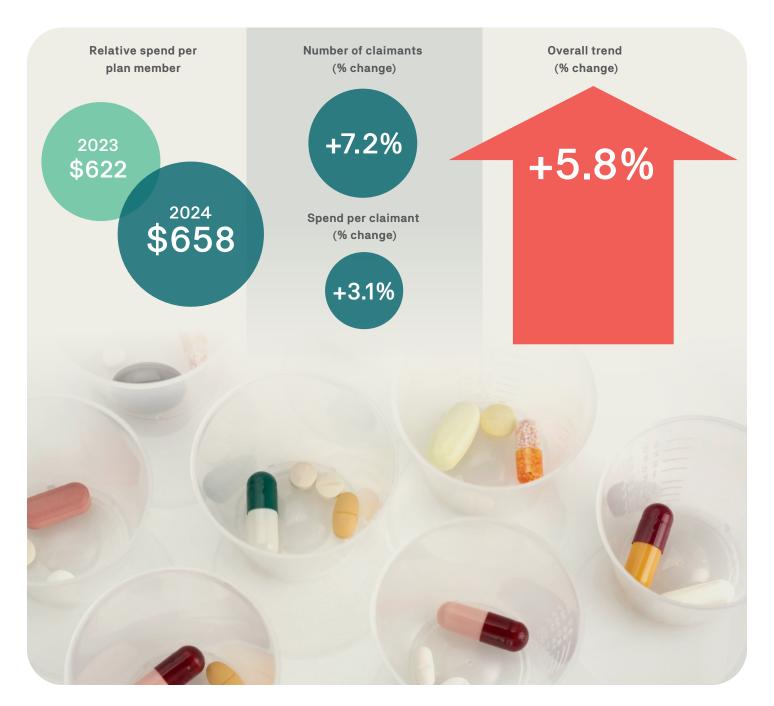
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Overall Drug Trend

Overall drug trend is the year over year change in the relative annual drug spend per plan member. This year, the overall drug trend increased by 5.8%. This trend is driven by a 7.2% increase in the number of claimants, and a 3.1% increase in spend per claimant.

The overall trend for 2024 is higher than last year's overall trend of 5.2%.



Traditional vs. Specialty Drug Trend

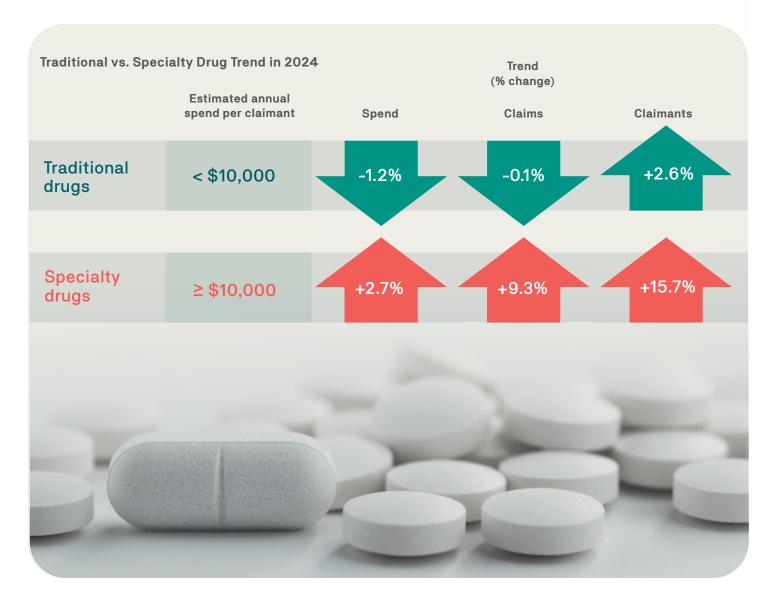
In 2024, there was a small decrease in the overall spend for traditional drugs and an increase on the specialty side. Claims volume remained stable for traditional drugs, with only a 0.1% reduction. Nevertheless, the percentage of claims for specialty drugs increased by 9.3%.

The year-over-year spend per plan member decreased by 1.2% for traditional drugs and increased by 2.7% for specialty drugs.

Additionally, the percentage of members making at least one claim for a specialty drug increased significantly by

15.7%. In contrast, the percentage of members with a traditional drug claim increased slightly by 2.6% compared to 2023.

This rising trend for specialty drugs can be explained by the increasing number of specialty drugs, and newly approved indications for drugs that target inflammatory, skin conditions and cancer as well as the growing trends for TRIKAFTA®, a high-cost drug for the treatment of cystic fibrosis.



Traditional vs. Specialty Drug Trend cont'd

Top 10 Drugs by Overall Spend

20	23		202	4	
Drugs: Chemical name (BRAND)	Therapeutic Class	Rank by Overall Spend	Drugs: Chemical name (BRAND)	Therapeutic Class	
Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	1	Semaglutide (OZEMPIC®, RYBELSUS®, WEGOVY®)	Diabetes, Weight Loss	
Adalimumab* (HUMIRA®)	Inflammatory conditions	2	Adalimumab* (HUMIRA®)	Inflammatory conditions	
Infliximab* (REMICADE®)	Inflammatory conditions	3	Infliximab* (REMICADE®)	Inflammatory conditions	
Ustekinumab (STELARA®)	Inflammatory conditions	4	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic supplies	
Lisdexamfetamine (VYVANSE®)	ADHD	5	Lisdexamfetamine* (VYVANSE®)	ADHD	
Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic supplies	6	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis	
Elexacaftor-Tezacaftor- Ivacaftor (TRIKAFTA®)	Cystic Fibrosis	7	Ustekinumab* (STELARA®)	Inflammatory conditions	
Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	8	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®, QUILLIVANT ER®)	ADHD	
Empagliflozin (JARDIANCE®)	Diabetes	9	Dupilumab (DUPIXENT®)	Skin conditions	
Dupilumab (DUPIXENT®)	Skin conditions	10	Empagliflozin (JARDIANCE®)	Diabetes	

^{*}Biosimilar(s) or generic(s) available

The top three drugs ranked by overall spend remained the same in 2024. Semaglutide continued to be at the top of the list (4.6% increase in overall spend), followed by adalimumab and infliximab. Although WEGOVY® appears in the data analysis, semaglutide (under brands OZEMPIC® and RYBELSUS®) approved for diabetes remain the main driver in spend. The proportion of semaglutide claims in 2024 was 99.3% for diabetes claims versus 0.7% for obesity claims. In terms of spend, the percentage of overall spend on semaglutide was 98.8% for diabetes and only 1.2% for obesity.

Despite their unchanged ranking, adalimumab and infliximab have seen a decrease in the overall spend in 2024 compared to the previous year.

Ustekinumab (STELARA®) moved down from 4^{th} to 7^{th} place. Flash Glucose Sensors (FREESTYLE LIBRE®) continued to move up. In 2024, it ranked in 4^{th} place by overall spend, due to a 7% increase in spend.

Despite the genericization of VYVANSE® (lisdexamfetamine) in mid 2024, it retained its 5th place

Traditional vs. Specialty Drug Trend cont'd

with no change in the year-over-year percentage of spend.

Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®) also continued to move up, from 7th to 6th place, due to an increase of 3.9% in overall spend, and a 12% increase in claimants. TRIKAFTA® expanded its indications in 2024 to include patients who have at least one mutation in the cystic fibrosis transmembrane conductance regulator

(CFTR) gene, rather than targeting one specific gene mutation. The expansion of its indication could potentially lead to an increased number of patients becoming eligible for treatment.

Dupilumab (DUPIXENT®) went up one place in terms of overall trend due to an increase in spend and in number of claimants, while empagliflozin (JARDIANCE®) went down from 9^{th} to 10^{th} place.

Top 10 Traditional Drugs by Overall Spend

20	23		2024			
Drugs: Chemical name (BRAND)	Therapeutic Class	Rank by Overall Spend	Drugs: Chemical name (BRAND)	Therapeutic Class		
Semaglutide (OZEMPIC®, RYBELSUS®)	Diabetes	1	Semaglutide (OZEMPIC®, RYBELSUS®, WEGOVY®)	Diabetes, Weight Loss		
Lisdexamfetamine (VYVANSE®)	ADHD	2	Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic supplies		
Flash Glucose Sensors (FREESTYLE LIBRE®)	Diabetic supplies	3	Lisdexamfetamine* (VYVANSE [®])	ADHD		
Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®)	ADHD	4	Methylphenidate* (RITALIN®, CONCERTA®, BIPHENTIN®, FOQUEST®, QUILLIVANT ER®)	ADHD		
Empagliflozin (JARDIANCE®)	Diabetes	5	Empagliflozin (JARDIANCE®)	Diabetes		
Rosuvastatin* (CRESTOR®)	High Cholesterol	6	Budesonide-Formoterol (SYMBICORT®)	Asthma/COPD		
Budesonide-Formoterol (SYMBICORT®)	Asthma/COPD	7	Rosuvastatin* (CRESTOR®)	High Cholesterol		
Escitalopram* (CIPRALEX®)	Depression	8	Onabotulinumtoxin-A (BOTOX®, XEOMIN®)	Muscle Relaxant		
Blood Glucose Test Strip (various brands)	Diabetic supplies	9	Estradiol* (various brands)	Hormone Replacement		
Onabotulinumtoxin-A (BOTOX®, XEOMIN®)	Muscle Relaxant	10	Blood Glucose Test Strip (various brands)	Diabetic supplies		

Traditional vs. Specialty Drug Trend cont'd

Semaglutide (OZEMPIC®, RYBELSUS®, WEGOVY®) continued to be the top traditional drug by overall spend in 2024. WEGOVY®, another brand of semaglutide which was approved by Health Canada for chronic weight management, arrived on the Canadian market in March 2024. This drug was highly awaited since its approval in 2021.

WEGOVY® is classified under the weight loss therapeutic class category; therefore, its coverage varies by plan design. Additionally, cost containment measures such as prior authorization or plan maximums may be leveraged. Prior authorization criteria ensure that the drug is utilized by the right patient population.

In addition to weight loss management, this drug gained an expanded indication in late 2024 for the reduction of nonfatal myocardial infarction risk in overweight adults with established cardiovascular disease. This expanded indication may contribute to the increased trend of semaglutide in the upcoming years.

See <u>Diabetes and Obesity</u> section for additional information.

The effect of the genericization of lisdexamfetamine (VYVANSE®) is more evident in the top 10 traditional drugs. This molecule moved down one place. However, the number of claimants increased by 20%.

Flash Glucose Sensor (FREESTYLE LIBRE®) showed an increase in the overall spend while lisdexamfetamine (VYVANSE®) had no change. Hence, both drugs switched places in their ranking in 2024.

Escitalopram (CIPRALEX®) moved out of the top 10 traditional drugs due to a 17% decrease in overall spend.

A new entrant to the top 10 traditional drugs is estradiol, an estrogen replacement therapy available in various forms such as oral tablets, topical gels, and transdermal patches. This molecule moved up 8 places, due to a 20% increase in claimants and 16% increase in spend. The average annual spend per claimant is \$241.

This rising trend for estradiol provides tangible evidence of the increasing awareness in women's health which

is supported by organizations, governments, public and private sectors.

Outside of the top 10, other traditional drugs that showed notable increases in spend in 2024:

+ Progesterone saw a 24% increase in overall spend and 32% increase in claimants. This drug is indicated as an adjunct to postmenopausal estrogen replacement therapy to reduce the risk of endometrial cancer.

This growing trend of another hormonal therapy for the treatment of postmenopausal symptoms further confirms the increased attention to women's health.

See Women's Health section for additional information.



