EXPRESS SCRIPTS CANADA®
DRUG TREND REPORT 2016

EXPRESS SCRIPTS®

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EXECUTIVE SUMMARY

In 2016, Express Scripts Canada's analysis of private-plan spending trends once again reflected opposing cost forces. Factors driving an increase in drug spend have outweighed downward pressure on drug costs. At the same time, high-cost drugs and high-cost patients continued to create troubling trend acceleration.

These new medicines offer high cure rates for formerly incurable diseases, transform previously fatal diseases into chronic conditions, and provide a much greater quality of life for many Canadians. But the often staggering costs of these drugs have created unmanageable financial burdens for families and plan sponsors. More and more patients are finding they can't afford the medications their doctors prescribe them. More plan sponsors are limiting employee access to treatment coverage in an attempt to protect plan sustainability without understanding that they have better options.

Parallel to these developments is the ageing of Canada's population and the related increase in chronic diseases. Of greatest concern to private plan sponsors is the rising number of working-age individuals with multiple chronic conditions that require numerous treatments often prescribed by many doctors and specialists without care coordination.

The combined result of these factors is treatment complexity that, without effective intervention, overwhelms plan members and potentially leads to worsening health and more expensive therapies. **These members need expert guidance at key decision points. Sponsors need to implement effective plan management solutions now, before cost increases become insurmountable.**

Over the last three years, these forces—extremely high-cost drugs and the rising number of plan members with multiple chronic conditions—have garnered increasing public attention. For plan sponsors, however, the perception of urgency has been lessened by the corresponding effect of generic pricing.

We are now at a crossroads—the cost impact of patent expiries is slowing, while that of high-cost drugs and patients with multiple chronic conditions continues to accelerate.

NOT EVERY PLAN MEMBER NEEDS CLINICAL GUIDANCE, BUT SOME NEED IT URGENTLY.

Astonishingly, just 14% of plan members account for 72% of total plan spending.

In 2011, members with annual claims of more than $10,000 represented 18.1% of total spending; by 2016, that number had increased by 60%, up to 28.8%.

The evidence shows that individuals with total annual claims between $1,000 and $10,000, and those whose annual claims are over $10,000, need help:

- Making treatment decisions;
- Managing their multiple chronic conditions (an average of 5.9 and 7.3 respectively);
- Coordinating care, provided by an average of 3.4 and 4.5 physicians respectively;
- Managing their many medications, an average of 8.3 and 10.5 respectively.

Innovative solutions are required to help these members make better decisions to manage their overall costs and health.

In this rapidly changing environment, most Canadians simply do not have the clinical knowledge they need to determine which drug is the most cost-effective, clinically appropriate option for their treatment. The difference between the best decision and a suboptimal decision can be tens of thousands of dollars. Express Scripts Canada's research shows that optimizing spending on traditional maintenance drugs through pharmacy services that engage patients and influence better decisions can help fund access to new high-cost drugs.

2016 DRUG TRENDS AT A GLANCE

- **Spending on high-cost specialty drugs (those used to treat complex, chronic conditions such as severe rheumatoid arthritis, hepatitis C and cancer) has grown from 13% of total drug spending in 2007 to 30% in 2016.**
- Tighter plan management and the successful completion of treatment for many hepatitis C Canadian patients moderated the specialty trend to 3.2% in 2016, a welcome respite after years of double-digit increases.
- Excluding hepatitis C medications, however, the specialty category trend was 10.7% in 2016.
- **One out of every five dollars spent on prescription drugs in 2016 paid for medication for diabetes or an inflammatory condition.**
- Trend on inflammatory conditions was 11.7% primarily due to an increase in utilization including expanding indications for high-cost, anti-inflammatory medications.
- The uptake of newer, more expensive diabetes drugs contributed to a trend of 13.7% in this category. **But our analysis also shows that an alarming number of patients were not treated in accordance with the Canadian Diabetes Association's Clinical Practice Guidelines, an example of an opportunity to potentially improve care while lowering costs with tighter plan management.**
- There was also double-digit trend growth on cancer and attention-deficit hyperactivity disorder medications during 2016.
- Biosimilars—drugs that provide alternatives to high-cost biologics that have reached patent expiration—are entering the market, but the associated cost savings is not comparable to that of generic drugs.
- **Cancer treatments dominate the drug development pipeline**, and **a continued shift from hospital-administered drugs (covered by public plans) to self-administered drugs is expected to mean more claims and higher costs in the future.**

SUMMARY

IN THIS COMPLEX ENVIRONMENT, ONLY TIGHTLY MANAGED PLANS CAN PROTECT ACCESS TO TREATMENT AND THE BENEFIT THAT CANADIAN EMPLOYEES VALUE MORE THAN ANY OTHER.

Given the number of challenges each plan member is currently facing, lightly managed plans—those that only react to claims—cannot control rising spending or help members achieve better health. But by focusing their plan management efforts on empowering these members to make more effective, informed decisions, sponsors can protect the long-term sustainability of their drug benefit while supporting better health outcomes for employees and their families.

