



2020

**PRESCRIPTION
DRUG TREND REPORT**

EXPRESS SCRIPTS CANADA



EXPRESS SCRIPTS®





A WORD FROM OUR PRESIDENT

Innovation distinguishes a leader from a follower. Express Scripts Canada is a leader in the pharmacy benefit management landscape, which means we stay ahead of the curve by focusing on innovation and using data to focus on what matters most to those we serve: better health benefits for less.

Better health is only possible when medications are accessible and prescription drug plans are affordable. Our annual Prescription Drug Trend Report is the industry's most comprehensive year-over-year summary of cost changes and use of prescription medication in Canada.

This year's Prescription Drug Trend Report confirms what we already know: innovative solutions are key to controlling the cost of prescription drug benefit plans, especially at a time when we have entered into an age of million-dollar-per-treatment drug launches. Innovations that deliver potentially breakthrough treatments with astronomical prices require us to be equally innovative in how we manage prescription drug benefit.

We've seen expanded indications for drugs in therapy categories like diabetes and more costly options in diabetic supplies continuing the increase in traditional spend. We also know that members who manage multiple conditions and take multiple medications for these conditions face annual drug costs that are 16.2 times higher than the average member. Another item of note can be found within the Top 10 Therapeutic Classes where the 19- to 35-year-old age group is driving the specialty spend.

While cancer treatment is still the primary pharmaceutical research focus in development, there are more than 30 new rare disease treatments on the horizon. While rare diseases, also known as orphan disorders, affect fewer than five in 100,000 persons in Canada, the total impact is considerable. In fact, approximately one million Canadians live with a rare disease and, because they affect so few people, treatments are often immensely expensive.

We will continue to see breakthrough treatments with high prices on the horizon. We expect research to focus on the production of high-priced specialty drugs, which currently consume more than one-third of all drug spending.

As industry leaders, innovation is at the forefront of everything we do. As we look ahead, with the growing use of high-cost specialty drugs, benefit plan sustainability hinges on solutions that translate into lower costs and improved health outcomes. In addition to holistic pharmacy care, ESC will continue to leverage technology and work hand in glove with our clients and partners to create a better future – and health outcomes for Canadians – together.



Dr. Dorian Lo
President



DRUG TREND & UTILIZATION

OVERALL TREND

A slow but steady increase in overall private drug plan spending continued in 2019. Proactive approaches to swiftly increasing levels of specialty medication spending and other new challenges in the pharmacy landscape are critical.

Most significant among these challenges are the extremely high-cost gene-based therapies expected in the near future.

TRADITIONAL

+0.1%

(98% CLAIMS)

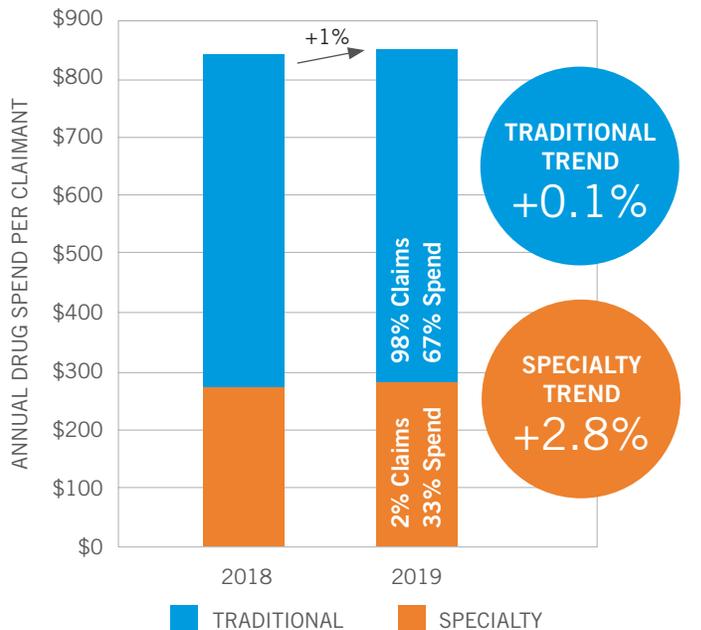
SPECIALTY

+2.8%

(2% CLAIMS)

**OVERALL
+1.0%**

SPECIALTY vs. TRADITIONAL SPEND FOR 2018 AND 2019





OVERALL TREND IN 2019

- 2019 trend driven by specialty (33%) and traditional (67%) spend; with an increase in specialty spending over 2018 (32%).
- After a decline in traditional spending in 2018, higher spending in both diabetes drugs and a 16% increase in diabetes supplies and monitoring technology pushed this trend upward.
- Utilization will continue to increase for certain diabetes medications like the SGLT-2 inhibitors as other benefits for patients with diabetes are established (e.g., to reduce cardiovascular risk).

FACTORS DRIVING TRADITIONAL DRUG SPEND

| COST/Rx | UTILIZATION | OVERALL TREND |
|---------|-------------|---------------|
| +0.4% | + -0.3% | = +0.1% |



- Uptake of higher cost drugs and supplies for common diseases such as diabetes



- OHIP+
- pan-Canadian Pharmaceutical Alliance price negotiations

FACTORS DRIVING SPECIALTY DRUG SPEND

| COST/Rx | UTILIZATION | OVERALL TREND |
|---------|-------------|---------------|
| -0.1% | + +2.9% | = +2.8% |



- Higher utilization of existing drugs with new indication approvals
- Oral oncology medications continue to be launched, shifting costs to private plans
- Increased use of specialty medications for asthma



- Emergence of provincial programs for biosimilars



A LOOK AHEAD: 2020 TREND

TRADITIONAL:

- Higher-cost asthma medications recommended as first-line therapy, replacing lower-cost reliever inhalers, will drive trend increase.
- Increased adoption of flash glucose monitoring systems over traditional glucose monitoring test strips will put additional cost pressure on prescription drug plans.

