

2021

**PRESCRIPTION
DRUG TREND REPORT**

EXPRESS SCRIPTS CANADA



EXPRESS SCRIPTS®

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A WORD FROM OUR PRESIDENT

2020 was an unprecedented year. It changed the way we lived, worked, learned and gathered with each other. What did not change, however, was the enormous responsibility we recognize we have to the clients and patients we serve to ensure our systems and operations transitioned seamlessly to a work-from-home model so Canadians could continue to utilize their drug card and receive delivery of their prescriptions.

Express Scripts Canada is committed to fostering partnerships and solutions that will have a lasting impact and redefine what it means to be the best health benefits manager in Canada. We continue to innovate on behalf of our clients as we improve efficiency and effectiveness as we strive to deliver a competitive advantage in the Canadian market to our clients. While 2020 brought with it many challenges, I firmly believe that with determination and focus we can turn them into opportunities and progress. We remain steadfast in our commitment to transform the health benefits management industry in Canada, supported by the strength of our global parent company, Cigna®, and the Evernorth brand.

The healthcare landscape is evolving with pharmacological interventions at a rapid growth, rate and pace; whole-person health is fundamental to wellbeing and care access is rapidly changing. With this evolution comes one thing you can count on: Express Scripts Canada's commitment to deliver differentiated value through innovation and affordable, predictable and simple solutions. The evolution of the landscape is also why we tap into the talent, experience and passion inside ESC.

Along with stay-at-home orders, conservation of critical healthcare resources and general population fears, non-critical medical resources are seeing significant drops in those seeking medical attention for many chronic conditions. There is confusion among patients and providers as to which medical services should be sought and which can be delayed. Unfortunately, the impact of these decisions could have profound consequences on the health of Canadians for years to come.

As an authority in health benefits management, Express Scripts Canada answers the biggest questions on the minds of those in the health benefits management industry. This includes determining potential threats to the health and wellbeing of members. For example, delays in diagnosis and treatment will increase the challenge for patients to manage their disease, as early treatment can often slow disease progression. This includes diabetes, multiple sclerosis and common cardiovascular diseases such as hypertension and heart disease. Therefore, those with chronic diseases need special attention and a course of action during the pandemic to reduce the impact on their health. This will eventually help to prevent an increase in morbidity and mortality due to these diseases.

Stay well, stay safe and, as we turn the corner on this pandemic, know that we are committed to drive better health outcomes for members while managing and reducing costs.



A handwritten signature in black ink, appearing to read 'D. Lo', written in a cursive style.

Dr. Dorian Lo
President

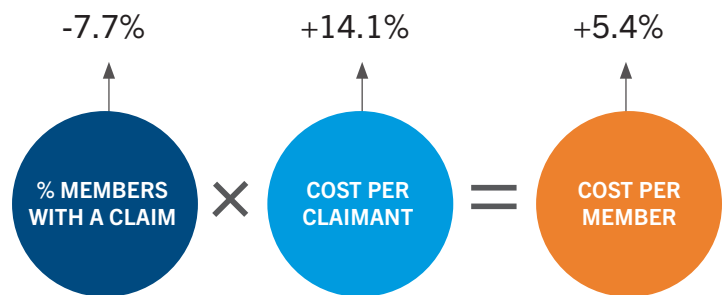
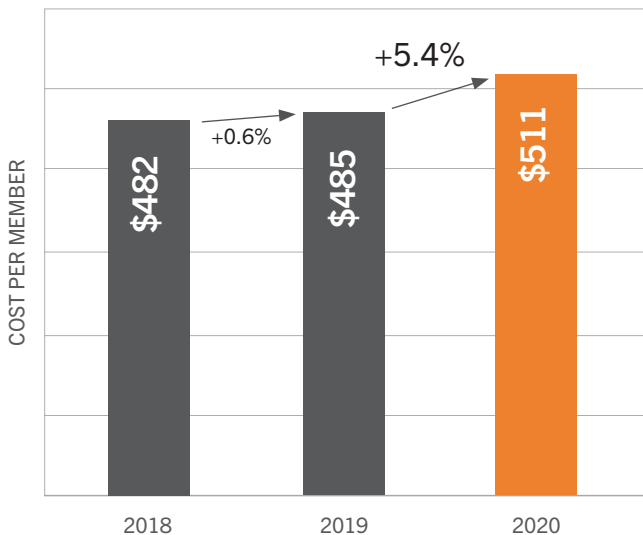


DRUG TREND & UTILIZATION

OVERALL TREND

OVERALL PRIVATE DRUG PLAN SPENDING SPIKED 5.4% DUE TO THE COVID-19 PANDEMIC

Heading into 2020, a 0.5%-1% trend increase was anticipated, similar to the 0.6% increase in drug trend from 2018 to 2019; however, due to COVID-19, there was a decrease in the percentage of members who claimed, which offset a significant growth in the cost per claimant. Overall, this balanced out at a 5.4% increase in the cost per member.



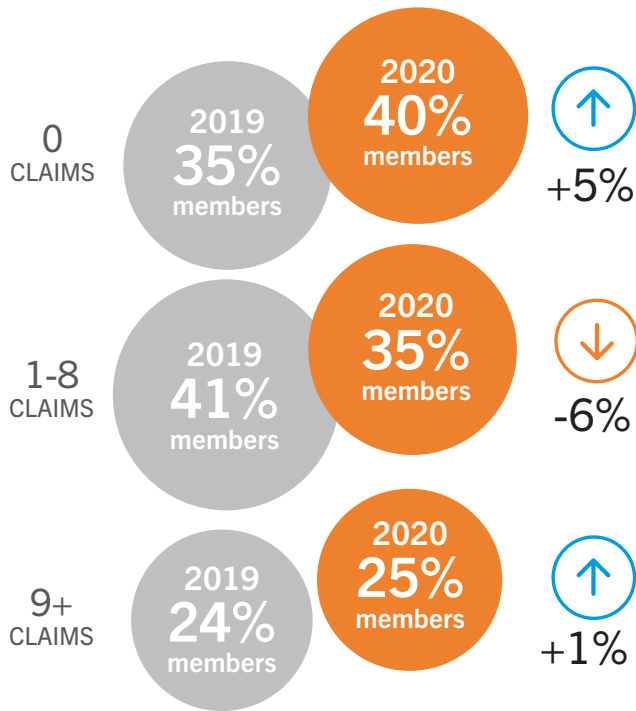


BREAKING DOWN THE IMPACT BY DIFFERENT MEMBER SEGMENTS

Based on annual claims, each member group has different needs and was impacted by COVID-19 in different ways.

Definition	1-8 drug claims annually	9+ drug claims annually
Drug claimant profile	<ul style="list-style-type: none"> occasional claims for antibiotics starting treatment for a chronic disease managing 1-2 chronic diseases 	<ul style="list-style-type: none"> managing multiple chronic conditions older members specialty drug claims and more complex needs
Average # therapeutic classes	1.8	4.9
Average # medications	2.1	6.8

FEWER MEMBERS ARE SUBMITTING DRUG CLAIMS DUE TO COVID-19, PUTTING DOWNWARD PRESSURE ON THE COST PER MEMBER

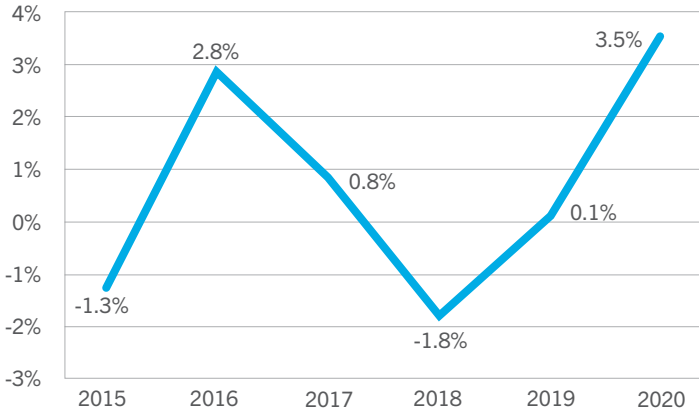


The cost per claimant increased due to fewer members submitting claims and higher costs associated with COVID-19 and specialty drugs:

- Decrease in cough and cold remedies (-60%), medications used for infections (-28%) and pain/inflammation (-19%).
- Chronic maintenance users now account for a higher proportion of the claimant base due to fewer acute-only claimants or new claimants for chronic disease medications.
- Onset of COVID-19 led to stockpiling of chronic medications and conversion of 90- to 30-days' supply claims across many provinces, resulting in additional claims and dispensing fees.
- Continued growth in specialty claims correlated with a rise in specialty drugs entering the market, and approved drugs being used for new indications.



TRADITIONAL DRUG TREND



FACTORS DRIVING TRADITIONAL DRUG TREND



30-days' supply limits on maintenance medications lowered cost per prescription but increased number of claims.