Traditional vs. Specialty Drug Trend cont'd

Top 10 Specialty Drugs by Overall Spend

20	23		2024			
Drugs: Chemical name (BRAND)	e (BRAND) Therapeutic Class		Drugs: Chemical name (BRAND)	Therapeutic Class		
Adalimumab* (HUMIRA®)	Inflammatory conditions	1	Adalimumab* (HUMIRA®)	Inflammatory conditions		
Infliximab* (REMICADE®)	Inflammatory conditions	2	Infliximab* (REMICADE®)	Inflammatory conditions		
Ustekinumab (STELARA®)	Inflammatory conditions	3	Elexacaftor-Tezacaftor-Ivacaftor (TRIKAFTA®)	Cystic Fibrosis		
Elexacaftor-Tezacaftor- Ivacaftor (TRIKAFTA®)	Cystic Fibrosis	4	Ustekinumab* (STELARA®)	Inflammatory conditions		
Dupilumab (DUPIXENT®)	Skin conditions	5	Dupilumab (DUPIXENT®)	Skin conditions		
Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease	6	Risankizumab (SKYRIZI®)	Inflammatory conditions		
Risankizumab (SKYRIZI®)	Inflammatory conditions	7	Vedolizumab (ENTYVIO®)	Inflammatory Bowel Disease		
Ocrelizumab (OCREVUS®)	Multiple Sclerosis	8	Ocrelizumab (OCREVUS®)	Multiple Sclerosis		
Omalizumab (XOLAIR®)	Asthma/COPD	9	Upadacitinib (RINVOQ®)	Inflammatory conditions		
Golimumab (SIMPONI®)	Inflammatory conditions	10	Aflibercept (EYLEA®)	Eye Disease (Macular Degeneration)		

^{*}Biosimilar(s) available

Inflammatory Conditions continue to dominate the top 10 Specialty Drugs. This includes conditions such as, rheumatoid arthritis and Inflammatory Bowel Disease. Interesting fact, many drugs classified under inflammatory conditions also have indications for skin conditions such as psoriasis and atopic dermatitis.

Despite the reduction in the percentage of overall spend and the availability of biosimilars, adalimumab (HUMIRA®), and infliximab (REMICADE®), remain the top 2 drugs on the list.

Similar to its decreasing trend in the overall top 10 drugs, ustekinumab (STELARA®) stepped down one place in the top 10 specialty drugs, with a 23% decrease in overall

spend, which contributed to elexacaftor-tezacaftor-ivacaftor (TRIKAFTA®) climbing from 4th to 3rd place.

Risankizumab (SKYRIZI®) spend continued to increase in 2024, ranking in 6th place. It saw a remarkable increase of 49% in claimants and a 50% increase in overall spend. This drug was approved for ulcerative colitis in late 2024 which will further expand the eligible patient population. There are currently no biosimilars available for this molecule.

Upadacitinib (RINVOQ®), a Janus Kinase (JAK) inhibitor for the treatment of various inflammatory conditions becomes the first of its class to enter into the top 10 specialty drugs in 9th place, due to a 44% increase in overall spend. This drug gained new indications for ulcerative colitis

Traditional vs. Specialty Drug Trend cont'd

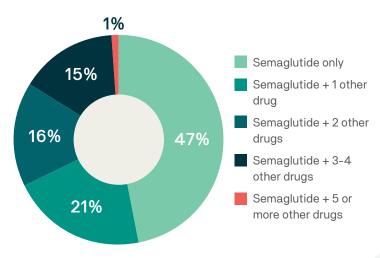
and Crohn's disease towards the end of 2023. The approval for inflammatory bowel conditions expanded the scope of its use, increasing the eligible patient population. RINVOQ® does not currently have generic alternatives.

Finally, aflibercept (EYLEA®) is a new entrant to the top 10 specialty drugs in 2024. This eye injection is intended to treat various eye diseases. Currently, biosimilars for this drug are under review by Health Canada. Upon approval, a decrease in spend is expected for this drug.

FOCUS ON DIABETES AND OBESITY

This image shows the proportion of members claiming semaglutide alone or in combination with other antidiabetic medications.

Percentage of semaglutide claimants and number of other diabetes drugs claimed in 2024



In 2024, analysis of semaglutide (OZEMPIC® and RYBELSUS®) claims identified that 47% of patients claimed semaglutide as their only diabetes drug treatment. This percentage has only increased by 1% from 2023. Semaglutide is only approved as monotherapy when first line treatment options are not tolerated. Following the increased uptake of semaglutide in the past years, many plan sponsors have put cost-containment measures

in place to ensure that semaglutide is used according to approved indications and guidelines. In 2024, the number of claimants using semaglutide as monotherapy has reached a plateau, which further confirms that these measures are effective.

WEGOVY®, which is semaglutide brand approved for chronic weight management arrived to the Canadian market in March 2024. However, the majority of semaglutide claims were for diabetes. (99.3% versus 0.7%). Uptake of WEGOVY® over the next years will depend on the plan sponsor's decision to add obesity coverage for their members.

New Definition of Obesity: Moving away from BMI and focusing on health outcomes

There has been concerns that current body mass index-based (BMI) measures of obesity may not provide accurate information about the health at the individual level. Indeed, BMI is criticized for not accounting for fat distribution, which increases health risk. *The Lancet Diabetes & Endocrinology Commission*¹ published an article in January 2025, that addresses this limitation and proposes a more accurate definition and diagnostic criteria. According to this article, clinical obesity should be diagnosed based on evidence of reduced organ function or significant limitations in daily activities.

Experts argue that defining obesity as a disease will help reduce stigma, and improve treatment access, including medication and surgery.

The new definition aims to shift the focus from size to health, encouraging a more personalized approach

¹Definition and diagnostic criteria of clinical obesity Rubino, Francesco et al. The Lancet Diabetes & Endocrinology, Volume 13, Issue 3, 221 - 262 (February 2025)

FOCUS ON DIABETES AND OBESITY cont'd

to obesity treatment. This could drive policy-makers to review eligibility criteria, and further target a specific patient population who would benefit most from treatment.

Ultimately this shift will help reduce the cost of treating later complications and organ dysfunction that would have been avoided if obesity treatment was initiated earlier.

What to Watch for:

MOUNJARO® (tirzepatide), another highly awaited drug, arrived in the Canadian market in late 2023.

+ This drug belongs to Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) receptor agonist therapeutic category. It has an advantage over the rest of the drugs within GLP-1 class of having a dual mechanism that targets glycemic levels and feelings of satiety. This drug has shown superior results over semaglutide in the management of diabetes as well as body weight reduction according to SURPASS-2 Trial.²

We will monitor the uptake of MOUNJARO® in the upcoming years and the introduction of novel diabetes treatment into the market.

Genericization of high-profile diabetes drugs

INVOKANA® (canagliflozin), JARDIANCE® (empagliflozin) and TRAJENTA® (linagliptin) currently have applications for generics submitted to Health Canada. JARDIANCE® is ranked at the 10th place by overall spend for 2024, and in 5th place in terms of traditional drugs.

Finally, two GLP-1 agonists, VICTOZA® (liraglutide) and OZEMPIC® (semaglutide) also have generic submissions currently filed with Health Canada.

With these popular diabetes drugs coming off patent in the next few years, and upcoming availability of generic versions priced at a discount compared to brand names, it is expected that drug plans will benefit from savings. Given the prevalence of diabetes in the population, generics will also help mitigate the impact of high-cost GLP-1's, which are dominating this therapeutic area.



² National Library of Medicine (U.S.). (2019, July 30-2021, February 15). A Study of Tirzepatide (LY3298176) Versus Semaglutide Once Weekly as Add-on Therapy to Metformin in Participants With Type 2 Diabetes (SURPASS-2). Identifier NCT03987919

Top 10 Therapeutic Classes

The 2024 top 10 therapeutic classes are almost identical as in 2023, with the exception of Cancer and Depression, which switched rank.

Top 10 Therapeutic Classes by Overall Spend

			% of overall	% of overall	Relative Trend (% change from 2023)		
Rank 2024	Rank 2023	Therapeutic Class	spend 2024	claims 2024	spend	claims	
1	1	Inflammatory conditions	11.7%	0.4%	-3.5%	+2.1%	
2	2	Diabetes	11.5%	7.2%	-2.6%	+1.7%	
3	3	Asthma/COPD	5.1%	3.9%	+2.0%	+0.1%	
4	5	Cancer	4.5%	0.6%	-0.8%	+0.6%	
5	4	Depression	4.4%	8.6%	-4.7%	-2.5%	
6	6	ADHD	4.0%	2.9%	-3.0%	+7.6%	
7	7	High Blood Pressure	4.0%	13.2%	-2.9%	-1.1%	
8	8	Skin conditions	3.9%	2.9%	+11.9%	-0.6%	
9	9	Diabetic supplies	2.9%	1.4%	+3.0%	-0.7%	
10	10	High Cholesterol	2.8%	7.1%	+3.7%	+2.3%	

ADHD: Attention Deficit Hyperactivity Disorder; COPD: Chronic Obstructive Pulmonary Disease

#1 - Inflammatory Conditions

Inflammatory conditions maintained the first place in terms of overall spend in the last years, and 2024 is no exception. The same decreasing trend in the percentage of overall spend was observed (-3.5%), despite a relative increase (+2.1%) in the percentage of overall claims for this category.

The top three drugs in this category remain: adalimumab, infliximab and ustekinumab.

Spend in 2024 has decreased for both adalimumab (-11%) and infliximab (-3%), driven by a decrease in the number of claimants. Biosimilar utilization is well established for these two drugs, in part due to biosimilar transition policies put in place in the last 5 years. In addition, there are now many newly marketed alternatives to treat

inflammatory conditions, which may shift claimants to other molecules.

Many new biosimilars have been approved for STELARA® (ustekinumab) in 2024. Claims for this drug have decreased by about 6% compared to 2023.

For more information, please refer to the <u>Biosimilars</u> section.

SKYRIZI® (risankizumab) and RINVOQ® (upadacitinib) continue to display a tremendous growth in terms of spend, 50% and 44% respectively compared to 2023, which can be explained by the approval of a new indication for SKYRIZI® (treatment of ulcerative colitis). The practicality of the oral administration for RINVOQ® may explain this uptake.

Top 10 Therapeutic Classes cont'd

BIMZELX® (bimekizumab) has been approved for two new indications in March 2024, active ankylosing spondylitis and non-radiographic axial spondyloarthritis (nr-axSpA). As a result, spend has increased by 71% compared to 2023 for this drug.

#2 - Diabetes & #9 - Diabetic Supplies

Diabetes still sits at the second place, despite a decrease 2.6% in the relative overall spend. The number of claimants has increased by 9.9% compared to 2023. This increase can be explained by the growing prevalence of this disease in the country. The number of patients taking diabetes medication and the overall spend were expected to follow the same trend.

For the third consecutive year, semaglutide (RYBELSUS® and OZEMPIC®) continued to drive the spend in the Diabetes category. The spend for these two drugs increased by 21%, which is lower than the 30% reported last year. Plan sponsors have put stricter cost-containment measures in place to ensure the proper use of these drugs. Of note, generic submissions for semaglutide were submitted to Health Canada and the first generic version of OZEMPIC® is expected in 2026. This will likely help bring the trend downward for this drug.

MOUNJARO® (tirzepatide) is another GLP-1 that has kept our attention in 2024. Data showed an important increase in claims, following the introduction of this drug to the market in late 2023. The shortage of OZEMPIC® at the beginning of 2024 may have prompted patients to move to this newer drug. In addition, this drug was highly anticipated as an alternative to OZEMPIC®. Stricter cost-containment measures have also been put in place to ensure the proper use of tirzepatide.

JARDIANCE® is the second drug in terms of spend in the Diabetes category. It has gained a new indication in 2024 (reduction in risk of end-stage kidney disease and renal death in adults with chronic kidney disease). This traditional diabetes drug costs about \$1,100 annually and there are no generics under review by Health Canada at this moment.

Despite the increased use of higher-cost drugs in this category, the overall spend was offset by the utilization of recently genericized higher cost diabetes molecules (dapagliflozin, sitagliptin and their combinations with metformin) as well as biosimilars for insulins. It is worth mentioning that a new insulin AWIQLI® has been brought to market in June 2024. It is administered once weekly, as opposed to once a day for other forms of long-acting insulins. The effect of this newer product in the diabetes category will be more evident in 2025.

For diabetic supplies, data showed a 3% increase in spend in 2024, but a 0.7% decrease in the number of claims. The number of claimants for this category has increased by 8%.