SPECIALTY:

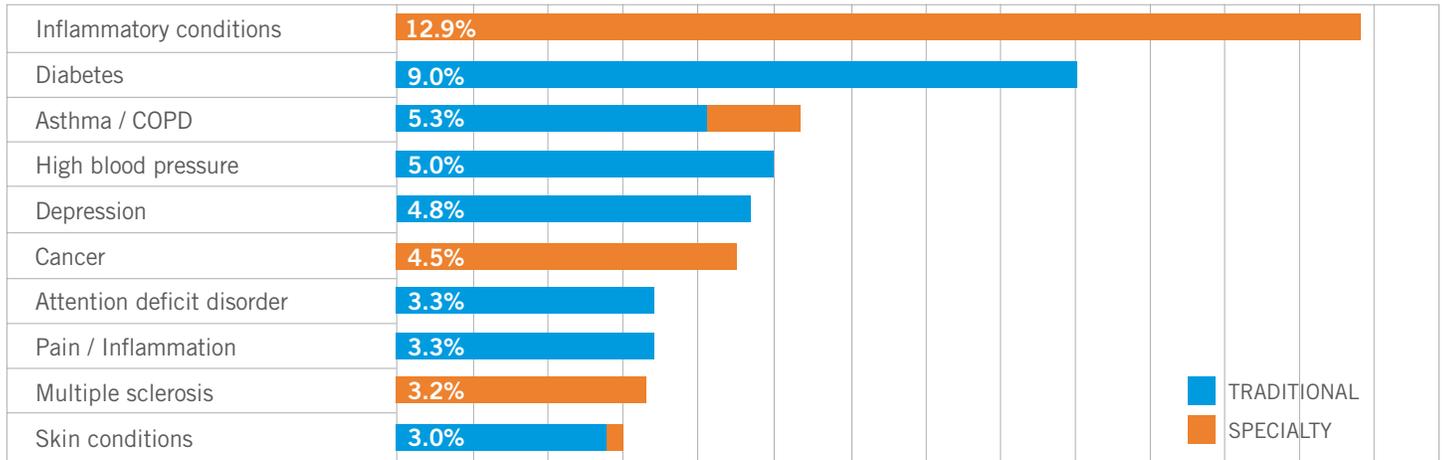
- PMPRB regulations will remove the U.S. and Switzerland (countries with higher patented drug prices) as drug price reference comparators, effective July 1, 2020. This should eventually drive lower prices.





TOP 10

TOP 10 THERAPEUTIC CLASSES IN 2019 (BY SPEND)



SPENDING BREAKDOWN BY THERAPEUTIC CLASS

The trend for 2019 was influenced by the introduction of new drugs, approval of new indications and first-time generics.

#1 – Inflammatory conditions

- Increased trend growth in this therapy class was driven by new biologics (like Skyrizi®) and new indication approvals for drugs such as Humira® and Cimzia®.

See Biosimilars for other possible trend factors for 2020.

#6 – Cancer

- More than 15 new drugs and almost twice the number of new indications for existing drugs were approved in 2019.
- Revlimid® still leads cancer spending (14.3% overall in this class; a generic is not expected until 2023).
- This trend may be mitigated by the introduction of generics and biosimilars for oncology drugs such as Sprycel®, Rituxan® and Afinitor®.

#9 – Multiple Sclerosis

- Costs in this class will lessen due to the launch of affordable generics that may be used instead of Gilenya®, which currently accounts for 18.5% of multiple sclerosis drug costs.
- The expiry of patents in the next few years for widely used brand name drugs such as Aubagio® and Tecfidera® may also lead to lower costs.

#10 – Skin conditions

- This therapy class had the highest increase in spending due to increased utilization and an expanded indication of Dupixent® to treat atopic dermatitis.

OTHER NOTABLE TRENDS

#13 – High cholesterol

- Utilization of PCSK9 inhibitors Praluent® and Repatha®, approved for cardiovascular protection in 2019, continues to grow. Despite increased utilization, however, cost per member declined in this category in 2019.

#27 – Migraine

- CGRP inhibitors (Emgality®, Aimovig®) introduced mid-year are more than 30 times more expensive than traditional preventative drugs.
- Total cost will increase with higher utilization of CGRP inhibitors as more experience is gained with these drugs.

#29 – Rare disease

- Costs will likely increase in the next year, but utilization will remain low for this category.
- ALS treatment Radicava® was introduced in Canada in 2019 at \$110,000 per year of treatment.
- Additional drug approvals in this therapy class will further increase costs.

See Pipeline for other possible trend factors for 2020.

TOP 10 THERAPEUTIC CLASSES ACCORDING TO TOTAL CLAIM COST (OVERALL SPEND)

| Rank 2018 | Rank 2019 | Therapeutic Class | % of Overall Spend | Trend | | |
|-----------|-----------|----------------------------|--------------------|-------------|-------|-------|
| | | | | Utilization | Cost | Total |
| 1 | 1 | Inflammatory conditions | 12.9% | 0.6% | -7.1% | -6.6% |
| 2 | 2 | Diabetes | 9.0% | 1.2% | 6.0% | 7.2% |
| 4 | 3 | Asthma / COPD | 5.3% | -2.6% | 0.4% | -2.2% |
| 3 | 4 | High blood pressure | 5.0% | 0.7% | -8.8% | -8.1% |
| 5 | 5 | Depression | 4.8% | 0.1% | -3.7% | -3.6% |
| 6 | 6 | Cancer | 4.5% | -1.0% | 7.2% | 6.2% |
| 11 | 7 | Attention deficit disorder | 3.3% | -1.8% | 2.2% | 0.4% |
| 7 | 8 | Pain / Inflammation | 3.3% | -0.5% | -3.8% | -4.3% |
| 10 | 9 | Multiple sclerosis | 3.2% | -4.5% | 6.3% | 1.8% |
| 13 | 10 | Skin conditions | 3.0% | -0.6% | 11.1% | 10.5% |