TOP 10 TRADITIONAL DRUGS

2019	2020
Methylphenidate HCL	Semaglutide*
Blood Glucose Test Strips*	Methylphenidate HCL
Sitagliptin-Metformin*	Lisdexamfetamine Dimesylate
Lisdexamfetamine Dimesylate	Sitagliptin-Metformin*
Rosuvastatin Calcium	Rosuvastatin Calcium
Liraglutide*	Flash Glucose Sensors*
Budesonide-Formoterol	Blood Glucose Test Strips*
Escitalopram Oxalate	Budesonide-Formoterol
Esomeprazole	Empagliflozin*
Atorvastatin Calcium	Escitalopram Oxalate

* Diabetic drug or supply

DIABETES DRUGS AND SUPPLIES

The #1 traditional drug in 2020 was Semaglutide, a diabetes medication available in either a once-per-week injection or once-daily oral tablet:

- Semaglutide and other GLP-1 agonists increase insulin secretion and sugar metabolism, with weight loss being a common side effect .
 - 41% increase in spend for all GLP-1 agonists

Semaglutide and Liraglutide (another GLP-1 agonist) shown to reduce risk of major adverse cardiovascular events associated with diabetes

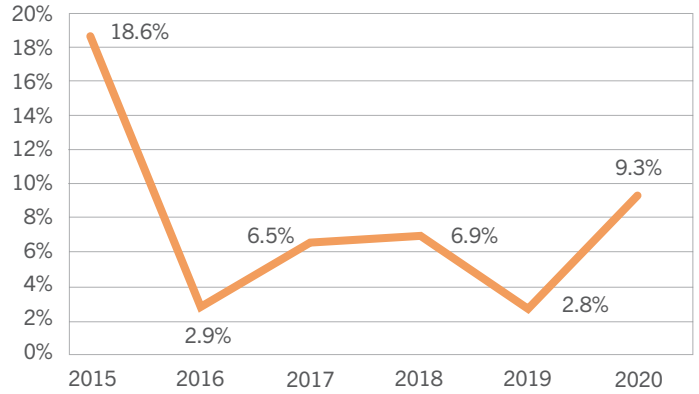
- High-dose Liraglutide (3 mg) approved by Health Canada for weight management in patients who have failed a previous intervention and have at least one weight-related comorbidity (e.g., hypertension, type 2 diabetes or dyslipidemia). Liraglutide (3 mg) is the only GLP-1 recommended in Obesity Canada's 2020 Clinical Practice Guidelines.

Flash glucose sensors overtook traditional blood glucose test strips in spend. Spend increased by 60% and the number of claimants increased by 33% :

- This technology is recommended for adults 18 years or older with diabetes.
 - Device is worn for two weeks at a time compared to traditional blood glucose monitors that require testing up to several times daily
- Average cost per claimant was about five times more than the cost for a diabetes test-strip claimant in 2020.



SPECIALTY DRUG TREND



FACTORS DRIVING SPECIALTY DRUG TREND

UTILIZATION **+7.6%** (+) COST/Rx **+1.7%** (=) SPECIALTY TREND **+9.3%**

- ↑ Many new drugs that came to market in 2020 were specialty drugs
- ↑ Additional treatment options now available for rare and untreatable diseases
- ↑ New indications approved for existing drugs

TOP 10 SPECIALTY DRUGS

2019	2020
Adalimumab	Adalimumab
Infliximab	Infliximab
Ustekinumab	Ustekinumab
Etanercept	Etanercept
Omalizumab	Omalizumab
Golimumab	Vedolizumab
Vedolizumab	Golimumab
Lenalidomide	Lenalidomide
Fingolimod	Ocrelizumab
Eculizumab	Secukinumab



WHAT TO WATCH IN SPECIALTY TOP 10



Most significant change in specialty spend was for multiple sclerosis medications:

- The introduction of generic alternatives for Fingolimod, a drug used to treat relapsing-remitting multiple sclerosis, caused it to fall off the top 10 list of specialty drugs in 2020.
- Ocrelizumab is indicated for both relapsing-remitting multiple sclerosis (which has many drug options) and primary progressive multiple sclerosis (which has few drug options). It also provides convenient six-month maintenance dosing compared to monthly for other drug options.

Biosimilars coming to market in 2021 have the potential to provide significant savings:

- Five biosimilar manufacturers for Adalimumab (#1) completed pan-Canadian Pharmaceutical Alliance negotiations in February 2021. The potential for generous savings will depend on biosimilar transitioning policies.
- In 2020, there were 28% more claimants for Adalimumab than Infliximab. These drugs may be used to treat similar inflammatory diseases. Infliximab biosimilars have been available since 2015 and the few provinces with transitioning policies have shown reduced spend for this drug.

See *Biosimilars* section for more info.

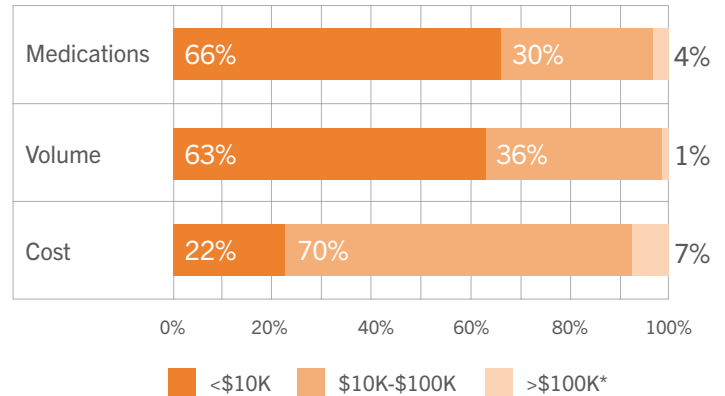
SPECIALTY SPEND BY ANNUAL COST

The following categories are useful for understanding total annual medication claims costs:

- More than \$100,000 annually
- From \$10,000 to \$100,000
- Less than \$10,000

The \$10,000 to \$100,000 category accounts for 30% of all specialty medications and makes up 36% of volume and 70% of the specialty drug spend.

SPECIALTY DRUG SPEND BY ANNUAL COST



*DUE TO ROUNDING, NUMBERS MAY NOT ADD UP TO 100%





**SPECIALTY SPEND BY ANNUAL COST:
2019 VS. 2020 DATA**

>\$100K ANNUAL COST

- Overall spend increased by 23.3% due to increased uptake in drugs used to treat cystic fibrosis (Orkambi® and Symdeko®).
- Significant increase in spend on rare disease medications (57%), with uptake of Crystvita®, a drug used to treat X-linked hypophosphatemia, rising with expanded use to treat children as young as six months of age.

\$10K-\$100K ANNUAL COST

- Overall spend increased by 9.4%, driven by:
 - 8.8% for inflammatory conditions
 - 16.3% for cancer
 - 43.2% for skin conditions

Skin conditions: Increase in spend attributed to Dupixent®, which received an expanded indication for the treatment of atopic dermatitis in children as young as 12 years of age. 2020 saw two additional indications for this drug, further expanding its potential patient population.

Multiple sclerosis: Spend on Ocrevus® increased by 78.9%. Rise could be attributed to Canadian multiple sclerosis guideline updates that promote disease-modifying therapy soon after diagnosis.

Asthma: Spend increased by 10.2%. While Xolair® is this category’s highest-cost medication, uptake of two other similar medications, Fasenna® and Nucala®, contributed most to this increase spend.

Inflammatory conditions: Spend for Stelara® increased by 15.5%. Stelara® was approved for a new indication in 2020 to treat patients with ulcerative colitis.

<\$10K ANNUAL COST

- Overall spend in this segment increased by 8.2%, driven by specialty medications for migraines.

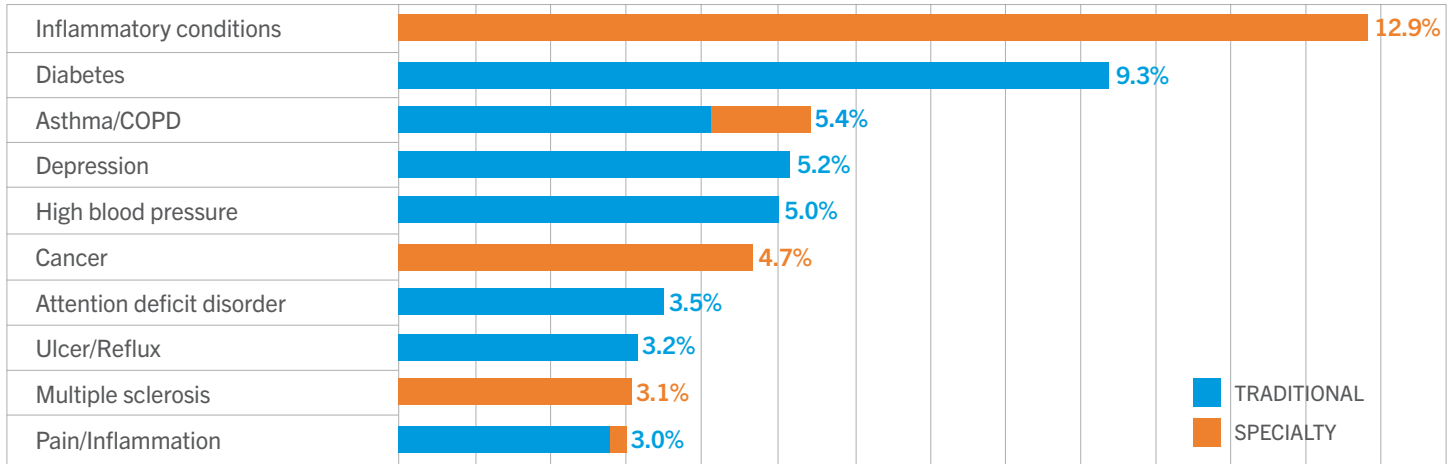
MOST COMMON DISEASE STATES AND HIGHEST-COST MEDICATIONS IN EACH SEGMENT

>\$100K ANNUAL COST	
Most common disease states: Cystic fibrosis and rare diseases accounted for nearly 70% of spend in this category	Highest-cost medications: Four medications = 66.7% of the spend: Soliris® (23.3%), Orkambi® (16.3%), Symdeko® (15.6%) and Vimizim® (11.5%)
\$10K-\$100K ANNUAL COST	
Most common disease states: Inflammatory conditions, cancer, multiple sclerosis, asthma/COPD, HIV/AIDS, endocrine or metabolic disorders and skin conditions	Highest-cost medications: Top three medications = 34.9% of spend: Humira® (16.7%), Remicade® (11.2%) and Stelara® (7%)
<\$10K ANNUAL COST	
Most common disease states: Inflammatory conditions, cancer, blood disorders, eye disease and macular degeneration, organ transplant, HIV/AIDS, muscle relaxants and infertility	Highest-cost medications: Top five medications = 25% of spend: Eylea® (6.3%), Botox® (6.2%), two oral medications for inflammatory conditions – Otezla® (4.3%) and Xeljanz® (4.2%) – and lastly Lapelga® (4.0%)