Similar to last year, flash glucose sensors generated the biggest proportion of spend in this category (66%). These devices have seen a 7% increase in spend since 2023, and an 8% increase in the number of claimants. In comparison, the classic blood glucose test strips have seen a 10% decrease in spend and a 1% decrease in the number of claimants. As a reminder, flash glucose sensors are more convenient for patients to use, but their annual cost is about 6 times more than test strips.

#3 – Asthma/Chronic Obstructive Pulmonary Disease (COPD)

The relative percentage of overall spend in the Asthma/COPD category has increased by 2% in 2024 while the percentage of overall claims remained stable.

This year again, SYMBICORT® (a combination of budesonide and formoterol) generated the most spend, with an increase of 3% in spend also driven by an 11% increase in the number of claimants.

Tezepelumab (TEZSPIRE®) is a subcutaneous injection that is approved as an add-on treatment for severe asthma in patients aged 12 years or older. Spend for this drug has doubled in 2024 alongside an increase in the number of claimants.

Our analysis also showed a slight decrease in spend (-7%) for XOLAIR® (omalizumab) despite stability in the number of claimants.

Top 10 Therapeutic Classes cont'd

#4 - Cancer

In 2024, despite a slight decrease in the relative percentage of overall spend (-0.8%), Cancer has climbed from 5th to 4th place. This category has seen a 12.1% growth in the number of claimants.

VERZENIO® (abemaciclib) has generated the most spend in this category in 2024. This drug, previously approved for advanced or metastatic breast cancer, can now be used for the treatment of early breast cancer at high risk of disease recurrence. As a result, spend more than doubled for this drug.

Oral targeted therapies also drove spend up in this category, such as ribociclib and osimertinib. On the other hand, other targeted therapies, such as ibrutinib and palbociclib, contributed to bringing the spend for cancer down due to a combination of less claimants using these drugs in 2024 but also the availability of generic palbociclib. For instance, generics have been approved for palbociclib in September 2024, priced 25% lower than the brand. A further decrease in spend is expected in 2025 for this drug.

BRUKINSA® (zanubrutinib) is another oral targeted therapy for which spend has increased significantly in 2024. It is indicated to treat various types of lymphoma, and more recently, to treat follicular lymphoma in combination with GAZYVA® (obinutuzumab). Given that most treatment options for this type of cancer are given in a hospital setting, this can explain the increase in spend where patients and prescribers favour treatments that can be taken at home.

#5 - Depression

Depression dropped from 4th to 5th place in the 2024 top 10, mainly due to a decrease in relative overall spend of 4.7%. Despite the reduction in spend, the number of claimants has increased by 5%, but this increase was offset by the fact that most drugs in this category have generic versions available.

Escitalopram (CIPRALEX®, and generics) was still the drug generating the most spend in this category, despite a 17% decrease in 2024. It is followed by vortioxetine (TRINTELLIX®) and sertraline (ZOLOFT®, and generics).

However, spend and number of claimants remained stable for these two drugs (between 0 and 2%). Finally, SPRAVATO® (esketamine) continued to see a 23% increase in spend and 2% in claimants in 2024.

#6 - Attention Deficit Hyperactivity Disorder (ADHD)

The relative overall spend for Attention Deficit Hyperactivity Disorder (ADHD) decreased by 3%. However, this class saw an increase of 17.6% in the number of claimants.

Lisdexamfetamine (VYVANSE®) is the drug generating the most spend for 2024 in this category; it is in 3rd place in the traditional drugs top 10. Generics were approved midyear and data immediately showed a positive impact on spend. There was no change in spend for this chemical in 2024, but a 17% increase in the number of claimants. Indeed, spend per claimant decreased by 18% compared to 2023 and about 13% of spend for this chemical was driven by generics. Most provinces established interchangeability for this molecule by the end of 2024, which contributed to driving the generic uptake. For context, generics are priced about 15% to 50% less than the brand, depending on the strength. A more complete portrait of the effect of the availability of generics for this drug will be available in 2025.



Top 10 Therapeutic Classes cont'd

Methylphenidate, which includes CONCERTA®, RITALIN®, BIPHENTIN® and their generics as well as QUILLIVANT ER® and FOQUEST®, followed closely although the increase in spend and claimants has been lower in 2024. A new extended-release formulation, JORNAY PM®, has been approved in November 2024. It is the first evening-dosed methylphenidate product and is focused on providing better control of symptoms upon awakening.

For more information, please refer to the <u>ADHD</u> section.

#8 - Skin Conditions

Skin conditions remained at the 8th place in terms of spend for 2024, but data shows that spend continues to grow year over year (11.9% for 2024).

DUPIXENT® (dupilumab) was still the drug generating the most spend for this therapeutic class, with an increase of 28% in spend. About 30% more members have claimed this drug in 2024, compared to 2023. This drug gained more and more indications as time goes and its use has

expanded to all age groups (including children aged 1 year and older for eosinophilic esophagitis).

Tralokinumab (ADTRALZA®) also contributed to the trend observed for skin conditions, competing with dupilumab (DUPIXENT®). Indicated for the treatment of moderate to severe atopic dermatitis, spend for this drug increased by 61% in 2024, outpacing DUPIXENT® growth. This increase was mostly driven by an increase of 37% in new claimants.

Finally, topical roflumilast (ZORYVE®) has also seen a tremendous increase in spend in 2024 (more than doubled), as more patients are claiming this drug to treat psoriasis. Towards the end of 2024, its use was expanded to treatment of seborrheic dermatitis which makes it the first approved drug for this condition usually treated with off-label, low-cost drugs.

#10 - High Cholesterol

High cholesterol spend increased by 3.7%, which was mostly driven by a 9.9% increase in claimants.

In 2024, the top two chemicals by spend were the traditional drugs rosuvastatin and atorvastatin. Their low cost (average annual spend per claimant was \$95 and \$120) had little effect on trend.

Proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors, such as PRALUENT® (alirocumab) and REPATHA® (evolocumab) monoclonal antibodies, were mostly responsible for this upward trend. Data showed an increase between 5% and 10% in the number of claimants for these drugs, which treatment cost is about 30 times the cost of traditional high cholesterol treatments. LEQVIO® (inclisiran) also showed significant uptake in 2024, with a two-fold increase in the number of claimants (and even higher increase in spend).

EVKEEZA® (evinacumab) is a monoclonal antibody that has been approved for homozygous familial hypercholesterolemia in 2023. Although this disease is rare, the high cost of this drug (over \$400,000 per patient annually) also contributed to the increase in spend for this category.



Attention Deficit Hyperactivity Disorder: A Rising Health Condition

Attention Deficit Hyperactivity Disorder (ADHD), is a neurodevelopmental disorder that affects approximately 5% to 9% of children and adolescents, and 3% to 5% of adults.³

This condition can manifest into three different forms: inattention, hyperactive impulsive or a combination of both.

Common ADHD symptoms³

Forgetfulness, loses things required for activities

Difficulty with organization at school, work and personal life

Talking excessively, frequently interrupting others, difficulty to await turn

Difficulty in sustaining attention in tasks/activities, reluctance to engage in tasks that require a sustained mental effort

Easily distracted, difficulty to complete tasks or manage time

ADHD causes symptoms that can impede greatly on an individual's quality of life, through negative repercussions on education and workplace productivity. Additionally, ADHD can also increase the risk of developing the following:

- + Addiction
- + Accidents, through recklessness or inattention (especially driving)
- + Difficulty with personal relationships
- + Anger management problems
- + Low self-esteem, depression, or other mental health disorders

ADHD, as a therapeutic class, entered the top 10 therapeutic class by overall spend in 2019 and since then spend has been rising, until it reached the 6th place in 2024.

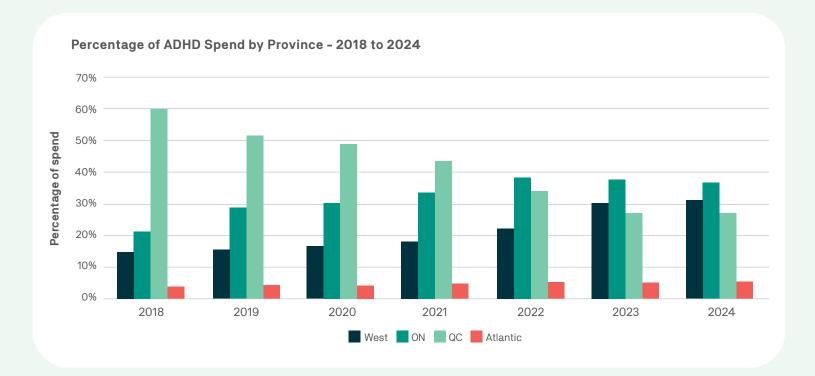
The number of claimants for ADHD treatment increased by 41% from 2018 to 2024, which increased claims by 30% and overall spend by 19%. The greatest growth of claimants was observed after 2020, coinciding with the start of the COVID-19 pandemic and the updates of Canadian ADHD practice guidelines.³

The next few sections will explore trends in our ESC claims data from 2018 to 2024 on the ADHD therapeutic class by provincial, age, and gender differences, and highlight some potential factors that may be contributing to these changes. Furthermore, newer treatments and solutions to better manage spend for this condition will be discussed.

Provincial Differences in the Consumption of ADHD Treatments

When interpreting claim breakdown by region, ESC's data shows that prior to the pandemic, the majority of ADHD claims were submitted in Quebec compared to other provinces. However, a shift occurred as of 2020, where the proportion of ADHD claims for Western provinces and Ontario increased, and Quebec claims decreased. In 2024, regional disparities still exist, but they are less drastic. The COVID-19 pandemic may have contributed to this shift, with more treatment prescribed across the country to address the struggles people were experiencing with remote work. Access to professional evaluation and diagnosis through virtual consultations may also have contributed to this change.

³ Canadian-ADHD-Practice-Guidelines-4.1-edition-January-2021.pdf



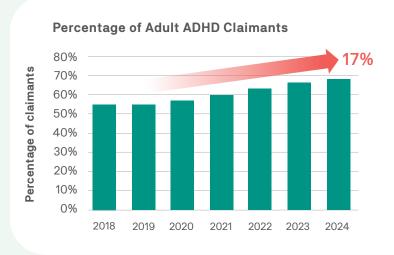
ADHD: No longer Just a Childhood Disease

Historically, ADHD has been predominantly thought to be impacting children and adolescents exclusively. However, recent data emerging in the last few years have challenged this narrative, bringing adult ADHD to the forefront. Now, ADHD is largely being recognized as a chronic illness that may start in childhood, or adolescence, but continues into adulthood.

Parents of children who have been diagnosed with ADHD may recognize some of the symptoms for themselves. ADHD is a hereditary disease: If a parent or sibling suffers from ADHD, the individual is up to 30% to 40% more likely to also be diagnosed with the condition.³

Furthermore, older adults who may have suffered from various symptoms throughout their life are now starting to realize that they may have never been diagnosed for this condition. Increasing awareness for ADHD and mental health in general has contributed to this realization. This awareness may have grown even more during the pandemic lockdowns, where some individuals encountered productivity challenges working from home.

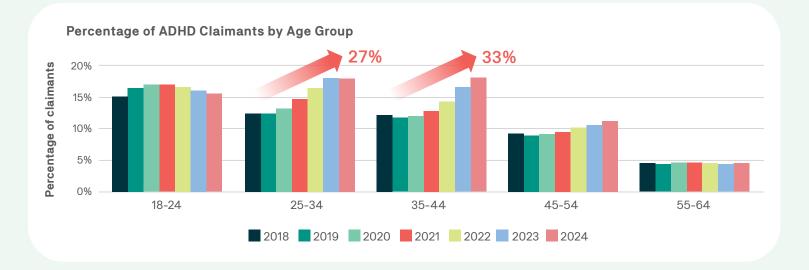
Looking at ESC data, the percentage of adult ADHD claimants remained relatively stable in 2018 and 2019. Starting from 2020, our data showed a gradual increase in ADHD claimants, corresponding to a 17% increase in adult ADHD claimants between 2020 and 2024.