■ THERAPY CLASS DOMINATED BY TRADITIONAL DRUGS
 ■ THERAPY CLASS DOMINATED BY SPECIALTY DRUGS

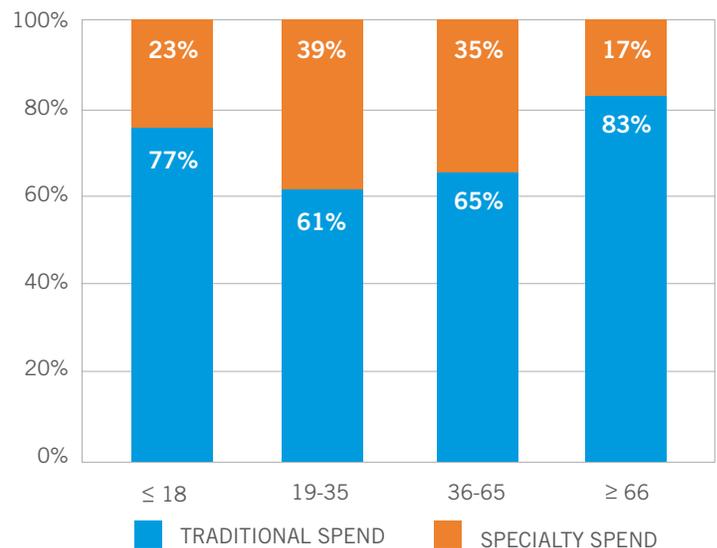
TARGET COST CONTAINMENT BY AGE GROUP

- Specialty spending is highest among 19- to 35-year-olds and 36- to 65-year-olds due to complex chronic conditions that require lifelong treatment, such as multiple sclerosis or ulcerative colitis.
- Over 66 year olds are more likely to need treatment for multiple chronic conditions such as high blood pressure, diabetes and high cholesterol that are commonly treated with traditional drugs.

Proactively managed plans are essential to contain costs

- Half of rare diseases are diagnosed during childhood, putting this therapy class in the Top 10 for children under 18 years old.
- Inflammatory conditions are prevalent in every age group, especially adults 19 to 65 years old.

TRADITIONAL vs. SPECIALTY SPEND PER AGE GROUP





TOP 10 THERAPEUTIC CLASSES PER AGE GROUP

| Rank | ≤ 18 | 19-35 | 36-65 | ≥ 66 |
|------|----------------------------|----------------------------|-------------------------|-------------------------|
| 1 | Attention deficit disorder | Inflammatory conditions | Inflammatory conditions | Diabetes |
| 2 | Infections | Birth control | Diabetes | High blood pressure |
| 3 | Asthma / COPD | Depression | High blood pressure | Cardiovascular disease |
| 4 | Inflammatory conditions | Attention deficit disorder | Asthma / COPD | High cholesterol |
| 5 | Allergy | Asthma / COPD | Cancer | Cancer |
| 6 | Cystic fibrosis | Infections | Depression | Asthma / COPD |
| 7 | Birth control | Skin conditions | Multiple sclerosis | Inflammatory conditions |
| 8 | Skin conditions | Multiple sclerosis | Pain / Inflammation | Ulcer / Reflux |
| 9 | Acne | Allergy | Ulcer / Reflux | Pain / Inflammation |
| 10 | Rare disease | Diabetes | High cholesterol | Diabetic supplies |

■ THERAPY CLASS DOMINATED BY TRADITIONAL DRUGS ■ THERAPY CLASS DOMINATED BY SPECIALTY DRUGS

OTHER NOTABLE TRENDS TO WATCH



- Depression for 19- to 35-year-olds represents the third highest spending rank for this class among all age groups.
- Attention-deficit disorder (ADD) therapy was the most prevalent treatment for those 18 and under. It also still ranked high for young adults 19 to 35 years old.
- The proportion of specialty spend is highest for 19- to 35-year-olds and 36- to 65-year-olds.

THE DRUG TREND 80/20

Just 20% of plan claimants drive 80% of overall drug plan costs.

THE 20%

The average annual drug costs are 16.2 times higher for these members, who:

- Manage multiple conditions, an average of 5.9.
- Take multiple medications, an average of 8.6 of which 12% are specialty drugs.

These members struggle with the complexity of treating their chronic conditions, so education and adherence support is critical.

Proactively managed prescription drug plans can help contain costs and protect members' health by:

- Helping patients manage their multiple chronic conditions;

- Co-ordinating care provided by physicians and other health-care professionals;
- Helping patients manage their many medications; and
- Controlling costs for plan sponsors to protect benefit sustainability.

80/20 RULE

| | Typical Claimant | Top 20% Claimant |
|--------------------------------|-----------------------------|-----------------------------|
| Average per claimant | 80% of claimants, 20% spend | 20% of claimants, 80% spend |
| Annual cost per claimant | \$210 | \$3,409 |
| # of conditions | 2.5 | 5.9 |
| # of physicians | 2.0 | 3.7 |
| # of unique medications | 3.2 | 8.6 |
| % of claimants using specialty | 0.8% | 12% |



BIOSIMILARS

Biosimilars present significant savings opportunities for drug benefit plans.