Tightly managed plans align drug utilization with clinical guidelines, empower members at critical decision points and provide comprehensive care to members with multiple chronic conditions. These plans leverage clinical expertise and data analytics. In addition, they incorporate synergistic management techniques, including formulary, utilization and clinical management tools to provide the best possible patient care at the lowest possible cost.

SECTION **I.**

INSIGHTS INTO PATIENT-SPECIFIC **CHALLENGES AND OPPORTUNITIES**

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SECTION I.

INSIGHTS INTO PATIENT-SPECIFIC CHALLENGES AND OPPORTUNITIES

The issue of rising drug costs dominated the news in 2016, amplified by highly publicized examples of staggering therapy costs and patients who found themselves paying thousands of dollars for medications. With the widespread introduction of new, higher-cost treatment options for many common conditions as well as for rarer diseases, benefit plan members need expert guidance more than ever. **Sponsors need to take swift, definitive action to maintain plan sustainability.**

In the face of increasing complexity and astronomical costs, plan management solutions can provide members with the information and support they need to make the best, most cost-effective decisions for their health.

PATIENT-LEVEL CHALLENGES

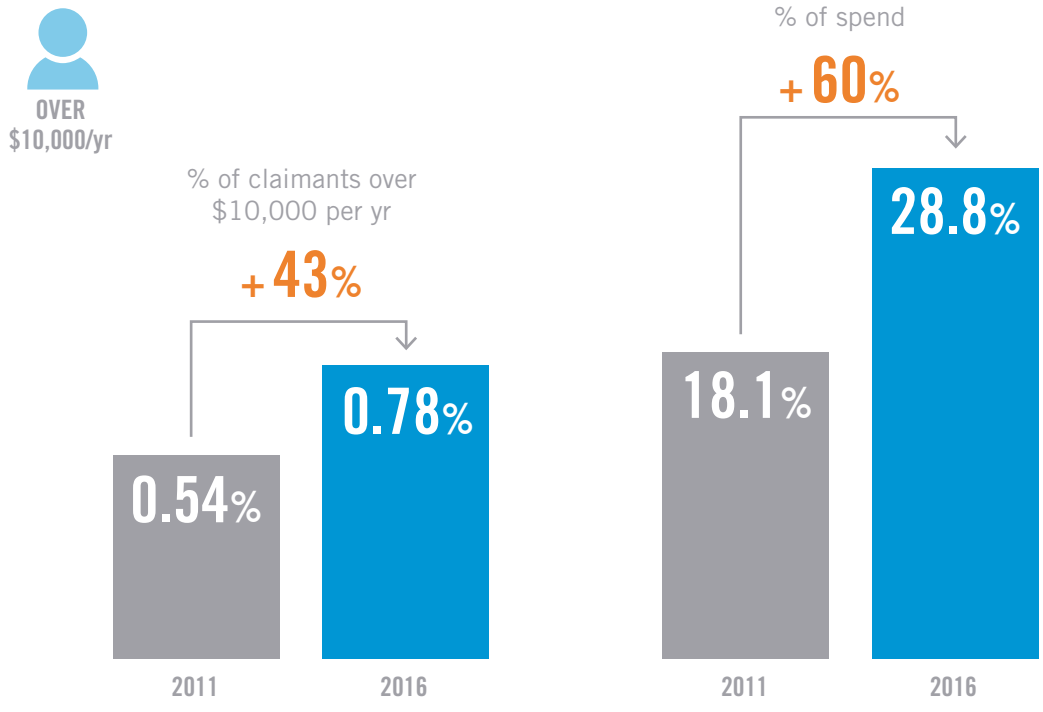
Express Scripts Canada's patient-centric **research reveals key insights into challenges that individuals face in the Canadian drug landscape.**

CHALLENGE 1. THE NUMBER OF HIGH-COST CLAIMANTS IS RISING.

Our extensive research into claim **patterns reveals that the prevalence of high-cost claimants (plan members with annual drug spending of over $10,000 per year) increased by 43% in five years**, from one out of every 185 in 2011 (0.54% of claimants) to one out of every 128 in 2016 (0.78% of claimants). Strikingly, the intensity of spending by these claimants increased at an even higher rate: they represented 18.1% of total spending in 2011 and 28.8% in 2016, an increase of 60%. With this rate of growth, it's obvious that the treatment of these members—who typically require many medications on an ongoing basis to manage their multiple chronic conditions—will drive spending increases for years to come.

INCREASING PREVALENCE IN HIGH-COST CLAIMANTS OVER TIME

Significant increase in number of high-cost claimants and intensity of spend



> IN THE FACE OF INCREASING COMPLEXITY AND ASTRONOMICAL COSTS, PLAN MANAGEMENT SOLUTIONS CAN PROVIDE MEMBERS WITH THE INFORMATION AND SUPPORT THEY NEED TO MAKE THE BEST, MOST COST-EFFECTIVE DECISIONS FOR THEIR HEALTH.