³ Canadian-ADHD-Practice-Guidelines-4.1-edition-January-2021.pdf

Among the different adult subgroups, the largest increase in the overall percentage of claimants was observed in those between 25-34 and 35-44 years of

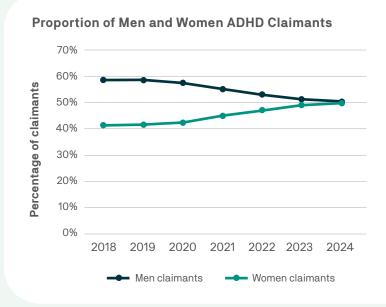
age. In the last 4 years alone, the percentage of ADHD claimants aged 25–34 years and 35–44 years increased by 27% and 33% respectively.



Gender Disparity in ADHD Claimants

ADHD symptoms present differently between men and women, especially during childhood. On average, girls are prone to inattentive type of ADHD, while boys have more hyperactive, impulsive symptoms. The latter symptoms are those typically associated with ADHD and thus, more easily diagnosed.³ However, these gender disparities in rates of diagnoses in childhood have been observed to lessen by adulthood.⁴

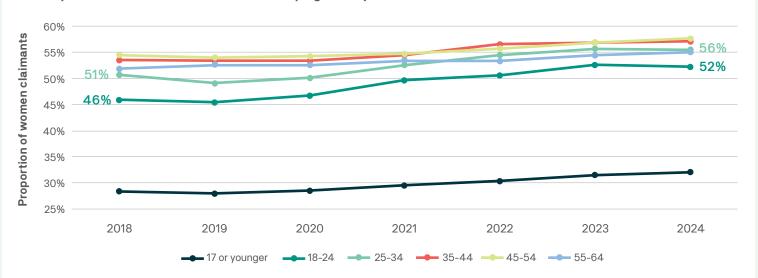
There has been a steady increase in the proportion of women in the last 7 years, where the proportion between men and women has evened out to a 50-50 split.



³ Canadian-ADHD-Practice-Guidelines-4.1-January-2021.pdf

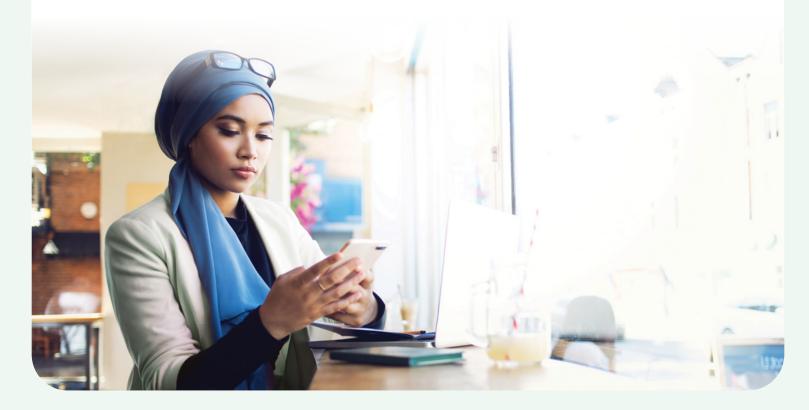
⁴ Martin, Joanna. "Why are females less likely to be diagnosed with ADHD in childhood than males?." The Lancet. Psychiatry vol. 11,4 (2024): 303–310. doi:10.1016/S2215-0366(24)00010-5





The same upward trend in the number of women ADHD claimants was observed across all age categories.

Among the different age categories, women ADHD claimants aged 25-34 years and 35-44 years saw the greatest increase between 2020 and 2024, at 24% and 27% respectively. This increase may be attributed to improved recognition of the gender-specific characteristics of ADHD among patients and care providers over the years.



Treating ADHD: What's New?

Latest guidelines from the Canadian ADHD Resource Alliance recommend the use of long-acting psychostimulants, such as methylphenidate or amphetamines, as first-line treatment, as they have similar efficacy and tolerability profiles. After trials of both amphetamine or methylphenidate, second line options include atomoxetine, guanfacine and short/intermediate-acting psychostimulants.

Despite both first-line treatments being available in generic versions, there is still new development in the pharmaceutical industry for these drugs. Many new formulations of methylphenidate are now available in Canada, which may continue to drive the spend for ADHD. For instance, QUILLIVANT ER®, marketed in June 2024, is available as chewable tablets, and oral suspension, and offers an additional product for pediatric patients unable to swallow full capsules or tablets. JORNAY PM® is another new formulation of methylphenidate aimed to control ADHD symptoms upon awakening as the drug is taken in the evening. On the other hand, VYVANSE® (lisdexamfetamine) and generics were marketed in Canada, and second-line treatment as atomoxetine and guanfacine also had generic versions available. This may provide cost savings to plans.

Currently, there are not many upcoming drugs for ADHD in Canada. However, centanafadine SR, an investigational drug currently in phase 3 trials, is expected to launch in the US in 2026. It is the first drug that inhibits dopamine, norepinephrine and serotonine reuptake for the treatment of ADHD. This first-in-class drug might provide a better tolerability compared to actual treatments available for children and adolescents. In addition, it is believed to have a lower abuse potential than other commonly prescribed treatments for ADHD.



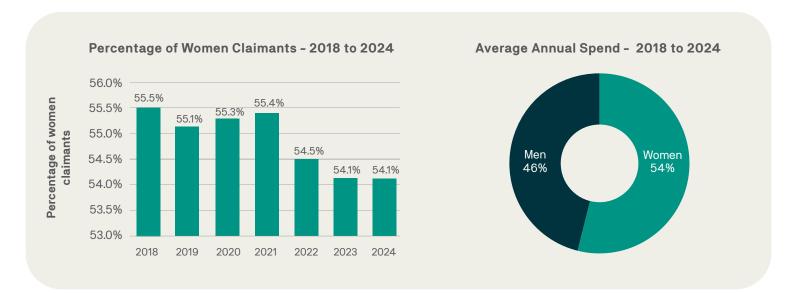
- + ADHD affects individuals throughout their life and causes many symptoms that may negatively impact education and workplace productivity. As the prevalence of ADHD diagnoses and associated needs increase, it is important to employ strategies to manage costs without compromising access to necessary and effective treatment.
- + Multiple plan management solutions can be considered to balance access to treatment for members and drug plan sustainability. Mandatory generic substitution can help direct patients to lower-cost alternatives of effective treatments whereas managed tiered formularies or clinical programs like Step Therapy can play a key role in better management in the face of this growing therapeutic class.





Women make up approximately half of the Canadian population, and in 2023, there were about 9.6 million women employed, according to Statistics Canada.⁵ Conditions that affect women only or in a disproportionate manner therefore have an impact on half of the population, and by extension, a significant portion of the workforce, with potential consequences on productivity, absenteeism and disability.

ESC's data show that between 2018 and 2024, women claimants represented a little more than half of the total claimants. For the same period, the average annual spend was 54% for women versus 46% for men.



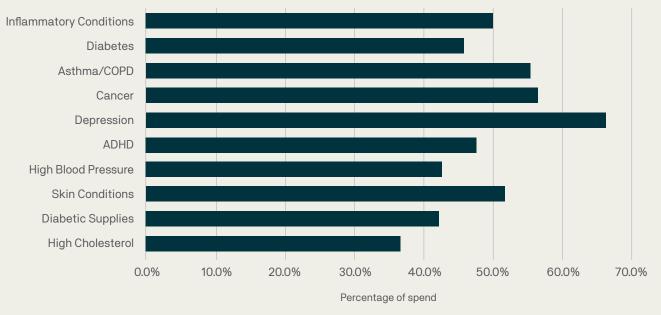
It does seem logical that if women represent a bigger proportion of claimants, they submit more claims and therefore, spend for this gender group will be higher. But this begs the question: do women and men really consume medication at the same rate and in the same manner?

Breaking down further data helps us get a better understanding of the difference in drug consumption between men and women.

⁵ Statistics Canada - Labour force characteristics by gender and detailed age group, annual

Women are Affected Disproportionally by Some Conditions

Overall Top 10 Therapeutic Classes with Percentage of Spend by Women*



*Therapeutic classes ranked from first (top) to tenth position (bottom) in terms of overall spend

Looking at the top 10 therapeutic classes with Percentage of Spend by Women in 2024, data shows that some conditions do affect women disproportionally.

For example, Cancer claims in women represented 56.4% of overall spend for this therapeutic class ranked in 4th place of the overall Top 10. For Asthma/COPD in 3rd place, women claimants represented 55.5% of overall spend. The difference is even more striking for Depression, ranked in 5th place, where two thirds of spend was attributed to women claimants.

On the other end, some conditions seem to affect greatly male claimants: Diabetes, High Blood Pressure, High Cholesterol and ADHD. These classes have a higher proportion of spend attributed to men than women.

A separate analysis of the top 10 therapeutic classes by overall spend per gender revealed that there are important differences for men and women and that the overall top 10 may not give the full picture regarding gender disparities. One of the most striking differences is the place of Depression in women's top 10, in 3rd place, whereas it is only found at the bottom of the list for men (10th place).

More insights about depression in women can be found in the section: <u>Depression is more prevalent in</u> women.

Multiple Sclerosis in another interesting class to look at: it currently sits in 8th place in terms of spend for women claimants but this class is not part of the top 10 for men. In fact, multiple sclerosis does not even make the top 20 for men. Globally, women are at least twice most likely to be diagnosed with this disease. In Canada, about 75% of patients living with Multiple Sclerosis are women.⁶ The higher prevalence in women explains the higher volume of spend for this class in this population.

The data also shows the differences in the ADHD class, which are addressed in the section: <u>Attention Deficit Hyperactivity Disorder</u>.

⁶ Prevalence and incidence of MS in Canada and around the world (MS Canada)

Top 10 Therapeutic Classes by Spend in 2024 for Women and Men

Rank 2024	Women	Men
1	Inflammatory Conditions	Diabetes
2	Diabetes	Inflammatory Conditions
3	Depression	High Blood Pressure
4	Asthma/COPD	Asthma/COPD
5	Cancer	ADHD
6	Skin Conditions	Cancer
7	ADHD	Skin Conditions
8	Multiple Sclerosis	High Cholesterol
9	High Blood Pressure	Diabetic Supplies
10	Hormone Replacement	Depression

Finally, looking at the top 10 for men, classes related to cardiovascular diseases such as High Blood Pressure, High Cholesterol and Diabetic Supplies, make up for almost a third of the top 10 while only High Blood Pressure is in the top 10 for women (9th place). It has

been established in the literature that men are more vulnerable to cardiovascular diseases in general.

However, heart disease is the first cause of premature death in women in Canada. Interestingly, symptoms of heart disease in women are often missed because they may differ from those in men. Major hormonal variations such as those occurring during pregnancy and menopause may contribute to the development of additional risk factors for heart disease in this population.

AGE - AN IMPORTANT FACTOR IN WOMEN'S HEALTH JOURNEY

Another interesting way to look at the gender data is through the age lens. The table below displays the life cycle of a woman, broken down in four life stages:

- + Childhood and teenage years, covering birth to 17 years of age. This population represented 15% of women claimants in ESC's 2024 book of business.
- + Early adulthood, from 18 to 24 years of age, represented about 7% of women claimants.
- + Family and career building years, ranging from 25 to 44 years old (32% of women claimants).
- + Late adulthood (45-64 years old), which represented 46% of women claimants.

	O-17 Childhood & Teenage				18-24 Early Adulthood		25-44 Family & Career E	_	45-64 Late Adulthood		
А	DHD	14.3%	ADHD	12.1%	Inflammatory	13.2%	Diabetes	13.0%			
C	ystic Fibrosis	10.8%	Inflammatory	11.8%	Conditions		Cancer	6.5%			
In	nfections	7.5%	Conditions	11.070	Depression	6.5%	Depression	5.3%			
A	sthma/COPD	6.2%	Birth Control	10.5%	Multiple Sclerosis	5.3%	Hormone	4.40/			
			Depression	8.4%	Infertility	4.5%	Replacement	4.1%			
	15% of women 50 of sp			% pend	32% of women 27 of sp			5% pend			

⁷ Our Strategy (Heart and Stroke)

The percentage of overall spend in women claimants during various life stages is displayed in the bigger circles. Finally, for each life stage, we have illustrated the percentage of overall spend for the main therapeutic classes alongside the percentage of overall women claimants represented in that life stage.