BIOSIMILARS LAUNCHED IN 2019 IN CANADA

| Biosimilar | Medicinal Ingredient | Reference Brand Name Biologic | Common Indication | % of total spend in 2019 | NOC |
|-----------------------------------|----------------------|-------------------------------|----------------------------------|--------------------------|----------------------------|
| Zirabev® | Bevacizumab | Avastin® | Cancer | 0.1% | June |
| Truxima® | Rituximab | Rituxan® | Cancer | 0.2% | April |
| Teva-Teriparatide® | Teriparatide | Forteo® | Osteoporosis / Skeletal disorder | 0.0% | August |
| Ogivri® Trazimera® Herzuma® | Trastuzumab | Herceptin® | Cancer | 0.0% | May August September |



If introduced, the following biosimilars will drive further competition around pricing as well as further saving opportunities for private payers.

BIOSIMILARS UNDER REVIEW BY HEALTH CANADA

| Medicinal Ingredient | Number of Biosimilars under review | Common Indication |
|----------------------|------------------------------------|-------------------------|
| Adalimumab | 3 | Inflammatory conditions |
| Bevacizumab | 1 | Cancer |
| Filgrastim | 2 | Blood disorders |
| Infliximab | 1 | Inflammatory conditions |
| Pegfilgrastim | 2 | Blood disorders |
| Rituximab | 2 | Cancer |
| Trastuzumab | 4 | Cancer |

Multiple biosimilar alternatives promise to create price competition

- Humira® claims made up 3.8% of total annual prescription drug costs in 2019. While one biosimilar (Hadlima®) was approved in Canada in 2018, its introduction has been prevented by ongoing patent lawsuit. Three additional brands are under review.
- A second biosimilar for Avastin® (Zirabev®) was also approved late in 2019. Low usage (6% of claims vs. 94% for the innovator drug) is due to its late market entry but is expected to increase with experience and expansion of approved indications.

Barriers to adoption of biosimilars

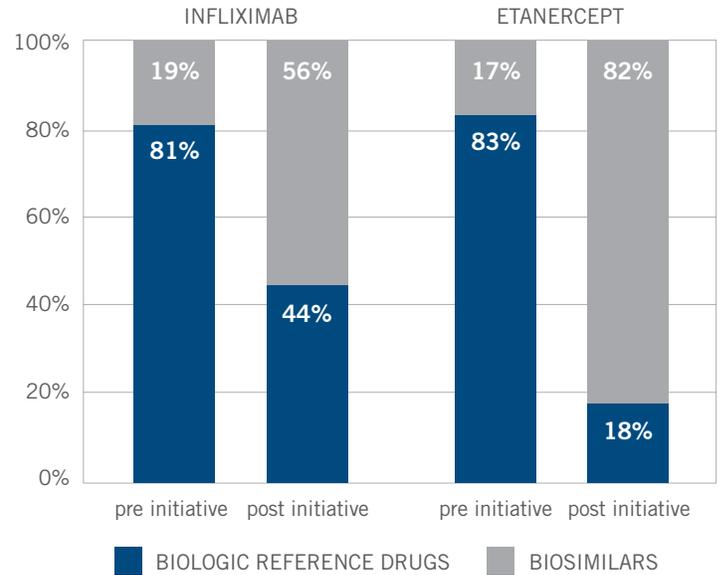
- Biosimilars cannot be substituted by a pharmacist for biologic reference drugs without a new prescription.
- Patients have yet to recognize that biosimilars are as safe and effective as biologic counterparts.

Biosimilars offer a cost savings of about 10-30% compared to innovator drugs.

BC makes the first move to improve sustainability and reduce costs

- A 2019 BC PharmaCare initiative required that patients taking three biologic drugs – Enbrel®, Remicade® and Lantus® – transition to biosimilars.
- This resulted in a continued increase in the use of biosimilars for infliximab and etanercept in 2020.

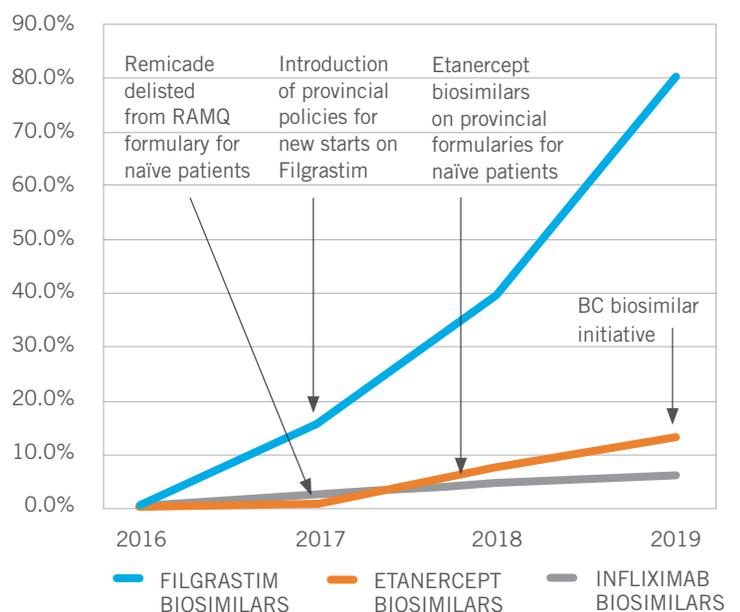
PROPORTION OF CLAIMS FOR INFILIXIMAB AND ETANERCEPT BEFORE AND AFTER BC BIOSIMILARS INITIATIVE



Muted but increasing uptake

- Filgrastim is experiencing the fastest growth. It is used more frequently because it is used to treat patients with cancer and administered for a finite period of time, unlike Remicade®, which is used on a chronic basis.