TOP 10

TOP 10 THERAPEUTIC CLASSES IN 2020 (BY SPEND)



TOP 10 THERAPEUTIC CLASSES (OVERALL SPEND)

Rank 2019	Rank 2020	Trend	Therapeutic Class	Trend		
				Total	Utilization	Cost
1	1	=	Inflammatory conditions	4%	7%	-2%
2	2	=	Diabetes	12%	11%	0%
3	3	=	Asthma/COPD	22%	19%	3%
5	4	↑	Depression	6%	10%	-4%
4	5	↓	High blood pressure	5%	11%	-6%
6	6	=	Cancer	12%	9%	2%
7	7	=	Attention deficit disorder	5%	6%	-1%
12	8	↑	Ulcer/Reflux	10%	11%	0%
9	9	=	Multiple sclerosis	3%	3%	0%
8	10	↓	Pain/Inflammation	10%	7%	2%

■ THERAPEUTIC CLASS DOMINATED BY TRADITIONAL DRUGS

■ THERAPEUTIC CLASS DOMINATED BY SPECIALTY DRUGS



SPENDING BREAKDOWN BY THERAPEUTIC CLASS

2020 saw the top three therapeutic classes remain the same as 2019 but with a rise in depression and significant drop in infections:

- New developments and indications resulted in growth of claims for medications treating chronic diseases.
- Despite an increase in biosimilar availability and additional indications approved for inflammatory conditions, savings are not immediate.

#1 – INFLAMMATORY CONDITIONS

- Decreased cost per claim driven by shift to lower-cost biosimilars for widely used Remicade® and Enbrel® to treat rheumatoid arthritis, Crohn's disease and psoriasis.
- 2021 will see market availability of biosimilars for Humira®, with the impact on spend dependent on biosimilar transitioning policies across the country.

#2 – DIABETES

- Indications for add-on/combo therapies and other disease-modifying factors (i.e., reducing cardiovascular disease and kidney disease risk) were approved in 2020.
- New Forxiga® indication for the treatment of heart failure in adults with or without diabetes will increase the potential patient population. This is the first time a diabetes drug class was approved for cardiovascular condition, regardless of the presence of diabetes.
- GLP-1 agonists continue to top spend in this disease state.

#3 – ASTHMA/COPD

- Updates in the Global Initiative for Asthma guidelines recommend that adult and adolescent patients with asthma should no longer be prescribed only a short-acting bronchodilator and that a low-dose combination corticosteroid and long-acting beta agonist also be prescribed for symptom relief.
- This, combined with stockpiling, drove an increase in the cost per claimant for use of Symbicort® and Salbutamol.
- Now approved in Canada as an add-on maintenance treatment for adults, adolescents and children (aged 6 years and older) with severe eosinophilic asthma Nucala® (Mepolizumab) saw a 42% increase in cost per claimant. It is the first interleukin-5 biologic approved for the condition in children in Canada.

OTHER NOTABLE TRENDS

#4 – DEPRESSION

- Driven by the impacts of the pandemic, and its associated isolation and financial stress.
- 10% increase in claims per claimant for antidepressants, including selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors.

#6 – CANCER

- Increase in spend driven by growth of novel anti-cancer agents that are increasingly targeted to specific patient populations at a significant price tag.
- Increased focus on developing oral therapies that can be administered outside of hospital settings.

#8 – ULCER/REFLUX

- Numerous recalls and backorders for Ranitidine and Famotidine occurred in 2020.
- Use of these widely generic, low-cost drugs dramatically decreased in 2020, replaced by higher-cost proton pump inhibitors like Pantoprazole and Dexlansoprazole.

#10 – PAIN/INFLAMMATION

- The pandemic delayed surgeries and dental procedures, which are often accompanied by pain relief medications.

#13 – DIABETIC SUPPLIES

- Increase in spend driven by the continued uptake of flash glucose sensors.

#16 – INFECTIONS

- Decrease in ranking could be attributed to lowered risk of community transfer of infections in schools and workplaces due to public health measures imposed during the pandemic.
- Those who became sick might not have visited a healthcare provider due to accessibility issues or fear of exposure.



OTHER NOTABLE TRENDS cont.

#26 – RARE DISEASE

- According to an article published in the *Journal of Rare Disorders* in 2020, there are approximately 7,000 classified rare disorders, of which 70% have no treatment. Ongoing research for rare disease treatments will result in market growth.
- Gene therapy Zolgensma® approved in late 2020 for the curative treatment of spinal muscular atrophy in infants, with a price tag of US\$2 million.
- Firdapse® and Ruzurgi® both introduced to treat Lambert-Eaton Syndrome.

#28 – PREVENTATIVE VACCINES

- Pandemic significantly reduced international travel and saw fewer patients seeking preventative vaccines for travel-related infections.

TOP 10 THERAPEUTIC CLASSES PER AGE GROUP

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

■ THERAPEUTIC CLASS DOMINATED BY TRADITIONAL DRUGS ■ THERAPEUTIC CLASS DOMINATED BY SPECIALTY DRUGS

COVID-19 AND RARE DISEASE IMPACT AGE GROUPS DIFFERENTLY

Children 18 years old and under:

- Infections fell from #2 to #7, likely due to decreased opportunities for community transmission.
- Inflammatory conditions surpassed asthma/COPD with higher-cost biologic therapies gaining pediatric indications.
- Rare diseases jumped from #10 in 2019 to #6 in 2020.

36- to 65-year-olds:

- Depression jumped from #6 to #3, reflecting increased stress, caregiving duties and isolation caused by the pandemic.

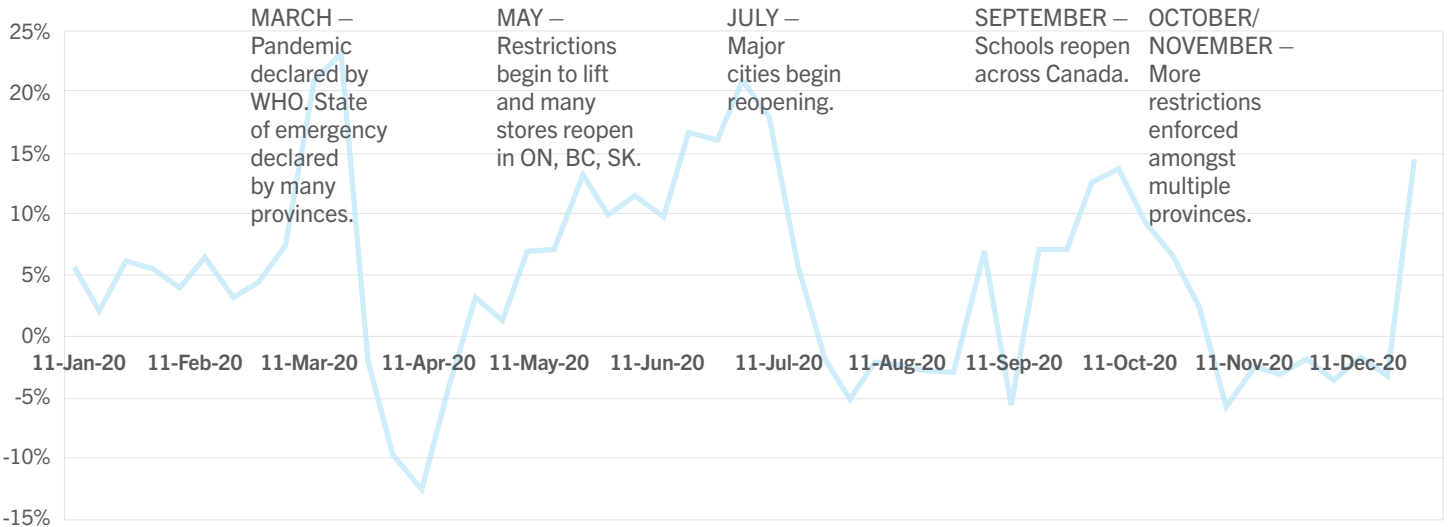
36- to 65-year-olds and 66 and older:

- Ulcer medications climbed by one position due to sourcing of higher-cost alternatives to Ranitidine and Famotidine.



COVID-19'S IMPACT ON DRUG CLAIMS

Provincial COVID-19 restrictions, including stay-at-home orders and supply limits on prescriptions, resulted in significant spikes and dips in claims volume in 2020.



BEFORE LOCKDOWN (January to March 2020)

- March's surge in claims volume was primarily driven by medication stockpiling as the World Health Organization (WHO) declared COVID-19 a pandemic and multiple provinces announced a state of emergency.
- The majority of provinces set temporary 30-days' supply limits* on prescriptions.

LOCKDOWN (April 2020)

- April saw a sharp drop in claims, reflecting the impact of pan-Canadian stay-at-home orders and earlier stockpiling of medications.