For obvious reasons, women's needs in terms of medication will vary as they progress through the different cycles of life. A toddler will not consume the same drugs as a young adult, for many reasons but notably, biology. This explains why Asthma and Infections are one of the main categories in the childhood stage while Birth Control and Inflammatory Conditions are among the top for young adults.

The spend pattern changes in later life stages, where Depression, Multiple Sclerosis and Infertility appear in the Family/Career building years. Meanwhile, chronic diseases such as Diabetes, and Cancer become the dominant conditions in Late Adulthood. In addition, menopause often starts in late adulthood, which explains why Hormone Replacement therapies make an important part of spend for this stage of life. A deeper dive on menopause will follow.



This thorough data review from the gender perspective highlights that there are important differences in women and men, in terms of health conditions and drug consumption. Not only women are affected at a greater rate than men by some conditions, but they are also impacted differently throughout life. These insights are important to consider when elaborating benefit plans and policies: measures need to be flexible and adapted to the women's population to maximize the value for members and plan sponsors.

DEPRESSION IS MORE PREVALENT IN WOMEN

Data shows that depression is 1.7 times more prevalent in women than men,⁸ which may be explained by many factors:

- + Today, despite major changes in the last decades, women still hold the greatest responsibilities in the household. Many women hold full-time work responsibilities, in addition to being responsible for childcare and even, elderly care in the later stages of their lives.
- Biology plays an important role: major hormonal changes such as those brought by pregnancy or menopause can lead to the development of depressive symptoms.
- + Finally, despite the increase in awareness about mental health disorders, especially following the COVID-19 pandemic, men still do not seek medical care as often as women for mental health issues. As a result, depression and other mental health issues are still underdiagnosed and undertreated in this population.⁹



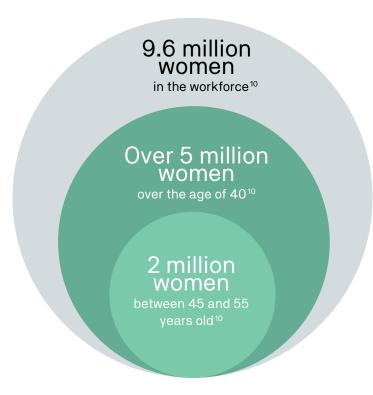
⁸ Why is depression more prevalent in women? | JPN

⁹ Anxiety & Depression Association of America

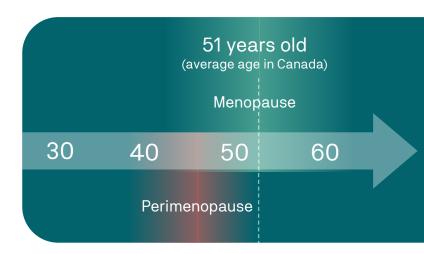
MENOPAUSE: IMPACTING WOMEN IN THE WORKFORCE

Menopause is a phase that almost all women will go through. According to the Menopause Foundation of Canada, 3 out of 4 women will experience symptoms that will interfere with their day-to-day activities and about a quarter will experience severe symptoms. Those severe symptoms, if not managed, drive up to 10% of women out of the workforce.

It is estimated that there are about 2 million women aged between 45 and 55 years old in the workforce. This period is critical in the lifespan of a woman: menopause and its symptoms manifest around this age while women are usually at an important stage in their career.



In Canada, the average age of menopause is 51 years old. But menopause is not a punctual event; a woman can experience symptoms for over 10 years. Although menopause is a physiological event in a woman's life, only a portion of women will seek medical care and even fewer will receive adequate treatment.



It starts with perimenopause, which is defined as the time leading to menopause. Hormone levels fluctuate, which may cause symptoms that have negative repercussions on health, workplace productivity and quality of life in general.

Eventually, perimenopause turns into menopause, defined as 12 consecutive months without periods. Ovaries stop producing reproductive hormones (progesterone and estrogen), which can provoke more or less intense symptoms. Some of the most common symptoms include:

- Vasomotor symptoms: the most common and wellknown are hot flashes and night sweats. Up to 80% of women report being affected by vasomotor symptoms during menopause
- + Urinary urgency
- + Weight gain
- + Insomnia
- + Mood swings, irritability and depression
- + Dryness (skin, eyes, mouth, vaginal)
- + Concentration and memory difficulties

Most women will experience symptoms for 7 years or less after their final period. However, 10% of women may suffer for more than 10 years.

Hormone therapy (HT) consists in taking hormone supplements, estrogen combined or not with progesterone, to alleviate menopausal symptoms.

¹⁰ Statistics Canada - Labour force characteristics by gender and detailed age group, annual

Most of these drugs have been marketed for quite some time, often available in generic forms and therefore, considered low-cost. HT is still controversial due to concerns of increased cancer risk. It is also contraindicated in women with a history of breast cancer, heart attack, stroke, blood clots and liver disease. In 2024, HT represented about 4.1% in spend for the Late Adulthood age bracket.

Newer treatments have been brought up to market in the last years. BIJUVA®, a capsule combining estradiol and progesterone, is indicated for the treatment of severe vasomotor symptoms. IMVEXXY® (estradiol) is an intravaginal insert that is indicated to treat symptoms related to vaginal atrophy. Finally, VEOZAH® (fezolinetant), became in December 2024 as the first non-hormonal therapy to have been approved

in Canada to relieve moderate to severe vasomotor symptoms. It is also believed to have a positive effect on mood and insomnia. These more recent therapies are most expensive than the traditional HT drugs.



The impact of menopause on women is important and can have negative repercussions on their productivity at work, career progress, and wellbeing. There are many opportunities to improve how the needs of these women are met, whether it is through the adoption of flexible work policies, increased access to newer treatments or health programs.



WOMEN'S HEALTH: FUTURE DEVELOPMENTS

The data reviewed for women's health showed that there are unmet needs in this population. The drug pipeline may address some of these needs.

Chemical	Expected Indication	Status
Elinzanetant Osanetant	Treatment of vasomotor symptoms in menopause; non-hormonal therapy	Under Health Canada review Clinical trial (Phase II)
Estetrol	Treatment of vasomotor symptoms in menopause; hormonal therapy but evidence suggests improved benefits and safety over existing estrogen therapies	Under FDA review; not submitted to Health Canada
Linzagolix	Endometriosis-associated pain and fibroids	Clinical trial (Phase III)
Brexanolone (oral)	Post-partum depression	Clinical trial (Phase III)

Elinzanetant is a similar molecule to VEOZAH® (fezolinetant), which has recently been approved as the first non-hormonal therapy to treat vasomotor symptoms. Osanetant is believed to have a similar mechanism of action as elinzanetant, but is still studied in clinical trials.

Linzagolix is similar to relugolix, which is found in MYFEMBREE® (in combination with estradiol and norethindrone), which has been approved in 2023 for the management of heavy uterine bleeding associated with fibroids and moderate to severe pain associated with endometriosis. However, linzagolix would have the advantage of being a non-hormonal monotherapy.

Finally, brexanolone is a GABA modulator currently approved in the United States as an intravenous infusion for the treatment of post-partum depression. The oral form is currently being evaluated in Phase III clinical trials.

In Canada, there is no specific treatment approved for this indication yet.

Awareness around women's health is rising. Women represent half of the workforce in the country and are disproportionally affected by health challenges due to biological and sociological factors. Moreover, their health varies throughout life stages along with their needs in terms of medical care and treatment. It is critical to understand these variations to develop the best possible solutions to serve this population adequately. Flexible benefit plans aimed to support women through their journey, programs oriented to promote health, effective prevention campaigns and adequate coverage for conditions impacting women are all measures that plan sponsors can put in place to meet the needs of this population.



Biosimilars

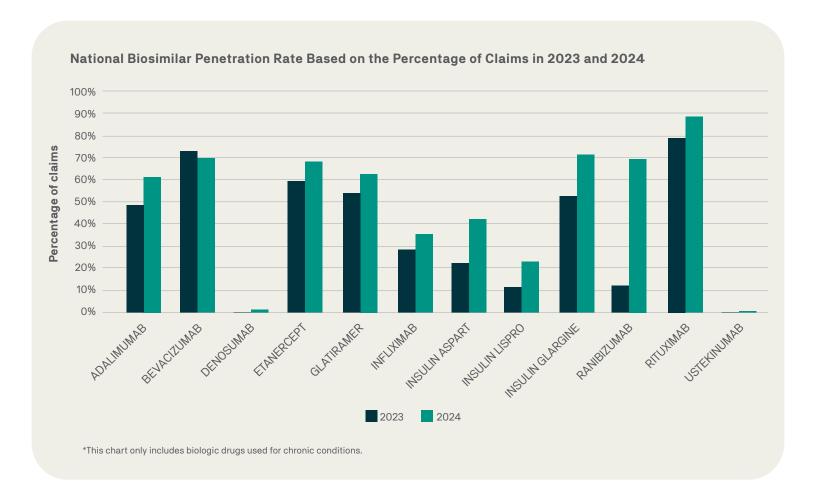
2024 Highlights

- + In August 2024, Manitoba was the last pharmacare province to join the public drug plans across Canada to implement a biosimilar initiative. All ten provinces have now made the switch to biosimilar drugs.
- + Multiple biosimilars of STELARA® (ustekinumab) were marketed in Canada in 2024 (JAMTEKI®, WEZLANA®, STEQEYMA®). As a result, many provinces added STELARA® to the list of biologic drugs targeted to their biosimilars policies.
- + Denosumab biosimilars have been marketed in Canada during 2024: JUBBONTI® (biosimilar of PROLIA®) and WYOST® (biosimilar of XGEVA®). Consequently, many provinces and territories added XGEVA® and PROLIA® to the list of biologic drugs targeted in their Biosimilar Initiative.
- + The first biosimilar of ACTEMRA® (tocilizumab), called TYENNE®, was approved by Health Canada in October 2024. At the time of writing this report, no province targeted this molecule yet as part of their biosimilar transition policy. This will be monitored throughout 2025.

Biosimilar Quick Reference Table							
Chemical Name	Corresponding Originator						
Adalimumab	HUMIRA®						
Bevacizumab	AVASTIN®						
Denosumab	XGEVA®, PROLIA®						
Etanercept	ENBREL®						
Glatiramer	COPAXONE®						
Infliximab	REMICADE®						
Insulin aspart	NOVORAPID®						
Insulin glargine	LANTUS®						
Insulin lispro	HUMALOG®						
Ranibizumab	LUCENTIS®						
Rituximab	RITUXAN®						
Tocilizumab	ACTEMRA®						
Ustekinumab	STELARA®						

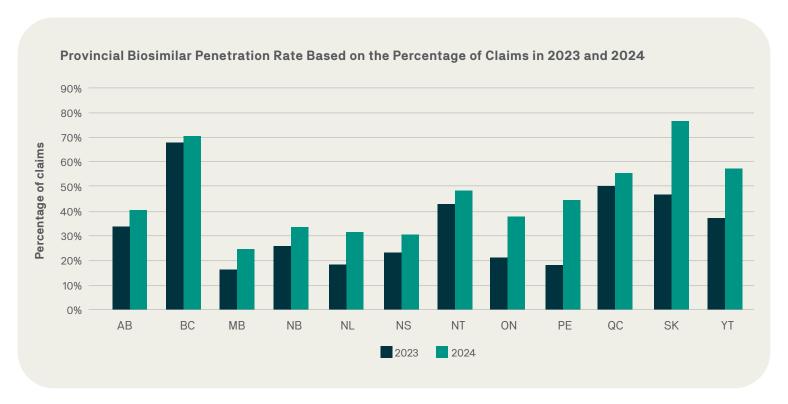


Biosimilars cont'd



- + The national biosimilar penetration rate is calculated by comparing the number of biosimilar claims for specific drugs in each year with the combined number of originator biologic and biosimilar claims. Based on the group of biologic drugs used to treat chronic conditions in the graph above, the overall biosimilar penetration rate continued to increase from 29% to 42% in 2024 in comparison with 2023.
- Ranibizumab biosimilars have the greatest variation in penetration rate, increasing from 13% to 70% in 2024 due to provincial switching policies that have been put in place. This drug is used to treat multiple
- eye disorders such as neovascular (wet) age-related macular degeneration (AMD). The first biosimilar for the originator drug LUCENTIS® was marketed in 2023, under the name BYOOVIZ®, and a second biosimilar was marketed in early 2024, under the name RANOPTO®.
- + Insulin biosimilars continue to penetrate the Canadian market, as more public plans have included these drugs in their biosimilar policies.
- + The uptake for ustekinumab biosimilars by private plans has not been seen yet (See <u>Ustekinumab</u> summary of provincial biosimilar transition policies).