UPTAKE OF BIOSIMILARS PER INGREDIENT BETWEEN 2016 AND 2019*



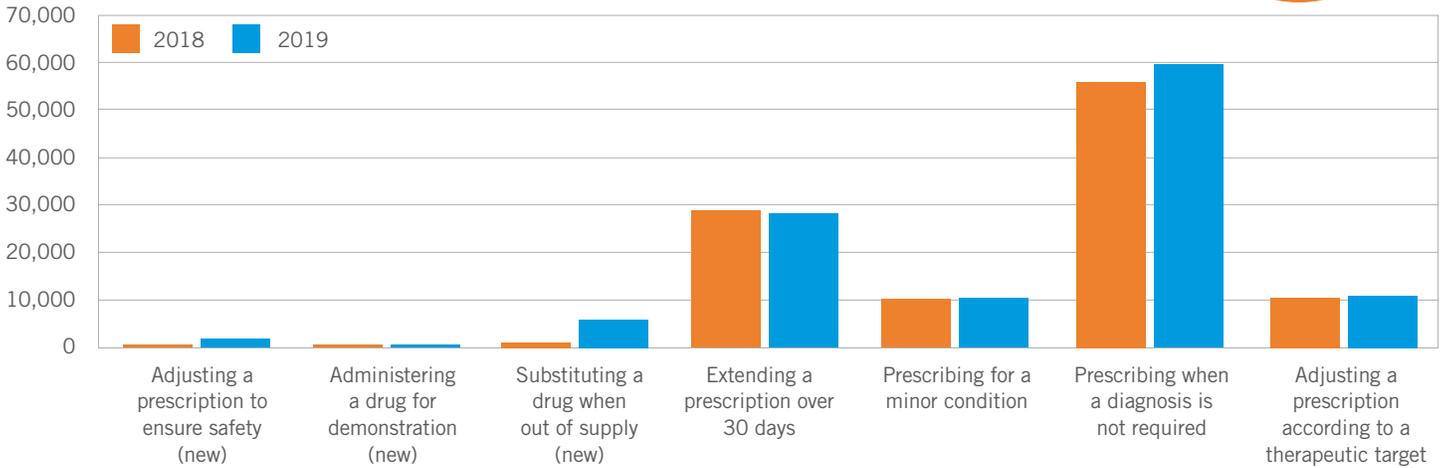
*Based on ESC's Book of Business

QUEBEC

Clinical services provided by pharmacists under Law 41 increased in 2019 largely due to major drug inventory shortages.

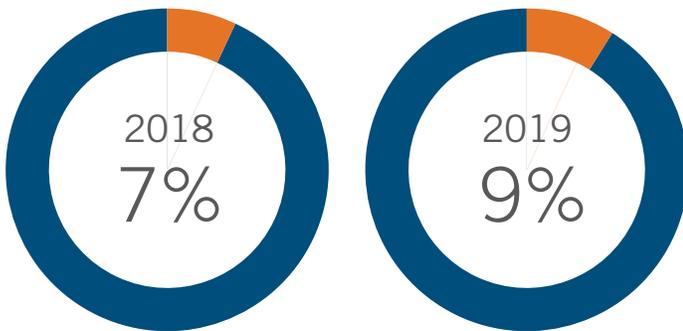
11% increase in clinical activity claims for 2019

NUMBER OF CLAIMS PER CLINICAL ACTIVITY TYPE IN 2018-2019



Remicade® coverage change

- Remicade® coverage rules were updated in February 2019 to apply the lowest price rule to all individuals starting treatment with infliximab: only Renflexis® is fully covered while members pay the difference out-of-pocket when starting on Remicade® or Inflectra®.
- Claims for Remicade® declined while claims for biosimilars Renflexis® and Inflectra® increased.



■ TOTAL NUMBER OF CLAIMS FOR REMICADE
 ■ TOTAL NUMBER OF CLAIMS FOR RENFLEXIS AND INFLECTRA

BILL 31 COULD ADD MORE SERVICES AND FEES

Currently in negotiation, Bill 31 would allow pharmacists to provide and bill for the following services:

- Administer medication intranasally;
- Consult with patients about stopping medication therapy at the request of a physician;
- Substitute one prescribed medication for another, including medications of different therapeutic classes;
- Prescribe and interpret lab analyses and other tests for the purpose of monitoring therapy;
- Assess patients' physical and mental condition to ensure proper use of medication;
- Adjust or renew prescriptions of all prescribers, including nurse practitioners and dentists;
- Prescribe and administer vaccines and, in emergency situations, certain other medications; and
- Prescribe over-the-counter drugs.

Implications

If covered under Loi sur l'assurance maladie, there will be no impact on private plans.

- If not covered, coverage by private plans will be mandatory (like clinical activities under Law 41); plans that reimburse over-the-counter drugs are expected to see the most impact.