REOPENING (May to June 2020)

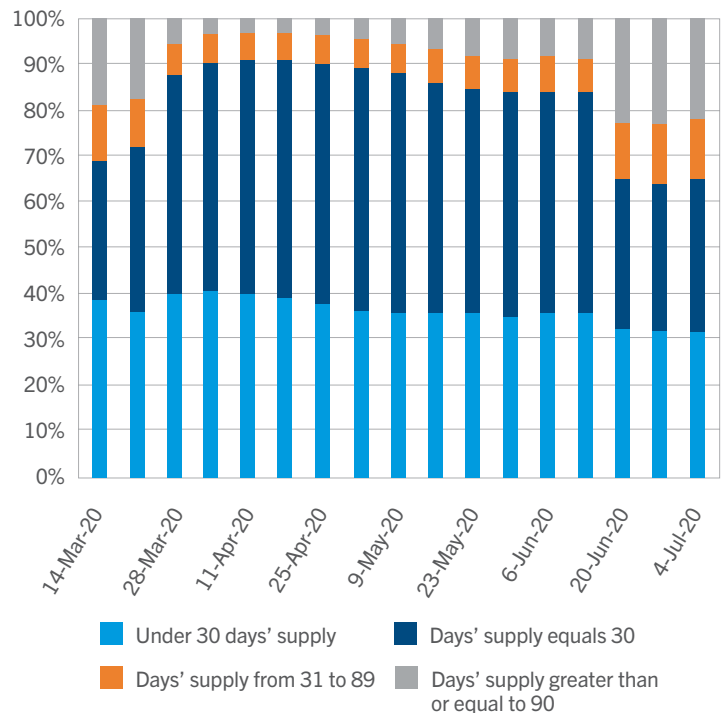
- May saw claims volumes increasing as restrictions were lifted and 30-days' medication supplies began to run out.
- The lifting of 30-days' supply limits in most provinces resulted in claim volumes dipping until September.

RETURN TO SCHOOL AND FALL HOLIDAYS (September to October 2020)

- Early September and October saw claims increase in step with back-to-school and Thanksgiving periods and as members prepared for the pandemic's second wave.

IMPACT OF DAYS' SUPPLY RESTRICTIONS

Days' supply limits drove up claims volume; what would have been a single claim resulted in three separate claims between March and June:



*Constraints on days' supply: 30-days' supply limits were imposed throughout the country (except B.C.). These restrictions were lifted between May and June.

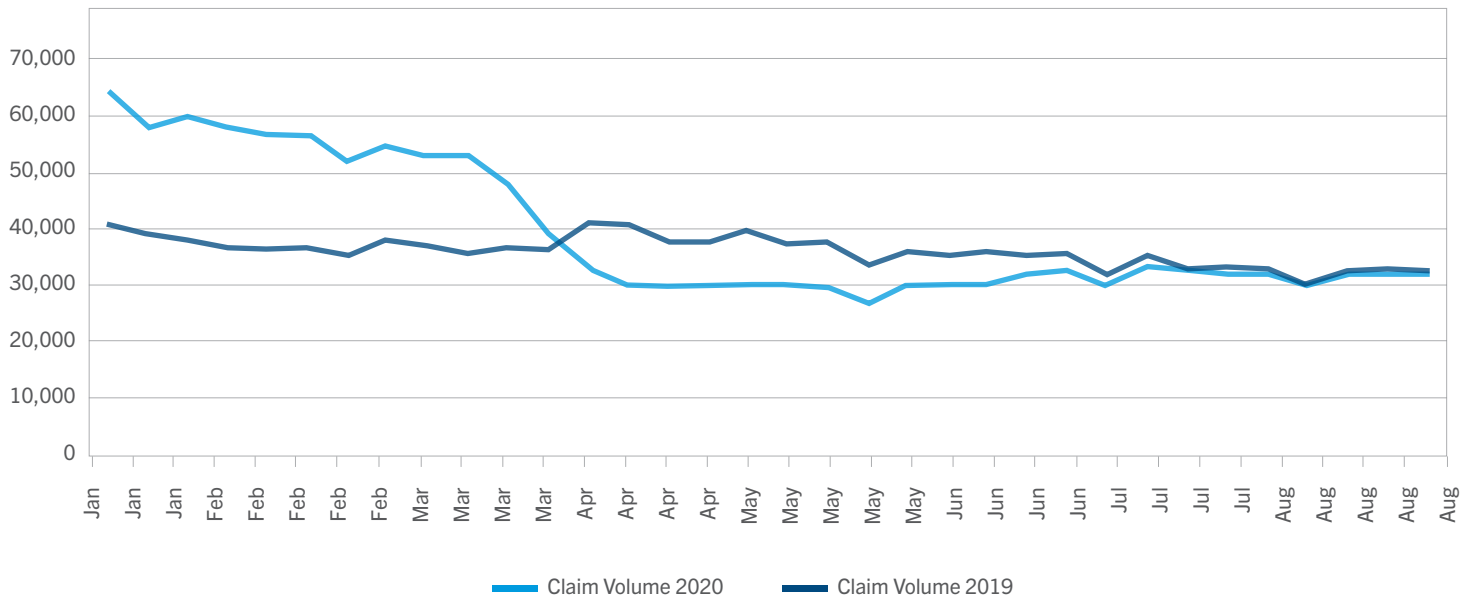


COVID-19'S IMPACT ON SPECIFIC THERAPEUTIC CATEGORIES

ANTI-INFECTIVES

- Steep decline in claims during the lockdown period.
- Likely attributed to increased hygiene practices, the closure of sites posing a higher risk of infections (i.e., schools, daycares, workplaces) and potential avoidance of clinics and hospitals for non-urgent illness.

WEEKLY CLAIMS VOLUMES



COVID-19'S IMPACT ON SPECIFIC THERAPEUTIC CATEGORIES cont.

ASTHMA/COPD

- Claims for asthma medication spiked in March.
- Combination of 30-days' supply limits and stockpiling contributed to sharp increase in claims.

HIGH BLOOD PRESSURE, DIABETES AND HIGH CHOLESTEROL

- Chronic medications for conditions such as high blood pressure, diabetes and cholesterol were highly affected by the 30-days' supply limits.
- Angiotensin receptor blockers, a class of commonly used blood pressure medications, were affected by frequent backorders as patients were forced to switch to alternatives.





PENT-UP DISEASE AND BACKLOG OF PATIENTS

2020 saw a significant drop in new claimants for chronic diseases like diabetes, cancer and depression. This drop in new claimants suggests there could be a growing backlog of members who, for a variety of reasons, are not necessarily seeking treatment for their conditions.

DEPRESSION

End of March to December saw an average 2% decline in weekly new depression claimants.

IMPLICATION: An estimated backlog of more than 100,000 Canadians who have not commenced treatment with medications used for depression.

DIABETES

End of March to December 2020 saw an average 1% decline in weekly new diabetic claimants.

IMPLICATION: An estimated backlog of more than 20,000 Canadians who have not commenced treatment with medications used for diabetes.

CANCER

End of March to December 2020 saw an average 2% decline of weekly new cancer claimants.

IMPLICATION: An estimated backlog of more than 10,000 Canadians who have not commenced treatment with medications used for cancer.

Possible impact: Treatment with newer drugs rather than less expensive first-line therapies.

Delays in cancer screening and the cancellation of surgeries may result in a shift towards treating more advanced cancers, with fewer therapeutic options at a higher cost.

HIGH CHOLESTEROL AND HIGH BLOOD PRESSURE

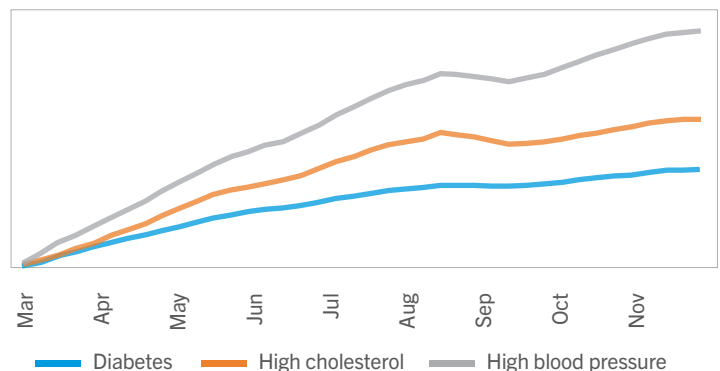
Cumulative backlog of claimants with delayed diagnoses and treatment of these conditions raises concerns related to possible consequences of increased risks of a heart attack or stroke.

Delayed treatment of diabetes is associated with a higher risk for therapy intensification.

Possible impact: Multiple medications required to treat the condition and the need for costly advanced treatment.

For most conditions, seeking care earlier in the course of illness improves outcomes and delays the progression to more serious outcomes.

CUMULATIVE BACKLOG OF CLAIMANTS



2021 TREND OUTLOOK

Dependent on return to “normal” and specialty drug influences

- Contributing factors include:
 - The timing of COVID-19 vaccinations
 - How quickly lockdown restrictions are lifted: lockdowns are associated with fewer claims for acute medications, such as antibiotics and cough and cold remedies
 - If the healthcare system reverts to pre-pandemic capacity levels
- An increase in new specialty drugs entering the market and existing specialty drugs being approved to treat a wider range of diseases
- Acceptance of biosimilar transitioning policies and new biosimilars coming to market



BIOSIMILARS

Increased approval and availability signals momentum of biosimilars in Canada.