Biosimilars cont'd

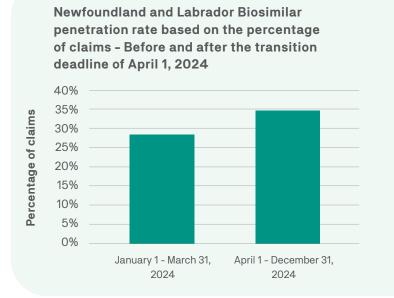


Saskatchewan's biosimilar penetration rate increased the most, from 47% to 76% in 2024. The transition periods ended in April 2023 for most of the drugs and in March 2024 for HUMALOG®. Since Saskatchewan is a pharmacare province, integration of private payers with the province is facilitated.

Prince Edward Island's biosimilar penetration rate saw a significant increase in 2024. This was mainly due to their public biosimilar switching policy, where patients had until June 2024 to switch to a biosimilar alternative. The province extended the date until September 30, 2024 for some of their targeted drugs.

Manitoba, a pharmacare province, also launched their biosimilar initiative, effective August 1, 2024, to generate cost savings. Although the transition period allowed by the province has not come to an end, data showed an increase in Manitoba's biosimilar penetration rate.

The **Newfoundland and Labrador** Prescription Drug Program (NLPDP), launched their biosimilar initiative in March 2023, allowing a 12-month transition period until funding and/or special authorizations end for ten originator biologics. Coverage was set to end on April 1, 2024. Therefore, the biosimilar penetration rate increased following this date.



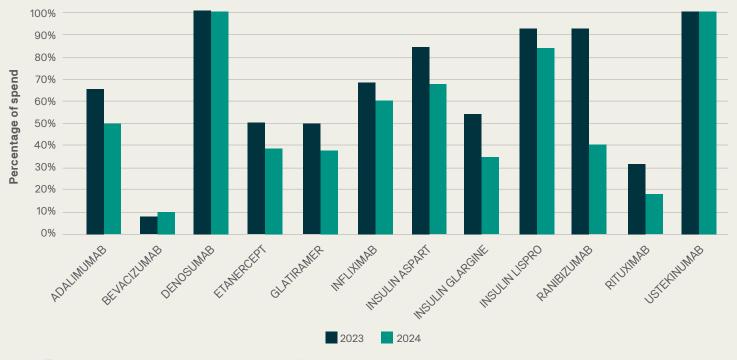
Biosimilars cont'd

Newly Marketed Biosimilars - Percentage of Claims by Province in 2024

Chemical Name	AB	ВС	МВ	NB	NL	NS	NT	ON	PE	QC	SK	YT
DENOSUMAB	2%	4%	2%	0.3%	2%	1%	*	1%	*	2%	0.2%	*
INSULIN ASPART	30%	52%	8%	17%	32%	29%	18%	44%	60%	48%	72%	37%
INSULIN GLARGINE	69%	91%	42%	65%	61%	59%	64%	62%	78%	77%	96%	69%
INSULIN LISPRO	13%	55%	5%	11%	8%	7%	38%	15%	18%	40%	54%	23%
RANIBIZUMAB	*	*	*	83%	5%	*	*	33%	*	99%	*	*
USTEKINUMAB	1%	2%	0.4%	*	0.1%	*	*	0.2%	*	0.3%	*	*

^{*}Insufficient claims

Percentage of Spend on Originator Biologics in 2023 and 2024



^{*}This chart only includes biologic drugs used for chronic conditions.

The overall percentage of spend on originator biologics in the graph above saw a decrease from 75% in 2023 to 66% in 2024, as biosimilar penetration continued to increase. The spend on originator biologics for ustekinumab and denosumab is expected to decrease next year with the ongoing provincial biosimilar initiative that target these drugs.

Biosimilars cont'd

Ustekinumab - Summary of Provincial Biosimilar Transition Policies

Despite biosimilar transition policies being in place in many provinces, the uptake of ustekinumab biosimilars has been minimal. A few factors can explain this:

- + Biosimilars for ustekinumab were approved for skin conditions and gastrointestinal conditions at a different time. For instance, JAMTEKI® received its notice of compliance in November 2024 for the gastrointestinal indications, shortly after being approved in May 2024 for plaque psoriasis and psoriatic arthritis. Furthermore,
- provincial biosimilar transition policies were rolled out at the same time as additional indications were approved by Health Canada. This may have contributed to the slow uptake of biosimilars.
- + Provinces like Alberta only cover ustekinumab for plaque psoriasis and not for gastrointestinal conditions. Less patients are targeted by the transition in such case.
- + Transition periods are still in effect in some provinces such as Ontario. The full effect of these transition policies may be more apparent later in 2025.

Province	Transition end date	Indications	Biosimilars
AB	November 1, 2024	Plaque psoriasis	JAMTEKI [®] WEZLANA [®]
BC	December 2, 2024	Plaque psoriasis	JAMTEKI® STEQEYMA® WEZLANA®
MB	May 27, 2025	Plaque psoriasis	JAMTEKI [®] WEZLANA [®]
NB	November 30, 2024	Plaque psoriasis	JAMTEKI® WEZLANA®
NL	May 1, 2025	Plaque psoriasis Psoriatic arthritis	JAMTEKI [®]
		Plaque psoriasis Psoriatic arthritis Ulcerative colitis Crohn's disease	WEZLANA®
NS	December 1, 2024	Plaque psoriasis Psoriatic arthritis	JAMTEKI®
		Plaque psoriasis Psoriatic arthritis Ulcerative colitis Crohn's disease	WEZLANA [®]
NT	June 1, 2025	Not specified	JAMTEKI [®] WEZLANA [®] STEQEYMA [®]
ON	January 31, 2025	Plaque psoriasis	JAMTEKI [®] WEZLANA [®]
PE	August 31, 2025	Plaque psoriasis	JAMTEKI [®] WEZLANA [®]
QC	November 6, 2024	Plaque psoriasis Psoriatic arthritis	JAMTEKI [®] WEZLANA [®]

Biosimilars cont'd

Denosumab - Summary of Provincial Biosimilar Transition Policies

Denosumab is the latest originator biologic drug targeted by most provincial and territorial biosimilar transition policies. The originator biologics PROLIA® and XGEVA® and their corresponding biosimilars JUBBONTI® and WYOST®, respectively, are used for the treatment of bone loss-related conditions.

Province	Transition end date*	Biosimilars
AB	PROLIA® - May 1, 2025	JUBBONTI®
BC	March 3, 2025	JUBBONTI® WYOST®
MB	February 26, 2025	JUBBONTI® WYOST®
NB	April 30, 2025	JUBBONTI® WYOST®
NL	September 1, 2025	JUBBONTI® WYOST®
NS	XGEVA® - April 1, 2025	WYOST®
	PROLIA® - October 1, 2025	JUBBONTI®
NT	June 1, 2025	JUBBONTI® WYOST®
ON	August 29, 2025	JUBBONTI® WYOST®
PE	PROLIA® - August 31, 2025	JUBBONTI®
QC	May 21, 2025	JUBBONTI® WYOST®

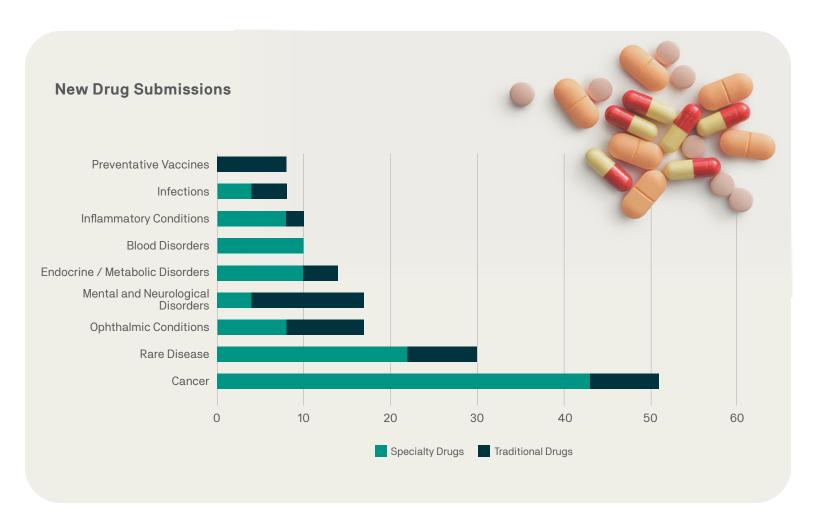
*If not specified, transition end date applies for both originator biologics

What to Watch Out for in 2025:

- + Impact of Manitoba's biosimilar initiative.
- + Uptake of ustekinumab and denosumab biosimilars by private plans following the end of the transition periods.
- + Additional new biosimilars coming to market, new transition policies and penetration rate by province.

Drug Pipeline

New drug treatments are coming out of the pipeline at an unprecedented rate. Advancements in technology have accelerated drug development, whereas streamlined processes in regulatory drug review have improved approval timelines, which made it possible to market new drugs for conditions like cancer, Alzheimer's disease, and rare diseases. While these innovative therapies hold promise in improving patient outcomes, they also have the potential to create challenges for drug plans in managing costs, access, and long-term sustainability once they enter the market.



Drug Pipeline cont'd

Cancer

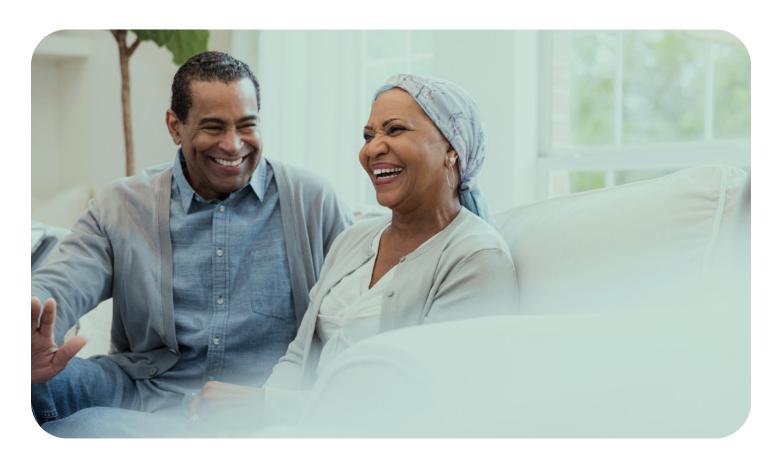
The drug pipeline continues to be dominated by specialty drugs for cancer. There is a growth in the development of self-administered cancer drugs as subcutaneous or oral formulations, which seeks to improve drug accessibility for patients and prescribers. In addition, cancer drugs are becoming highly focused on targeting specific driver mutations and/or biomarkers not only to improve the drug's safety profile, but also to improve overall patient survival and outcomes.