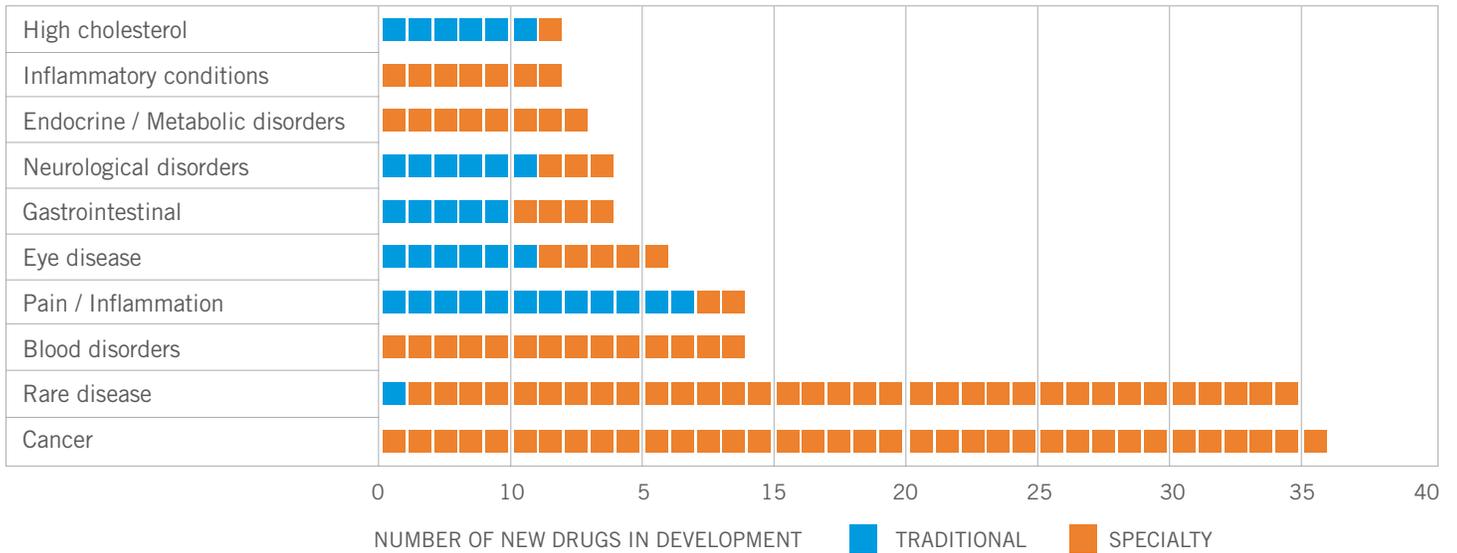
What to expect in 2020

- Two new clinical services to take effect – managing the care of patients post-hospitalization and in palliative care – could increase benefit plan costs.

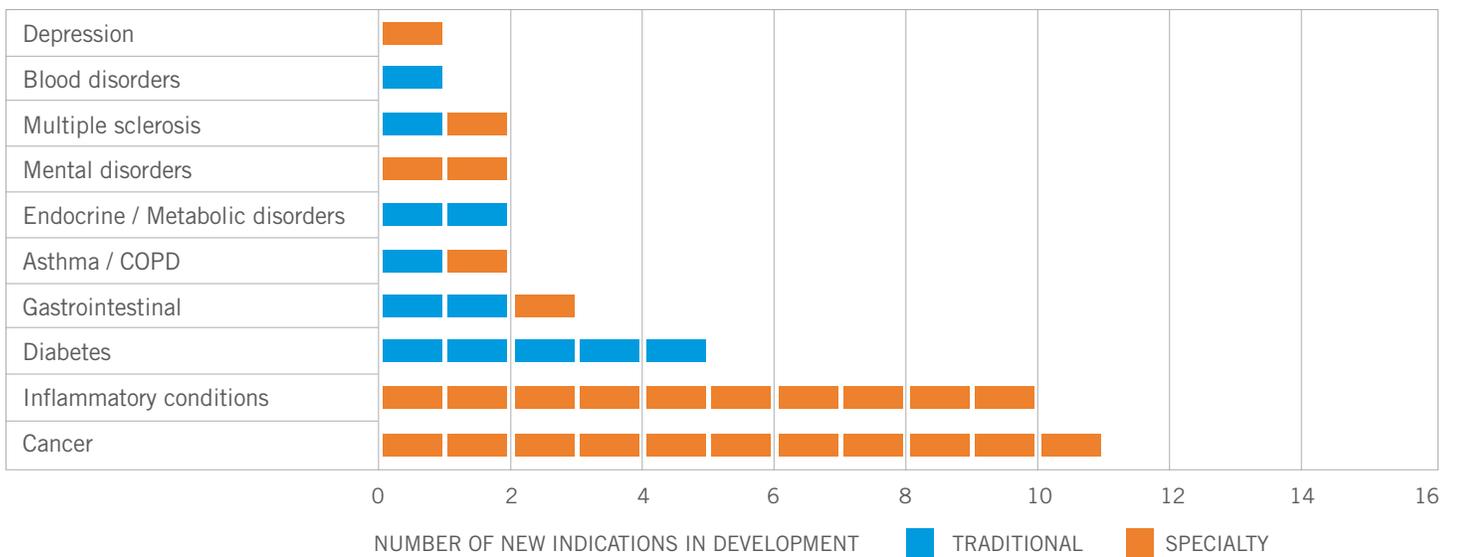


PIPELINE

NEW DRUGS IN DEVELOPMENT PIPELINE



NEW INDICATIONS IN DEVELOPMENT PIPELINE



THE DEVELOPMENT PIPELINE: TREATMENT COMES AT A HIGH PRICE

Speciality dominates 60% of the pipeline

Cancer treatment is still the primary pharmaceutical research focus, with numerous promising gene therapies in development. About 50% of drugs in the pipeline are designed for oral administration, continuing a shift in costs from provincial to private plans.

30+ new rare disease treatments on the horizon*

Rare diseases are serious, life-altering and often catastrophic conditions for patients and their families. Also known as orphan disorders, rare diseases affect approximately one million Canadians, of which about 50% are children, and treatments, if available, are often immensely expensive.

Nonalcoholic steatohepatitis (NASH) drug, the new blockbuster to come

Characterized by liver inflammation that may evolve into cirrhosis or cancer, the prevalence of NASH increases with age. It currently affects between 3% and 5% of Canadians, and accelerates with obesity, insulin resistance, dyslipidemia and hypertension.