BIOSIMILARS APPROVED IN 2020

Biosimilar	Chemical Ingredient	Reference brand	Indications
Idacio®	Adalimumab	Humira®	Inflammatory conditions
Amgevita®	Adalimumab	Humira®	Inflammatory conditions
Hyrimoz®	Adalimumab	Humira®	Inflammatory conditions
Hulio®	Adalimumab	Humira®	Inflammatory conditions
Noromby®	Enoxaparin	Lovenox®	Cardiovascular disease
Inclunox®	Enoxaparin	Lovenox®	Cardiovascular disease
Redesca®	Enoxaparin	Lovenox®	Cardiovascular disease
Nivestym®	Filgrastim	Neupogen®	Blood disorders
Avsola®	Infliximab	Remicade®	Inflammatory conditions
Trurapi®	Insulin aspart	NovoRapid®	Diabetes
Ziextenzo®	Pegfilgrastim	Neulasta®	Blood disorders
Nyvepria®	Pegfilgrastim	Neulasta®	Blood disorders
Riximyo®	Rituximab	Rituxan®	Cancer
Ruxience®	Rituximab	Rituxan®	Cancer
Osnuvo®	Teriparatide	Forteo®	Osteoporosis/Skeletal disorder
Apo-Teriparatide®	Teriparatide	Forteo®	Osteoporosis/Skeletal disorder
Kanjinti®	Trastuzumab	Herceptin®	Cancer



**RECENTLY APPROVED BIOSIMILARS EXPECTED
IN 2021**

- Six biosimilars expected to be marketed in 2021 expected to reduce costs.
- Infliximab biosimilar: Avsola®.
- Trurapi® (insulin aspart) joins insulin biosimilars Basaglar® (insulin glargine) and Admelog® (insulin lispro) introduces savings related to diabetes medication.
- Three biosimilars for Enoxaparin, a drug that reduces risk of deep vein thrombosis and pulmonary embolism, and is often used following surgeries including knee or hip replacement. Due to COVID-related delays of elective surgeries, uptake of Enoxaparin may be lower than expected.

BIOSIMILARS APPROVED BY HEALTH CANADA IN 2020

Most common indication	Number of biosimilars approved	Percentage of total indications
Blood disorders	3	18%
Cancer	3	18%
Cardiovascular disease	3	18%
Diabetes	1	6%
Inflammatory conditions	5	29%
Osteoporosis/Skeletal disorder	2	12%
Grand total	17	

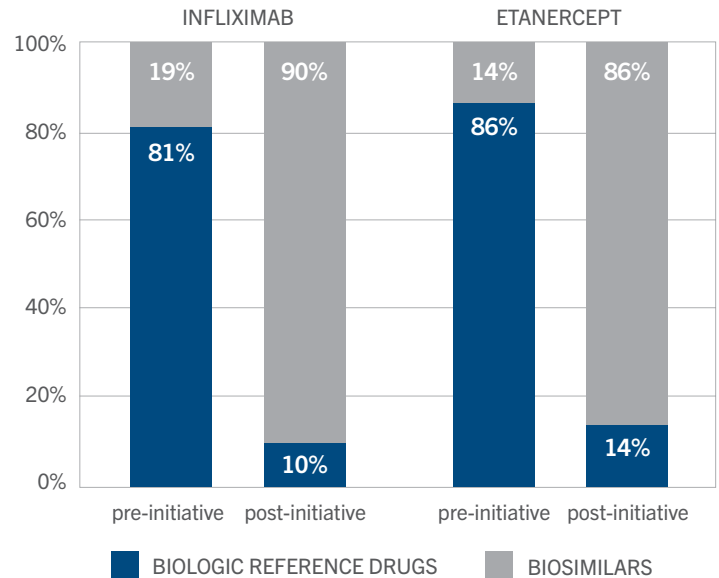
**IMPLEMENTATION OF PROVINCIAL INITIATIVES
CONTINUES**

BRITISH COLUMBIA

B.C. biosimilar initiative is successful

- Successful market uptake of Infliximab for gastrointestinal indications drove penetration from 56% in 2019 to 90% in 2020.
- Enbrel® (biologic reference for Etanercept) claims dropped from 18% post-initiative at the end of 2019 to 14% in 2020.

**PROPORTION OF CLAIMS FOR INFLIXIMAB AND ETANERCEPT
PRE AND POST B.C. BIOSIMILAR INITIATIVES**



Rituximab next for the B.C. biosimilar initiative

- Target implementation date: February 18, 2021.
- Compared to Remicade® and its biosimilars, Rituxan® is less costly. As a result, financial impact will be smaller.
- Targets indications of rheumatoid arthritis.

ALBERTA

- Alberta’s biosimilar initiative launched January 15, 2021, for provincial public plan recipients taking Copaxone, Filgrastim, Pegfilgrastim, Insulin glargine, Etanercept (all indications except psoriasis) and Infliximab.

Differences between Alberta and B.C. programs:

- Alberta’s program affects adults only; B.C. includes adults and children.
- Only government-sponsored plan members will be directly impacted in Alberta.

ONTARIO

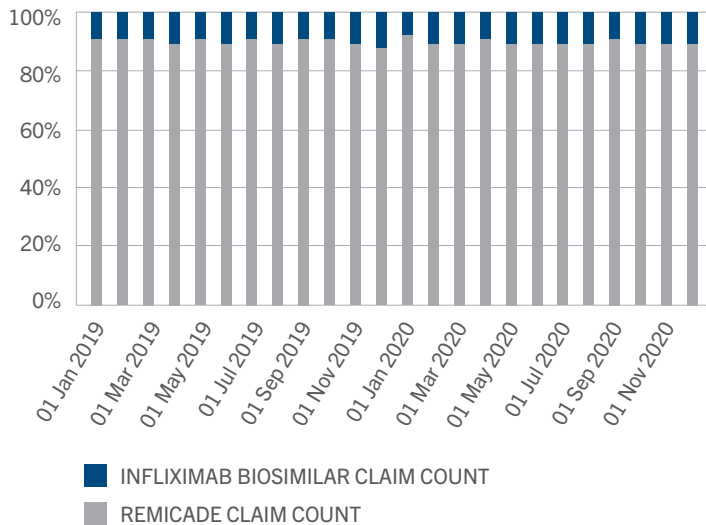
- Ontario’s biosimilar policy remains unannounced.
- Currently managing reference biologics through Exceptional Access Program (EAP) and access to biosimilars through Limited Use Codes.



QUEBEC

- RAMQ’s grandfathering approach targets a much smaller group of first-time users of Remicade® and has reduced impact on biosimilar uptake.

REMICADE VS. BIOSIMILARS



BIOSIMILARS UNDER REVIEW BY HEALTH CANADA

If introduced, the following biosimilars would drive further pricing competition and resulting savings opportunities for private payors.

BIOSIMILARS UNDER REVIEW BY HEALTH CANADA

Medicinal ingredient	Number of biosimilars under review	Common indication
Bevacizumab	2	Cancer
Rituximab	1	Inflammatory conditions
Pegfilgrastim	1	Blood disorders
Trastuzumab	1	Cancer
Etanercept	1	Inflammatory conditions
Adalimumab	1	Inflammatory conditions

DELAYED INITIATIVES REDUCE SAVINGS IMPACT ON PRIVATE PLANS

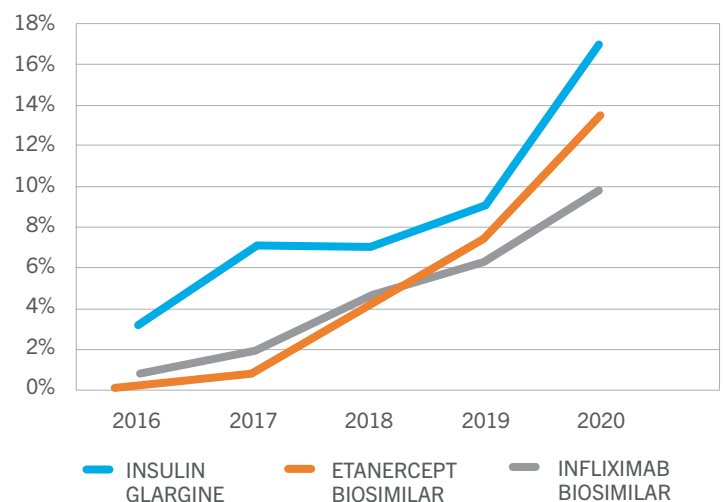
- The Alberta and Ontario programs were delayed plus their directly implicated populations are limited. Both of these factors led to decreased savings opportunities.
- Compared to the mandatory biosimilar policies in B.C., Alberta and Ontario’s less aggressive programs will result in relatively lower savings in these jurisdictions.

BIOSIMILAR POLICIES TO WATCH IN 2021



- New switch policies will affect Ontario Drug Benefit (ODB) recipients. The ODB already requires new patient use of biosimilars for Rituximab, Infiximab and Etanercept.
- Due to its smaller cost differential and limited number of affected conditions treated with this biosimilar, B.C.’s 2021 launch of the Rituxan® biosimilar is not expected to match the financial impact of the previous Infiximab and Etanercept initiatives.
- A June 2020 Institut national d’excellence en santé et services sociaux (INESSS) statement on non-medical switching reported Quebec clinicians were generally not in favour of a switching policy.
- To succeed long term, biosimilar brands must provide resource-intensive Patient Support Programs (PSPs) or Patient Assistant Programs (PAPs) comparable to those currently provided by biologics originators.

UPTAKE OF BIOSIMILARS PER INGREDIENT BETWEEN 2016 AND 2020*



*Based on ESC’s Book of Business data



BIOSIMILARS APPROVED IN CANADA

2014	2015	2016	2017	2018	2019	2020
Inflectra® (Infliximab) Dormant: Remsima® (Infliximab)	Basaglar® (Insulin Glargine)	Grastofil® (Filgrastim) Brenzys® (Etanercept)	Admelog® (Insulin Lispro) Erelzi® (Etanercept) Renflexis® (Infliximab) Glatect® (Glatiramer)	Lapelga® (Pegfilgrastim) Mvasi® (Bevacizumab) Hadlima® (Adalimumab)	Fulphia® (Pegfilgrastim) Truxima® (Rituximab) Ogivri® (Trastuzumab) Herzuma® (Trastuzumab) Trazimera® (Trastuzumab) Zirabev® (Bevacizumab) Teva-Teriparatide® (Teriparatide)	Osnuvo® (Teriparatide) Kanjinti® (Trastuzumab) Avsola® (Infliximab) Riximyo® (Rituximab) Nivestym® (Filgrastim) Ziextenzo® (Pegfilgrastim) Ruxience® (Rituximab) Apo-Teriparatide® (Teriparatide) Idacio® (Adalimumab) Nyvepria® (Pegfilgrastim) Trurapi® (Insulin Aspart) Noromby® (Enoxaparin) Amgevita® (Adalimumab) Hyrimoz® (Adalimumab) Inclunox® (Enoxaparin) Hulio® (Adalimumab) Redesca® (Enoxaparin)

Increase in biosimilar approvals throughout the years offers potential savings to plan sponsors.