Type 1 Diabetes

There has been a paradigm shift in the clinical management of type 1 diabetes (T1D) outside of insulin therapy. Teplizumab is the first investigational therapy under review by Health Canada which could delay the progression of insulin-dependent T1D by a minimum of two years. Research confirmed that there are three stages of

T1D, starting from early Stages 1 and 2, to Stage 3, where patients present with clinical symptoms of diabetes and their body can produce little to no insulin. Teplizumab was approved by the FDA in January 2023, and the drug works by modulating the immune cells, thus preventing the self-destruction of pancreatic beta cells responsible for insulin production in the body.

STELARA® (ustekinumab) is one of the top 10 specialty drugs in our Drug Trend Report for the last 3 years. The drug is undergoing phase 3 trials and preliminary results suggest ustekinumab's efficacy in slowing down T1D progression in the early stages of the disease, through the inhibition of inflammatory pathways. Existing biologic therapies indicated for various inflammatory conditions are also pursuing this indication for T1D in phase 2 trials, which include SIMPONI® (golimumab), CIBINQO® (abrocitinib), and TALTZ® (ixekizumab).



Drug Pipeline cont'd

Alzheimer's Disease

There have been no new treatments approved for Alzheimer's disease in the past two decades. Since the regulatory withdrawal of aducanumab in 2022, patients and their families have been anticipating access to an effective disease modifying therapy for Alzheimer's disease in slowing disease progression.

Health Canada is currently reviewing lecanemab and donanemab, two new disease modifying treatments (DMTs) for early-stage Alzheimer's disease. These drugs are administered via intravenous infusion and have demonstrated improvements in cognition and function in patients.

Lecanemab and donanemab have already been approved by the FDA in January 2023 and July 2024, respectively. However, they are associated with amyloid-related imaging abnormalities (ARIAs). ARIAs can present as microbleeds or swelling, and thus require frequent monitoring on MRI, which can be logistically difficult to implement due to the increasing wait times in Canada for MRI scans. These new DMTs will likely transform the clinical management of Alzheimer's disease and could result in higher costs compared to genericized, oral conventional treatments.

An unexpected drug being investigated in late phase trials for early Alzheimer's disease is semaglutide. Semaglutide is a GLP-1 receptor agonist (GLP-1 RA) that have market indications for type 2 diabetes (OZEMPIC®) and obesity management (WEGOVY®). WEGOVY® has gained a new indication to reduce the risk of non-fatal myocardial infarction in overweight adults (BMI≥27kg/m²) with established cardiovascular disease. Semaglutide has been the top 1 drug by overall spend in our Drug Trend Report since 2022. If approved, this new indication of semaglutide could further expand patient eligibility and have a significant impact on plans.

Metabolic Dysfunction-Associated Steatohepatitis

There are no approved drug treatments in Canada for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) despite the millions of patients affected by this condition. In the United States, resmetirom was approved in March 2024 as the first treatment for MASH. Health Canada has not yet received a submission for resmetirom.

Several drugs in various late-stage clinical trials have been competing for the next successful launch from the pipeline. One agent to watch for is survodutide, which has the potential to be best-in-class treatment for MASH, ahead of its GLP-1 RAs counterparts, semaglutide and tirzepatide that are also being investigated for this condition.

Paroxysmal Nocturnal Hemoglobinuria

The treatment landscape for paroxysmal nocturnal hemoglobinuria (PNH) has seen significant progress in recent years. Initially, PNH treatments were limited to intravenous therapies such as ULTOMIRIS® (ravulizumab) or SOLIRIS® (eculizumab). In the last year, drugs coming out of the pipeline have since shifted to subcutaneous and oral formulations allowing for self-administration.

Crovalimab is the first subcutaneous C5 inhibitor submitted to Health Canada for the treatment of PNH. The drug has already been granted FDA approval in June 2024. Crovalimab could replace ravulizumab and eculizumab as first-line treatment in PNH, reducing the overall treatment burden to patients.

Iptacopan and danicopan are the first two oral disease-modifying therapies in PNH. Danicopan has since been approved by Health Canada in July 2024 under the trade name VOYDEYA®. Given that danicopan is indicated as an add-on treatment to either ravulizumab and eculizumab, which are both associated with high annual costs, danicopan's market entry may further increase the overall spend per member for this rare disease.

Drug Pipeline cont'd

Other Rare Diseases

The rare disease pipeline has been experiencing significant activity, with numerous therapies making significant progress through clinical trials and regulatory reviews. These therapies often address conditions with limited or no current treatment options, and have high annual costs. Furthermore, the development of self-administered formulations seen in the last year remains true for this year.

Drug Name	Route of Administration	Indication	Estimated Average Annual Cost (US\$)
Elafibranor	Oral tablet	Primary Biliary Cholangitis	167,000
Omaveloxolone	Oral capsule	Friedreich's Ataxia	468,000
Deutivacaftor-tezacaftor- vanzacaftor	Oral granules/tablet	Cystic Fibrosis	N/A
Sepiapterin	Oral powder for suspension	Phenylketonuria	N/A

Friedreich's ataxia is a rare genetic and neurologic disorder that causes loss of motor sensation and function. Symptom management of disease-related complications has been the mainstay of treatment until the FDA approval of omaveloxolone in February 2023. Omaveloxolone is the first treatment approved for the treatment of Friedreich's ataxia.

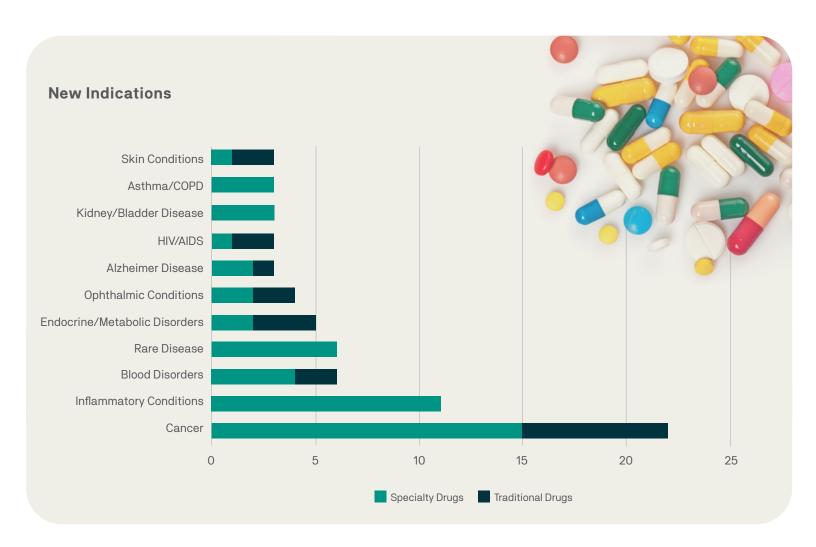
Elafibranor for primary biliary cholangitis, deutivacaftortezacaftor-vanzacaftor for cystic fibrosis, and sepiapterin for phenylketonuria are new alternative treatments that could potentially offer patients additional clinical benefit in this rare disease space.



Drug Pipeline cont'd

New Indications

Another emerging trend in the pipeline over the last few years is drug repurposing. Manufacturers have figured out a way to prolong the life cycle of a single drug by exploring other indications in different therapeutic areas. We have seen this trend more intensely applied in metabolic disorders and cancer as seen in last year's Drug Trend Report but now it touches other therapeutic areas such as Asthma/COPD, inflammatory bowel diseases, and diabetes.



Drug Pipeline cont'd

Asthma/COPD

Advanced biologic therapy used in severe allergic asthma such as DUPIXENT® (dupilumab), NUCALA® (mepolizumab), and FASENRA® (benralizumab) are now being evaluated in the treatment of chronic obstructive pulmonary disease (COPD). There is a subset of patients with COPD that have a specific type of inflammation called type 2 that could respond to these biologic therapies. DUPIXENT® is leading the way, as it is on the regulatory review stage with the FDA, while the other two drugs are starting their phase III trials.

Inflammatory Bowel Diseases

DUPIXENT® (dupilumab) is undergoing phase II trials for the treatment of ulcerative colitis. Research suggests a possible link between the presence of type 2 inflammation in ulcerative colitis patients who show greater disease activity, poorer clinical outcomes and response to therapy.

Drugs that have been approved for the treatment of ulcerative colitis are also seeking expanded indications for the treatment of Crohn's disease due to parallel inflammatory disease pathways. Late-stage trials for Crohn's disease indication are ongoing for VELSIPITY® (etrasimod), OMVOH® (mirikizumab), and SIMPONI® (golimumab) which have been approved by Health Canada for ulcerative colitis.

As manufacturers continue to explore new indications for existing drugs, therapeutic class designations begin to be blurred as in the case of dupilumab that has indications that span from skin conditions, to asthma/COPD, and potentially inflammatory conditions.



Legislative Updates

Pharmacist Scope of Practice Updates



Expanding pharmacists' scope of practice will enable pharmacists to offer additional services to patients, which in turn will alleviate the strain on the provincial health system. Private plans may see additional drug or clinical service claims depending on the legislation and provincial rules.

As of August 30, 2024, pharmacists in British Columbia were authorized to order certain laboratory tests for medication management. This change in regulation will equip pharmacists with additional clinical tools to enhance their medication management services offering.

The Government of Saskatchewan is investing in a new pilot training program, which will allow pharmacists to prescribe and manage medication(s) for a variety of chronic conditions. These conditions include asthma, diabetes, chronic obstructive pulmonary disease (COPD) obesity heart failure and hypertension

Ontario had expanded their list of minor ailments in late 2023. In 2024, the Ministry of Health expanded the minor ailment services to allow pharmacists to conduct assessments remotely, with the goal of serving patients living in rural areas. Additionally, the Ministry of Health is consulting on several changes to the scope of practice for pharmacists, including further expanding the list of minor ailments, as well as authorizing pharmacists to order certain laboratory tests and perform point-of-care tests.

In Quebec, Bill 67, which will expand the clinical scope of practice for pharmacists, has been officially adopted on November 7, 2024. The expanded activities include: removing timelines on prescription extension services, prescribing medications more broadly, authority to administer medications for therapeutic purposes, and drug substitution in a broader range of situations. L'Ordre des pharmaciens du Québec is currently drafting the regulatory framework of these new activities, in collaboration with other stakeholders.



Legislative Updates cont'd



Women's Health at the Forefront

Manitoba introduced universal coverage for contraceptives including oral and injectable formulations, hormonal IUDs, implants, as well as medical abortion pills effective October 1, 2024. Provincial coverage will shift drug spend for this therapeutic class from private to public plans. The province will also provide free public coverage of hormone replacement therapy (HRT) as part of the national pharmacare bilateral agreement.

Quebec's Ministry for the status of women announced their intention to improve access to abortion services. The government aims to increase access to abortion pills, in part by creating a telehealth service to speed up the process, especially for people who live far from abortion clinics.

British Columbia was the first province to offer universal coverage for contraceptives for its residents effective April 2023. As part of negotiations to implement the National Pharmacare Act, the province also intends to provide free treatment of menopausal symptoms with hormone replacement therapy (HRT).

Universal coverage for contraceptives and hormone replacement therapy (HRT), as well as the efforts towards enhancing the delivery of abortion services reflect the recognition of women's health as a priority for public funding and services.

See Women's Health section for more.

Provincial Biosimilar Initiatives

Provinces and territories of Canada continue to add or expand on existing biosimilar policies with almost all jurisdictions implementing biosimilar transitioning programs by 2024. The impact on private plans varies depending on the province and plan design.

Manitoba has joined the rest of the Canadian provinces, announcing the implementation of a biosimilar transition policy in 2024. As a pharmacare province, this policy allows integration opportunities for the private sector. The transition period expands until mid-2025. Therefore, the impact on private plans may not be fully observed until next year.

See Biosimilar section for more.

Legislative Updates cont'd

Canada's Drug Agency (CDA) formerly Canadian Agency for Drugs and Technologies in Health (CADTH) is a pan-Canadian health organization created and funded by Canada's federal, provincial, and territorial governments. CDA is responsible for driving better coordination, alignment, and public value within Canada's drug and health technology landscape.