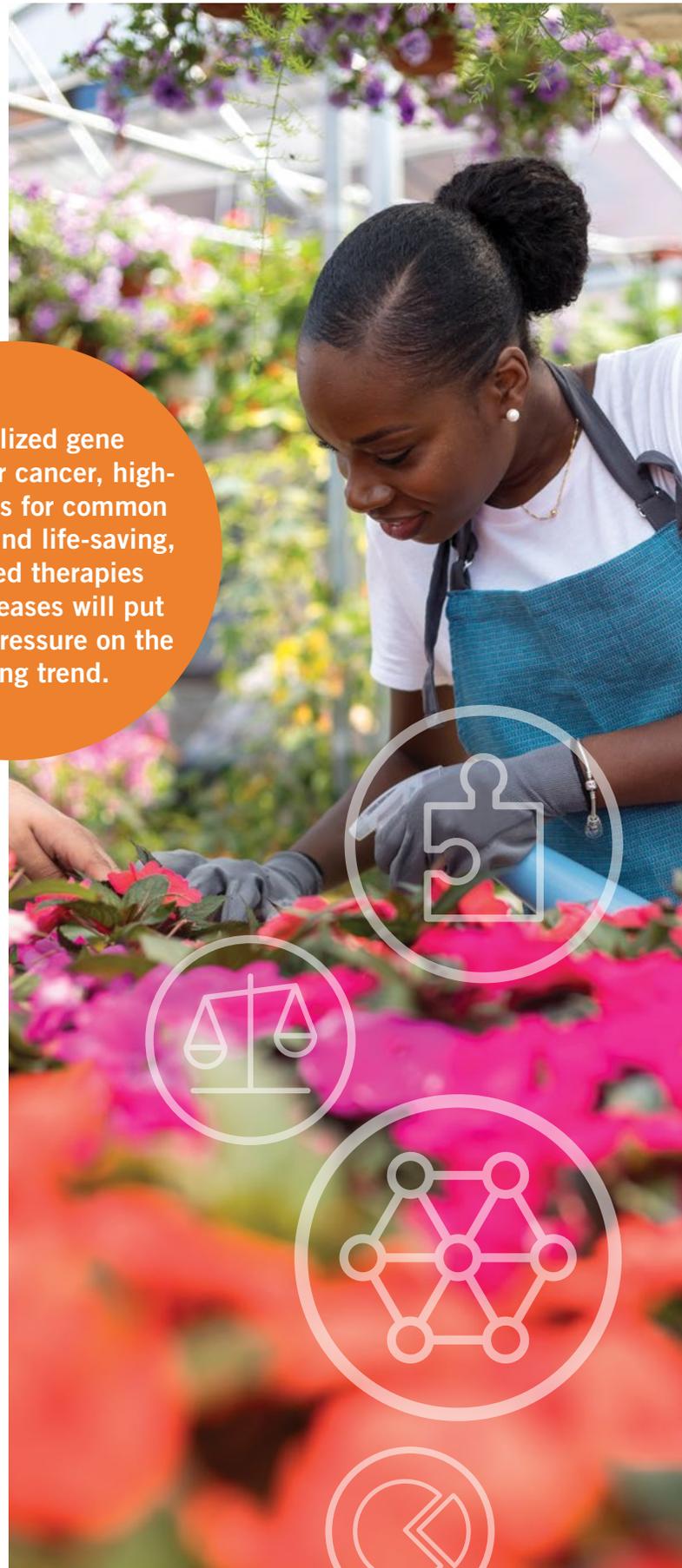
If the indication is expanded to treat NASH, Ocaliva® would result in higher costs due to the dosage and frequency of administration. Its availability would increase utilization and spending (estimated \$100,000-year treatment).

PCSK9 sets the tone – tracking new therapeutic classes for high cholesterol

- This class of drug was approved to treat elevated cholesterol.
- With other drug classes currently being developed for hereditary diseases and elevated cholesterol due to lifestyle, this therapy class will have a significant impact on spending in the next few years.

**Includes drugs in Phase III clinical trials or under review by FDA and/or Health Canada.*

Personalized gene therapies for cancer, high-priced drugs for common conditions and life-saving, high-priced therapies for rare diseases will put continued pressure on the spending trend.





At Express Scripts Canada, innovation is at our core – it is at the heart of who we are and what we do. From high-cost specialty medications to challenges with adherence to addressing the opioid crisis head on, we are constantly piloting, measuring and perfecting new ways to address our clients’ and patients’ challenges.

OPIOIDS

The opioids crisis is a national emergency, taking the lives of almost 14,000 Canadians from January 2016 to June 2019.

LEADING THE WAY FOR SAFER OPIOID USE

Express Scripts Canada’s Opioid Management Solution has seen a:

- 32% reduction in the average days’ supply per claim for first-time, short-acting opioid users.

Express Script Canada’s Opioid Management Solution minimizes opioid exposure and prevents progression to misuse.

Limit “first fill” to seven-day supply*:

1. minimizes early exposure
2. encourages patients to use a short-acting opioid first
3. ensures safe starts of long-acting opioids

**Initial fill for a member who has not received an opioid in the last 180 days.*

PROBLEM: Acute pain can usually be treated with 3 or fewer days’ supply**, but average “first fill” is more than 18 days.

***Centers for Disease Control Guidelines (2016) for prescribing opioids for chronic pain.*

CURRENT LANDSCAPE

10% Opioid claimants in ESC book of business

22% Claimants who receive short-acting opioids with initial day fill that is greater than 7 days (monthly average)

25% Claimants for long-acting opioids who did not take short-acting opioids (monthly average)

20% Percentage of users starting a 10-day supply of opioids who become long-term users*

* <https://www.canada.ca/en/health-canada/services/substance-use/problematic-prescription-drug-use/opioids/data-surveillance-research/harms-deaths.html>

ADHERENCE

MEDICATIONS DON'T WORK IF THEY AREN'T TAKEN CORRECTLY

Nonadherence affects the most prevalent chronic conditions (high blood pressure, diabetes, depression) in our book of business, impacting control of disease in early stages. The more medications a person takes, the more likely they are to be nonadherent to at least one. For example:

38% of members with depression are nonadherent.