QUEBEC

COVID-19 significantly impacted pharmacy services, with patients increasingly seeking treatment and medication refills from pharmacists.

AS OF MARCH 17, 2020, PHARMACISTS EXPAND AUTHORITY UNDER LAW 31

ADMINISTER MEDICATION DURING AN EMERGENCY

- Subject to deductible and copay
- Private payors billed for these claims, with the amount billed including both fees for the prescription and administration of drug.

Fee to administer medication during an emergency
\$18.59

PRESCRIBE AND ADMINISTER A VACCINE

- There is no fee agreement for this service, except for those included in the Programme québécois d'immunisation (PQI), such as the influenza vaccine, for which private payors are not billed.

OTHER NEW CLINICAL ACTIVITIES ALLOWED BY LAW 31

- Assess patients' physical and mental condition to ensure proper medication use.
- Take a sample by inserting an instrument into the pharynx, for example to test for strep throat.
- Prescribe over-the-counter medications, as warranted by the clinical situation or circumstance.

IMPACT for new clinical activity of pharmacists prescribing OTC medications:

COVID-19 and recalls significantly increased claims for specific drug categories.

- **Constipation** (PEG-3350, Sodium Docusate).
- **Allergic rhinitis** (Cetirizine, Loratadine, Fluticasone nasal spray, Mometasone nasal spray, Triamcinolone nasal spray).
- **Gastroesophageal reflux disease** (Tums®, Gaviscon®, Ranitidine, Famotidine, Esomeprazole, Omeprazole)
Recall of prescription Ranitidine products in 2020 led to possible switch towards OTC versions of drugs such as Esomeprazole.
- **Topical treatments** (Hydrocortisone, Clotrimazole).

LAW 41

- COVID-19 increased claims for pharmacists' clinical activities as patients sought care at pharmacies for refills and minor ailments.
- Significant decrease in claims for travel-related consultations.

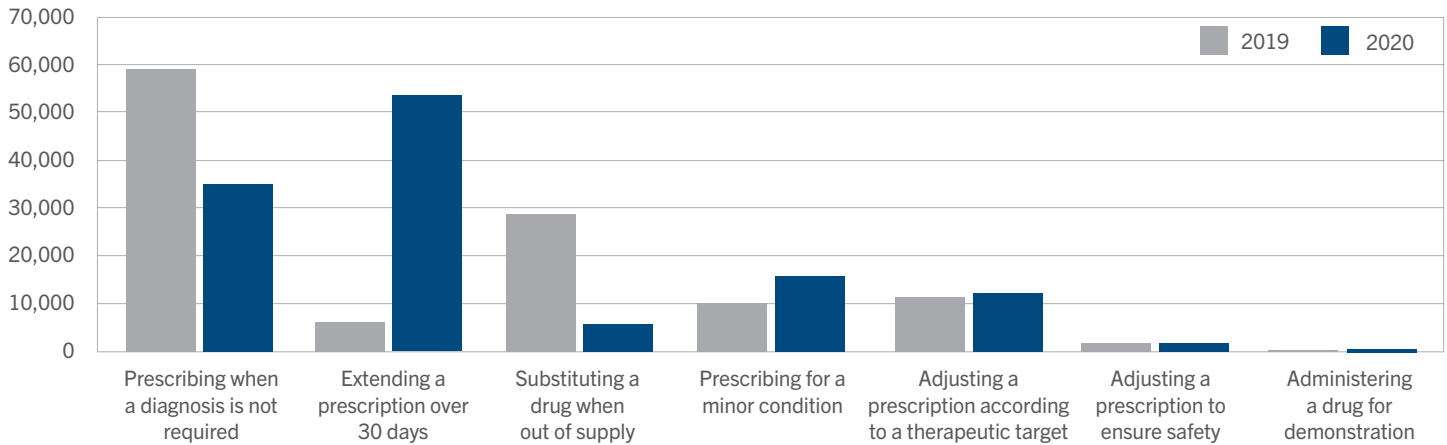




CLAIM ACTIVITY FOR LAW 41 CLINICAL ACTIVITIES

There was a 5% increase in clinical activity claims from 2019 to 2020.

NUMBER OF CLAIMS PER CLINICAL ACTIVITY TYPE IN 2019-2020



SUMMARY OF INCREASE IN CLAIMS

EXTENDING A PRESCRIPTION OVER 30 DAYS



552%

- COVID-19 reduced physician accessibility; patients sought pharmacists to secure refills of essential medications.

ADMINISTERING A DRUG FOR DEMONSTRATION



153%

- Significant increase in claims over 2019.
- Claims for this clinical service will be paid by private payors in 2021.

PRESCRIBING FOR A MINOR CONDITION



51%

- Pharmacist consultations for hemorrhoids and for urinary tract infections as patients turned to pharmacists rather than family doctors to seek treatment.

SUMMARY OF DECREASE IN CLAIMS

SUBSTITUTING A DRUG WHEN OUT OF SUPPLY



81%

- Drug shortages less impactful in 2020 compared to 2019.

PRESCRIBING WHEN A DIAGNOSIS IS NOT REQUIRED



42%

- Significant decrease in claims could be attributed to:
 - lack of travel consultations due to COVID-19-related restrictions and
 - fewer consultations for lice treatment could relate to closure of schools and day cares during lockdowns.

PRESCRIBING WHEN A DIAGNOSIS IS NOT REQUIRED

Percentage change in claim volume 2019-2020

ALTITUDE SICKNESS	-79%
MALARIA PROPHYLAXIS	-65%
TRAVELLER'S DIARRHEA	-52%
LICE TREATMENT	-49%

PRESCRIBING FOR A MINOR CONDITION

Percentage change in claim volume 2019-2020

HEMORRHOIDS	120%
URINARY TRACT INFECTION	96%
DYSMENORRHEA	93%



RAMQ BIOSIMILAR AMENDMENTS IN 2020

Changes to coverage of reference biologics (Remicade®, Enbrel®, Neupogen® and Rituxan®) limited new-user access to these products. Quebec's policies did not force non-medical switching for current patients.

INFLIXIMAB

- As of August 19, 2020, Remicade® is only reimbursed for patients with idiopathic juvenile arthritis or patients who had been reimbursed by RAMQ or an insurer for Remicade® before this date.
- Only Renflexis® or Inflectra® are reimbursed for indications such as Crohn's disease, rheumatoid arthritis and psoriatic arthritis.

ETANERCEPT

- As of August 19, 2020, Enbrel® will not be reimbursed for patients with conditions like psoriatic arthritis or plaque psoriasis unless reimbursement was received by RAMQ or an insurer for Enbrel® before this date.
- For these indications, only Erelzi® is reimbursed.
- Since August 18, 2017, ankylosing spondylitis and rheumatoid arthritis patients have been directed to start on Brenzys®.

FILGRASTIM

- As of September 30, patients are only approved for Grastofil® or Nivestym® for any new start of Filgrastim.

RITUXIMAB

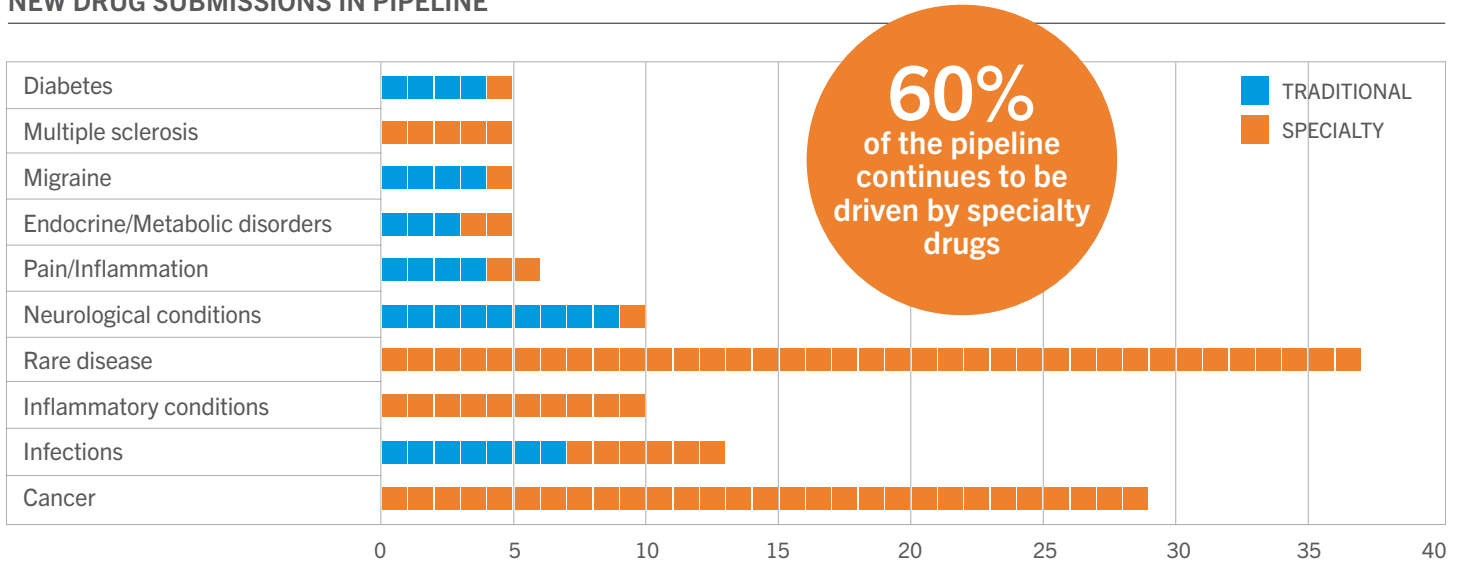
- As of September 30, patients are only approved for Riximyo® or Ruxience® for any new start of Rituximab for rheumatoid arthritis.