CANADA'S DRUG

AGENCY

Canada's Drug Agency

announced its official launch

in September 2024 with the expansion of its existing mandate and functions to include the

developments of new programs

focused on appropriate use,

data and analytics, system

coordination and

Target Zero initiative

Target Zero is an initiative that aims to achieve zero days between Health Canada's regulatory approval of a drug and CDA's reimbursement recommendation. This initiative aims to improve the timeliness of patient access to new drugs.

As part of this initiative, CDA can now initiate a parallel review process for any drug application that is filed before Health Canada's regulatory decision, if the sponsor consents to information sharing between the two agencies.

Specific Work related to National Pharmacare

CDA confirmed through a statement that the organization can undertake national pharmacare-related work as part of Bill C-64.
These activities would include: developing a list of essential drugs and related products to inform the creation of a national formulary, creating a national bulk purchasing strategy, and establishing a pan-Canadian strategy on the appropriate use of prescription medications.

Real-World Evidence Strategy

CDA published a report of industry task force on realworld-evidence (RWE) that outlines key actions for the organization, and the broader health care community, that can enable the use of industry-sponsored real-world evidence (RWE) to help improve the understanding of the safety and effectiveness of new

treatments. The task force represents a first-of-its-kind collaboration between the pharmaceutical industry, Canada's Drug Agency, and Health Canada.

New Model Validation Tool to Support Economic Evaluations of Health Technologies

CDA has developed a comprehensive and accessible tool to support the validation of economic models used in health technology assessments (HTAs). While this tool is not a requirement for submissions to the Drug Reimbursement Review program, it will help to ensure a more consistent and reproducible approach to model validation for economic evaluations of all health technologies.

Announcement of Recipients of Funding to Enhance Rare Disease Registries

Canada's Drug Agency has awarded funding to selected rare disease registries in Canada to improve the pan-Canadian evidence landscape and support the National Strategy for Drugs for Rare Diseases.

The awarded rare disease registries span diverse disease areas and will undertake varied improvement initiatives, all with the goal of generating high quality and fit-for-purpose data that can be used to help answer regulatory and reimbursement questions and facilitate decision-making, as rare diseases affect a small patient population.

Legislative Updates cont'd



In March 2023, the Government of Canada announced a \$1.5 billion investment to fund the first-ever National Strategy for Drugs for Rare Diseases.

The Government of Canada has developed a common list of new drugs that will be elected by the provinces and territories to ensure that the national strategy delivers the maximum possible benefits to all patients with rare diseases.

This list is updated as the pan-Canadian Pharmaceutical Alliance (pCPA) concludes its price negotiations and is designed to facilitate the listing and reimbursement of rare disease drugs within Canada's existing pharmaceutical management system.

The federal government published a common list of drugs which currently includes: POTELIGEO®, OXLUMO®, EPKINLY®, WELIREG®, YESCARTA®, and KOSELUGO®. Each province selects all or some of the drugs from the published federal list.

All provinces and territories have signed the bilateral agreement with the government to provide access to rare disease drugs. This bilateral agreement intends to invest an allocated fund over three years to improve access to new and existing drugs for rare diseases as well as improving screening and diagnostics for rare diseases.



Legislative Updates cont'd





NATIONAL PHARMACARE

On February 29, 2024, the Government of Canada introduced Bill C-64 (Pharmacare Act) which became a law on October 10th. This legislation informs the creation of a universal, single-payer, first-dollar coverage, and allows the federal government to continue negotiations with the provinces and territories to cover contraception and diabetes medication as an initial phase.

On February 27th 2025, Manitoba became the first province to sign the national pharmacare agreement with the federal government to provide a universal coverage to a range of contraceptives and diabetes medications for its residents. Following suit, British Columbia, Prince Edward Island, and Yukon signed the national pharmacare agreement in March 2025. As part of Manitoba and British Columbia's federal agreements, the provinces will also enhance pharmacare coverage by providing free public coverage of hormone replacement therapy to treat menopausal symptoms.

On the other hand, some provinces such as Alberta and Quebec have expressed their plan to opt out of pharmacare, as they prefer to invest the program's funding to further enhance their current provincial drug plan offerings.

Pan-Canadian Pharmaceutical Alliance (pCPA)

Launch of pCPA Temporary Access Process (pTAP)

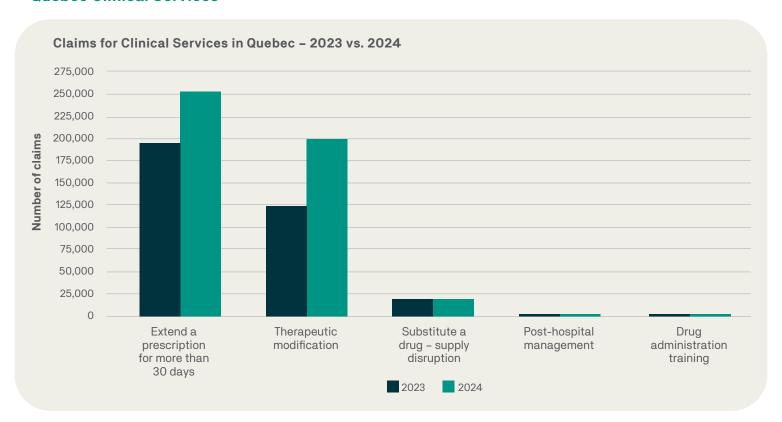
In April 2024, pCPA announced the launch of the Temporary Access Process (pTAP). This Process aims to allow temporary access to drugs that are promising early results while clinical evidence continues to be collected and reviewed.

New Process for Generic Drug Price Change Submissions

In November 2024, the pCPA has introduced a centralized process to submit price change requests directly, instead of submitting to individual public drug plans. The pCPA will review the requests, however, the final decision on price changes will remain at the discretion of participating drug plans.

Quebec

Quebec Clinical Services



Maintaining the same trend as in previous years, the clinical service claimed the most in Quebec remains the extension of a prescription for greater than 30 days, representing over 50% of all clinical services claimed. Coming in second and third place are the clinical services for therapeutic modification (for safety and/or efficacy reasons) and the drug substitution due to supply disruptions (including discontinuation of a drug, backorder, administration problems and safety reasons). Post-hospital management and drug administration training services collectively represented 2% of the claims volume for clinical services in Quebec.

Following the adoption of Bill 67 in Quebec in November 2024, which further expands the scope of practice of pharmacists, it is expected that more clinical services claims will be reimbursed should private plans have to cover these new services.

For more information, please refer to <u>Legislative</u> Updates section.

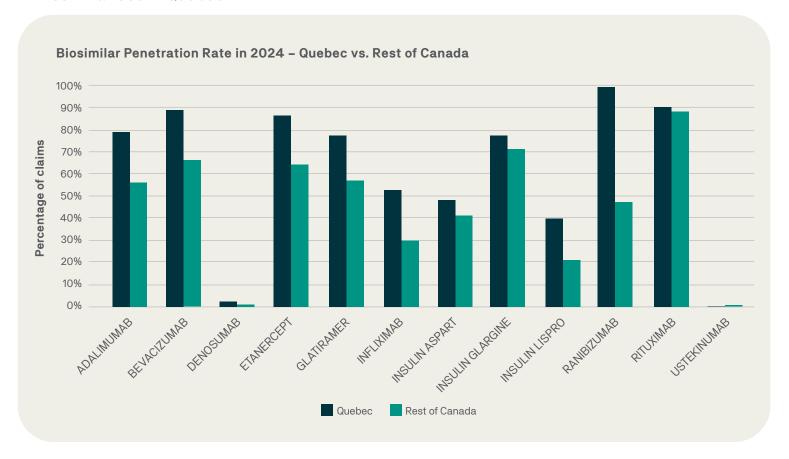
Quebec Overall Trend

2024	Quebec	Rest of Canada
Average days' supply per claim	28.3	40.5
Number of claims per claimant	19.6	12.6
Spend per claimant	\$1,262	\$915

In 2024, the spend per claimant was 38% higher in Quebec than in the rest of Canada. This represents a slight improvement from last year's data (41%). The shorter days' supply and the higher number of claims per claimant in Quebec are the main drivers of this difference.

Quebec cont'd

Biosimilar Use in Quebec



The use of biosimilars was more widespread in Quebec than in the rest of Canada for most biologic drugs used to treat chronic conditions.

Since the transition period ended in May 2024 for LUCENTIS®, the uptake of ranibizumab biosimilars was close to 100% in the province whereas in the rest of Canada, it did not reach 50% yet.

The province had also put in place a transition policy for STELARA® (ustekinumab), which ended on November 6, 2024. Patients must be transitioned to one of the

three biosimilars on the RAMQ Formulary. Despite these measures, there has been little to none uptake in 2024 for the biosimilars: we expect to see higher numbers in 2025.

XGEVA® and PROLIA® (denosumab) is also subject to a transition period that will end in May 2025. Therefore, a higher penetration rate is expected in 2025 for their biosimilars WYOST® and JUBBONTI®.

For more information, refer to Biosimilars section.

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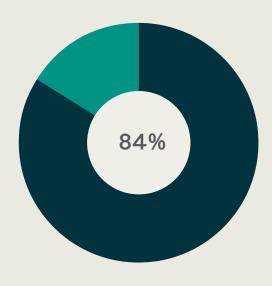
PLAN ADOPTION

Drug Plan Management Options

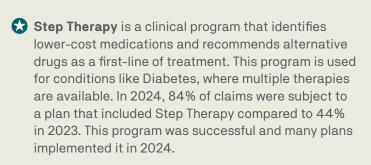
Express Scripts Canada is offering multiple options to support member experience and drug costs. Many traditional plan options are available for our clients to adapt their strategy while ensuring that their members' needs are met. Clinical programs offer enhanced member support while helping to manage costs at the same time. The uptake of traditional drug plan management options as well as clinical programs is detailed in the next section.

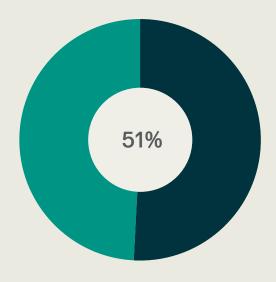
CLINICAL PROGRAMS:

Indicates cost saving measures



STEP THERAPY





OPIOID MANAGEMENT SOLUTION

Express Scripts Canada's Opioid Management Solution (OMS) is intended to promote early interventions and safer use of opioid medications. This program minimizes early opioid exposure, identifies high opioid dosages, and potential duplication of therapies at the point of adjudication. In 2024, 51% of claims were subject to a plan that included Opioid Management Solution.

PLAN ADOPTION

Drug Plan Management Options cont'd

PLAN MANAGEMENT OPTIONS:

★ Indicates cost saving measures



- Lifetime Maximums limit the amount that a plan will pay for drugs over a member's lifetime. In 2024, 9% of claims were subject to a plan that included a lifetime maximum.
- Annual Maximums limits the amount that a plan will pay for drugs for a member each year. In 2024, 11% of claims were subject to a plan that included an annual maximum.
- 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. The financial accountability of the member 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 2024, 70% of claims were subject to a plan that included co-insurance. Therefore, 30 % of the claims were fully covered.
- 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 2024 national uptake showed that 86% of claims were subject to a plan that included generic substitution.

Dispensing Fee Caps. The dispensing fee is a professional fee charged by the pharmacist to cover drug storage, preparation and professional services dispensed. The dispensing fee can vary depending on the pharmacy and the province. Therefore, some plans choose to add a cap to further manage costs. This is the maximum amount that the drug plan will reimburse towards the dispensing fee. If the member chooses a pharmacy that charges fees above the capped amount, the member will be responsible for paying for the difference. Dispensing fee caps may encourage plan members to seek pharmacies with lower dispensing fees. Some provinces require pharmacies to post their dispensing fees for the public, while others are not required to.

Summary of Dispensing Fee Capped Amounts in 2024





Biologic Drug: A biologic drug comes from a living organism or from its cells. An originator biologic drug is the first version of a biologic drug. A biosimilar is a drug demonstrated to be highly similar to an originator biologic drug that was already authorized for sale. Health Canada evaluates all the information provided to confirm that there are no clinically meaningful differences in safety and efficacy between the biosimilar and the reference biologic drug.

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.

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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