33% of members on high blood pressure medications are nonadherent. These are often prescribed with high cholesterol medications, which also have a high rate of non-adherence.

Medication adherence is ESC's priority. Determining who is at risk is half the battle.

AN ALARMING TREND

As many as 70% of Canadians are not taking their medications as directed by their physicians and up to 26% of prescriptions are never filled.

ESC LAUNCHES FIRST-OF-ITS-KIND ADHERENCE SOLUTIONS

An impactful solution relies on early detection.

More than 38% of adherent claimants are expected to become nonadherent by June 2020.

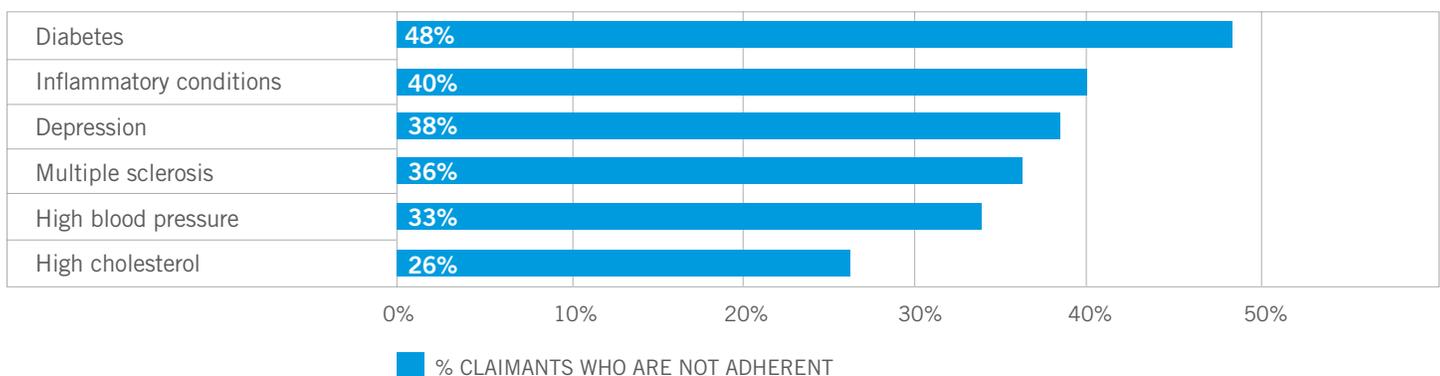
1 ESC's Medication Nonadherence Identification Report

This report provides information about the scale of nonadherence for an individual group, including a comparison to similar groups, making it easy to see if a group has superior, average or below average adherence. Through this analysis, we identify the most problematic medical conditions within the group and target programs to benefit this population.

2 ESC's Predictive Medication Adherence Report

Through ESC's proprietary predictive models, we detect those at risk for future nonadherence. With a focus on diabetes, high blood pressure and high cholesterol, it allows specific interventions to prevent nonadherence before it becomes an obstacle to someone's health.

PERCENTAGE OF CLAIMANTS WHO ARE NONADHERENT BY THERAPY CLASS





KEY TAKEAWAYS

1.

WHILE THE OVERALL PRIVATE DRUG TREND IS UP 1%, prescription drug benefits continue to be threatened by the growing use of very high-cost specialty drugs. Sustainability depends on benefit management solutions that translate into lower costs and improved health outcomes.

2.

THE TRADITIONAL SPEND TREND INCREASED, REVERSING A DECLINE IN 2018, due in part to expanded indications for therapy categories like diabetes and more costly options in diabetic supplies.

3.

SPECIALTY DRUGS CONTINUE TO MAKE UP 60% OF THE DEVELOPMENT PIPELINE. This category will continue to grow as research and technology advances, creating targeted drug solutions for debilitating medical conditions. Better managed plans address this reality to control benefits costs.

4.

EXPRESS SCRIPTS CANADA'S OPIOID MANAGEMENT SOLUTION DRIVES DOWN UNNECESSARY USE OF OPIOIDS, directing plan members to safer utilization. Preliminary results show a reduction of up to 32% in the average days' supply per claim for first-time, short-acting opioids.

5.

THE 2019 DATA SUPPORTS THAT WELL-MANAGED PLANS CAN LEVERAGE AND MANAGE BENEFIT INVESTMENT through proven approaches that optimize drug costs along with member health.







GLOSSARY

| | |
|-------------------|---|
| Trend | Measurement of the rate of change in gross cost per claimant over the previous year. Overall trend is composed of the utilization and cost per prescription trends. |
| Total Cost | Eligible drug cost including dispensing fee. This includes both the plan member's and plan sponsor's portions. |
| Claimant | Each unique individual with a prescription, including dependants who were continuously eligible for coverage throughout the course of 2019. |



Areas of interest that should be watched.

MEDICATION GROUPINGS

Therapeutic class: Grouping of medications based on most common indications.

Specialty drug: Medications used to treat chronic, complex conditions. Specialty medications include injectable and non-injectable drugs and 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 specialized handling or administration.

Traditional drug: Medications that are easy to self-administer and require less intensive clinical monitoring, such as those used to treat diabetes and high blood pressure.

Adherence: Medication adherence is the measure of whether or not a patient takes medications as directed by a physician. Medication adherence is calculated using the proportion of days covered (PDC), which measures the number of days of a time period that a medication is “on hand” and available to the patient. An individual is deemed to be nonadherent to a therapy when he/she has a PDC score of less than 80%. A claimant is determined to be nonadherent to a therapeutic class if he/she is not adherent to at least one medication in that class.



LEG EXTENSION
100





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