PIPELINE

NEW DRUG SUBMISSIONS IN PIPELINE



Specialty drugs continue to dominate pipeline

- There are over 30 drugs in development to treat rare diseases and over 25 drugs to treat cancer.
- These therapeutic classes are dominated by specialty drugs, including biologics and curative gene therapies.

The pandemic has shifted attention back to research and development to treat infections

- This therapy class typically sees little research due to existing drugs and small markets.
- However, five of the new specialty drugs under investigation are to treat COVID-19.

Life-changing effects of rare disease drugs come with steep price tags

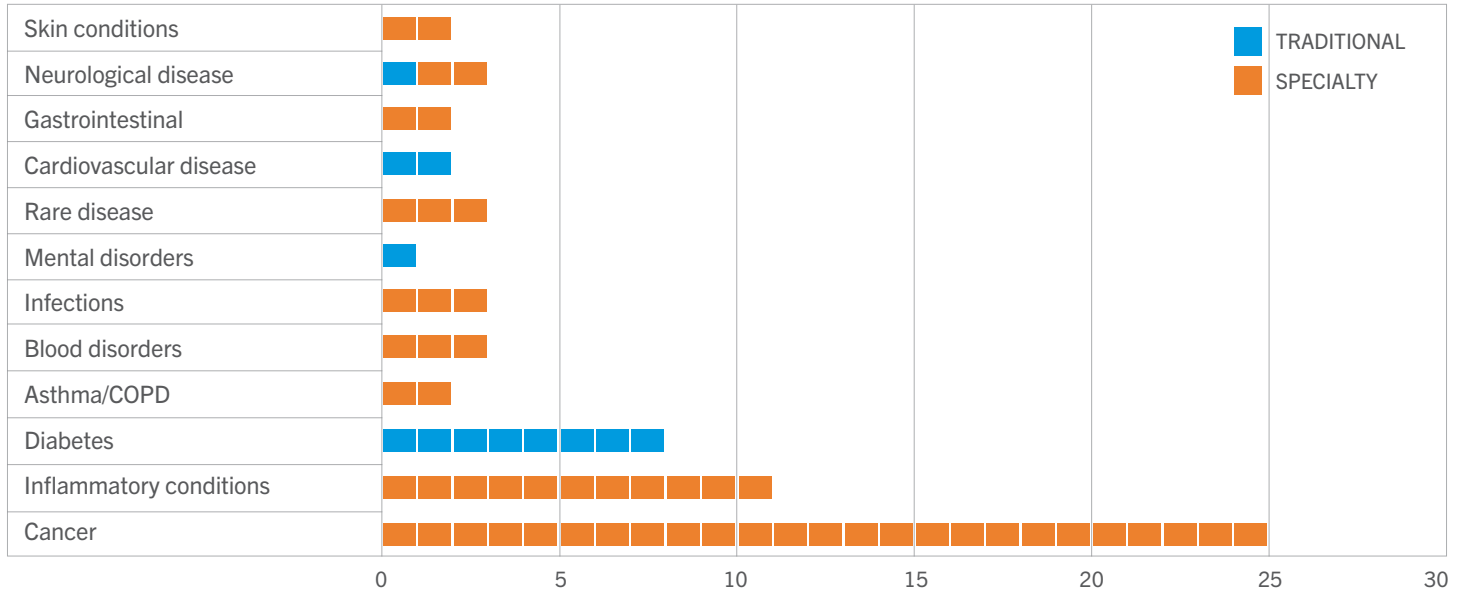
- Emerging research continues to focus on rare diseases.
- Within the 30+ drugs in development are three gene therapies: “curative” one-time treatments that can offer life-changing effects.

Emerging gene therapies to treat cancer come at a potential cost to private payors

- Four gene therapies are in development to treat hematological cancers.
- More than half of the new oncology drugs are oral formulations that allow patients to receive treatment at home.



NEW INDICATIONS IN DEVELOPMENT PIPELINE



Specialty drugs for cancer and inflammatory conditions dominate new indication pipeline.

ASTHMA/COPD

- Once dominated by traditional inhalers, high-cost biological therapies now target this therapeutic category.
- The drugs with expanded indications for asthma under investigation are all specialty biologic therapies.

Oral formulations overtake injectables for inflammatory conditions

- Most drugs with pending new indications for inflammatory conditions are orally administered specialty medications.
- This is more convenient for patients compared to injectable options for conditions like psoriatic arthritis, ulcerative colitis and psoriasis.





LEGISLATIVE UPDATES

COVID-19 delayed some national and provincial programs, but others were accelerated, increasing access to pharmacy care.

NATIONAL

Judicial review scrutiny delays amendments to Patented Medicines Regulations

- Intended to lower prices of patented medications in Canada through new price tests, factors to assess excessive pricing and PMPRB11, a modified list of comparator countries.
- Deemed beyond the scope of the *Patent Act*, a previous requirement for manufacturers to report rebates was removed.
- Guidelines delayed until July 1, 2021.

ALBERTA

Introduction of three provincial programs offer cost-saving measures

- Biosimilars program delayed from July 1, 2020, to January 15, 2021.
- Changes only apply to Albertans on government-sponsored plans, including Coverage for Seniors and Child and Family Services.

Coverage for Seniors program

- Eliminated provincial coverage for previously covered family members younger than 65, who were to seek coverage through workplace-administered private drug plans or an alternative government-sponsored program.

Standardizing Access to Medications for Ambulatory Patients (STAMP) program

- Aims to reduce Alberta Health Services (AHS) spending by \$2.3 million per year by requiring that patients pay for the cost of their medications and their administration, such as in the case of injections.
- Will restrict medications paid by AHS and transfers costs of cancer, Crohn's disease, fibromyalgia, osteoporosis, multiple sclerosis and other treatments to private payors and patients.
- Announced in October 2020, this program's impact to private payors could be substantial.

BRITISH COLUMBIA

Phase 2 of Biosimilars Program implemented

- Q1 2020 deadline for Infliximab Biosimilar Phase Two program targeted gastrointestinal indications (Crohn's disease and ulcerative colitis), which represented the largest portion of Infliximab patients.
- Rituximab (Rituxan®) initiative implemented in August 2020 with a mandatory switch deadline of February 19, 2021, for the affected indications: rheumatoid arthritis, granulomatosis with polyangiitis, and microscopic polyangiitis and relapsing-remitting multiple sclerosis.

ONTARIO

Reducing administrative burden to manufacturers and pharmacies regulation introduced in early 2020

- Extended the reversal window on Ontario Drug Benefit (ODB) claims.
- Allowed private label products to be designated as interchangeable.
- Facilitated short-term public funding of drugs in response to drug shortages.
- Reconciliation payments from pharmacies saw reduced dispensing fee and mark-up payments for all drug claims made for ODB-eligible members.



UPDATES TO PHARMACISTS' SCOPE OF PRACTICE

Pharmacists' scope of practice was updated to ensure continuity of care for patients during the COVID-19 response, including additional renewal and injection authority.

NEWFOUNDLAND AND LABRADOR

Amendments to regulations under the *Pharmacy Act* came into effect January 31, 2020

- Allowed pharmacists to prescribe vaccines for Hepatitis A, Hepatitis B, Hepatitis A and B, shingles (Herpes Zoster), Human Papillomavirus (HPV) and chicken pox (Varicella Zoster).

NOVA SCOTIA

Nova Scotia College of Pharmacists broadens pharmacists' injection authority

- Allowed pharmacists to inject all drugs administered by intramuscular or subcutaneous injection in patients older than two years.

ONTARIO

Ontario scope of practice expands authority for renewals and injections with minor ailments on the horizon

- Increased from a six months' supply to up to one-year supply.
- Allowed pharmacists to administer influenza vaccines to children aged two and up.
- Ministry of Health is currently reviewing regulatory amendments for minor ailments services.





USING MACHINE LEARNING TO IDENTIFY AREAS FOR INTERVENTION

Express Scripts Canada's proprietary predictive model can predict health behaviours and pave the way for early strategic interventions to help mitigate health outcome barriers such as nonadherence or opioid overuse.

STAGE 1: MEASURE A HEALTH BEHAVIOUR

ESC can measure factors such as adherence by therapeutic class. Visibility into these metrics enables plan sponsors to identify areas of risk.

STAGE 2: UNCOVER THE DRIVERS BEHIND BEHAVIOURS

ESC leverages machine-learning algorithms to track claimant behaviour over time and identify leading risk factors.

STAGE 3: PREDICT FUTURE BEHAVIOUR

The ability to forecast future claimant behaviour provides an opportunity to identify risk and introduce intervention strategies designed to improve health management and outcomes.



IDENTIFYING AT-RISK OPIOID USERS

The opioid crisis continues to be a national emergency, with 17,600 apparent opioid toxicity deaths between January 2016 and June 2020*. ESC’s predictive models can mine claims data to help identify at-risk claimants. This information can then be used to develop tailored strategies and interventions to better manage overall claimant health.

ESC tracked opioid user data for almost two years based on variables such as daily morphine dosage, treatment length and the complexity of patient health conditions.

ESC’s analytical model applies the Daily Morphine Equivalent Dose (MED)** to calculate the cumulative volume of opioids claimed by a member over a single day.

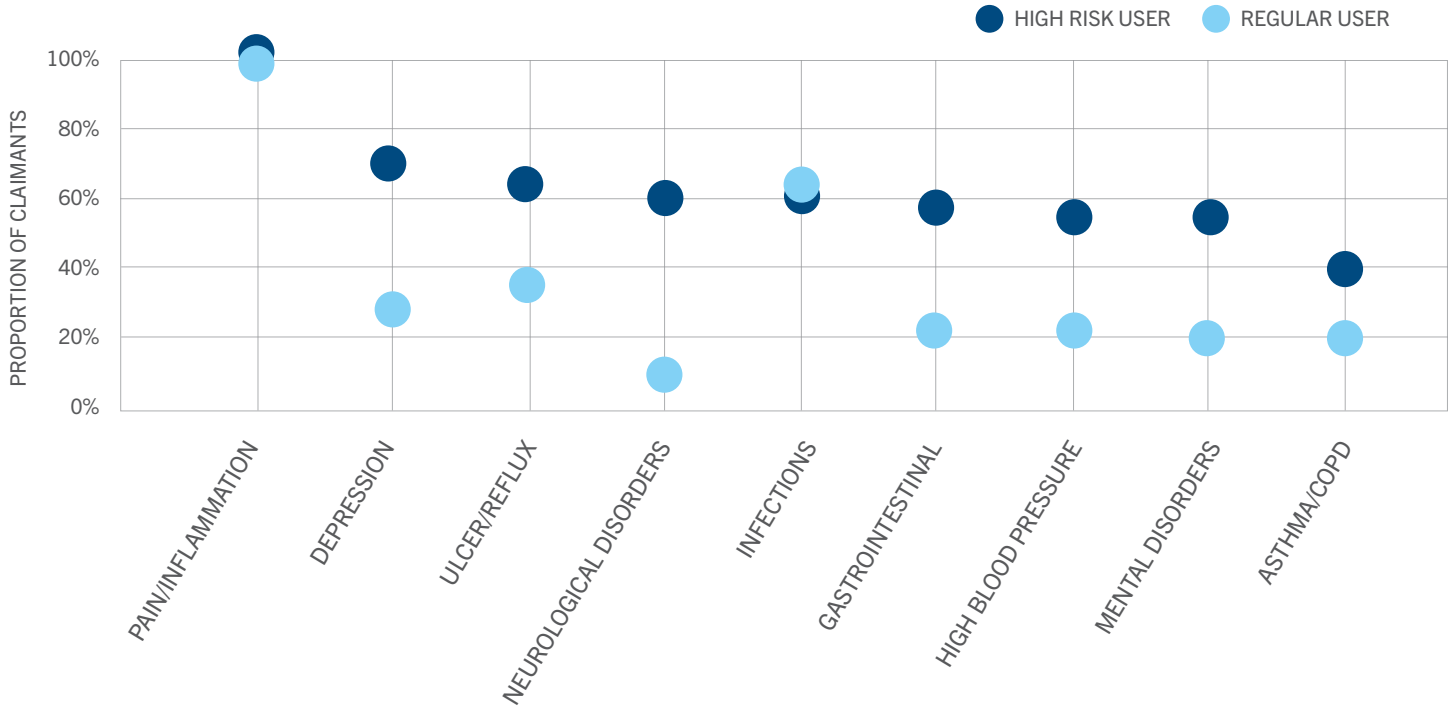
Risk factors: The model identified that male claimants in general, as well as male and female claimants aged 36 years and older, are more likely to be taking a “watchful dose” that might represent cause for concern.

ESC’s predictive model profiled claimants with a watchful dose, revealing that:

- About 25% of claimants who receive doses of over 200 mg MED are considered high risk for opioid-related complications due to their typically significant long history of complex opioid dosage and treatment.
- Among such high-risk users, 70% have more than 200 out of 365 days with a watchful dose
- High-risk users suffer multiple comorbidities: 70% of high-risk opioid users also take medications for depression, 60% have ulcer/reflux and 50% experience high blood pressure.

Conclusion: The unique behaviours and health patterns of early-stage, high-risk opioid users can enable more effective ways to provide interventions that facilitate safer opioid use and reduce long-term opioid impacts.

PREVALENCE OF THERAPEUTIC CLASSES



*Government of Canada, Opioid- and Stimulant-related Harms in Canada, December 2020

**A Daily Morphine Equivalent Dose over 200 mg per day is considered a watchful dose as per the clinical guidelines (https://nationalpaincentre.mcmaster.ca/opioid/cgop_b02_r10.html). There’s a greater likelihood of harm and prescribers are advised to more frequently monitor claimants for complications and efficacy. We found that 2% of opioid users are exceeding this watchful dose threshold.



DETECTING NONADHERENCE TRENDS

Medication adherence is vital to improving health outcomes and is a driver of overall claims volume and, by extension, drug costs.

ESC's predictive model makes early detection of nonadherence possible. By analyzing claims across hundreds of different variables over 12 months, this model predicts whether a claimant will be adherent in the next six months.

Despite the pandemic, adherence rates in 2020 across therapeutic classes were stable. Key findings include:

- More than 50% of Canadians taking medications for chronic conditions, such as high blood pressure and depression, were adherent. Nonadherent claimants for diabetes medications showed longer treatment length compared to adherent claimants.
 - When compared with retail pharmacies, the Express Scripts Canada Pharmacy® had an average 16% increase in medication adherence
- Compared to nonadherent claimants, adherent claimants have significantly more claims with 90 days' supply or greater.
- Treatment length for a chronic condition is a likely indicator to predict claimant adherence.
- About 70% of people with a diabetes claim also filled prescription medications used for hypertension, which helps prevent further complications associated with diabetes, including heart disease as well as damage to the eyes and kidneys.
- Claimants who are adherent to diabetic medications/drugs are also likely to be adherent to high blood pressure and high cholesterol medications.

Conclusion: Adherence is vital for better health. ESC's predictive model pinpoints claimants at risk of nonadherence. This capability allows for more cost-effective and efficient interventions focused on at-risk claimants, rather than a less targeted and potentially more costly broad strategy.

ESC's predictive models provide insight on the current status of claimant health and use advanced analytics to predict their future status. The models:

- Monitor hundreds of factors to track claimant behaviour changes.
- Provide actionable reports to proactively identify claimants who require outreach and further assistance to better manage and improve their health outcomes.

Allow plan sponsors or healthcare providers to apply actionable strategies to better manage overall claimant health.



WHAT TO WATCH

In any given year, some claimants shift from being adherent to nonadherent and vice versa.

- Most Canadians' adherence to diabetes, high blood pressure and high cholesterol medications is expected to be stable or slightly improve by mid-2021 with a 0.1%-3.5% increase by therapeutic class.
- Identifying at-risk claimants and undertaking interventions can improve overall adherence and achieve a stable-state adherence level.
- Such interventions could pave the way to improve health outcomes through targeted engagement of at-risk patients and help prevent long-term complications, potentially lowering overall plan costs.



KEY TAKEAWAYS

1.

OVERALL TREND SAW A 5.4% SPIKE IN 2020, as COVID-19 caused an increase in claims due to days' supply limitations and stockpiling. The timing of COVID-19 vaccinations, implementation and lifting of lockdown restrictions, and whether the healthcare system returns to pre-pandemic capacity levels, are among factors expected to continue influencing trend through 2021.

2.

SPECIALTY DRUGS CONTINUE TO MAKE UP 60% OF THE DEVELOPMENT PIPELINE, with drugs to treat rare disease and cancer the largest contributors. In addition, the overall specialty spend in the more than \$100,000 category was up 23.3% from 2019. The extremely high prices of these breakthrough treatments mean that plan design must be equally innovative to protect plan sustainability.

3.

POTENTIALLY, MORE THAN 100,000 CANADIANS LIVING WITH UNDIAGNOSED CHRONIC DISEASES DID NOT COMMENCE TREATMENT IN 2020 FOR CHRONIC DISEASES, AND COULD SEEK A DIAGNOSIS AND TREATMENT IN 2021 OR BEYOND. This alarming trend is reflected in 2020's significant drop in new claimants for chronic diseases like diabetes, cancer and depression. For these and other conditions, seeking care in the earlier stages likely improves health outcomes and helps decrease the risk of disease progression and related consequences.

4.

THE INCREASED APPROVAL OF BIOSIMILARS IN CANADA is a sign of this category's continuing momentum. Several biosimilars are currently under review by Health Canada. If approved, these medications would further drive savings opportunities for private payors.

5.

ESC'S INNOVATIVE SOLUTIONS include advanced models that can predict member behaviour, and are essential to support the development and implementation of personalized strategies to target members struggling with chronic or complex conditions.





GLOSSARY

Trend	The rate of change in total cost per member, including members who did not make a drug claim. Overall trend is impacted by both how many members make a drug claim and the eligible costs per claim.
Total cost	Eligible claim cost, including the ingredient cost, markup and dispensing fee.
Claimant	Any one individual for whom a claim is reimbursed; this may be the plan member or any one of the plan member's dependants.
Member	A unique individual who is eligible for prescription drug coverage through a health-care benefit plan.



Areas of interest that should be watched.

MEDICATION GROUPINGS

Therapeutic class: A group of medication used to treat the same diseases or conditions.

Specialty drug: Medications 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.

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




Adherence: Medication adherence is calculated using the Proportion of Days Covered (PDC), as measured by the number of days in a given period that a medication is “on hand” and available to the patient.

Nonadherence: An individual is deemed to be nonadherent to a therapy when they have a PDC score of less than 80%. A claimant is determined to be nonadherent to a therapeutic class if they do not adhere to at least one medication in that class.





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