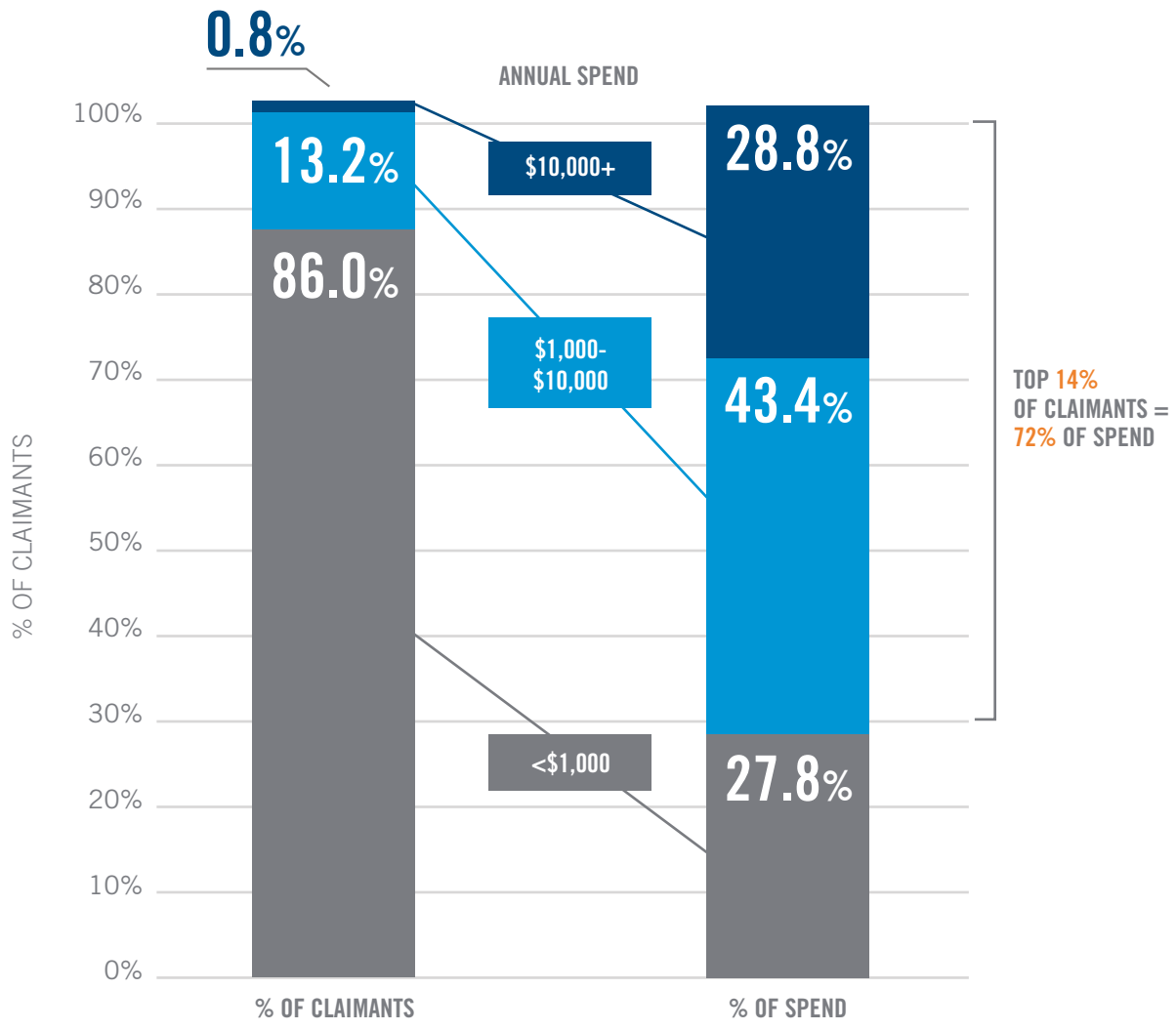
CHALLENGE 2. A SMALL FRACTION OF PLAN MEMBERS CONSUME THE MAJORITY OF PLAN RESOURCES.

Our analytics also identified that 86% of claimants had drug claims of less than $1,000 per year, collectively consuming 27.8% of total plan spending. Another 13.2% had annual drug spending between $1,000 and $10,000, representing 43.4% of total spending.

Remarkably, 14% of claimants account for 72% of total spending. Providing targeted support to these plan members presents the greatest opportunity to capture cost savings while achieving healthier outcomes. By focusing their plan management efforts on equipping these members to make more effective and informed decisions, sponsors can help ensure the long-term sustainability of their drug benefits.

TOP 14% OF CLAIMANTS REPRESENT 72% OF SPEND

Focus efforts on driving better decisions among these claimants



CHALLENGE 3. MEMBERS ARE STRUGGLING WITH GROWING TREATMENT COMPLEXITY AND COSTS.

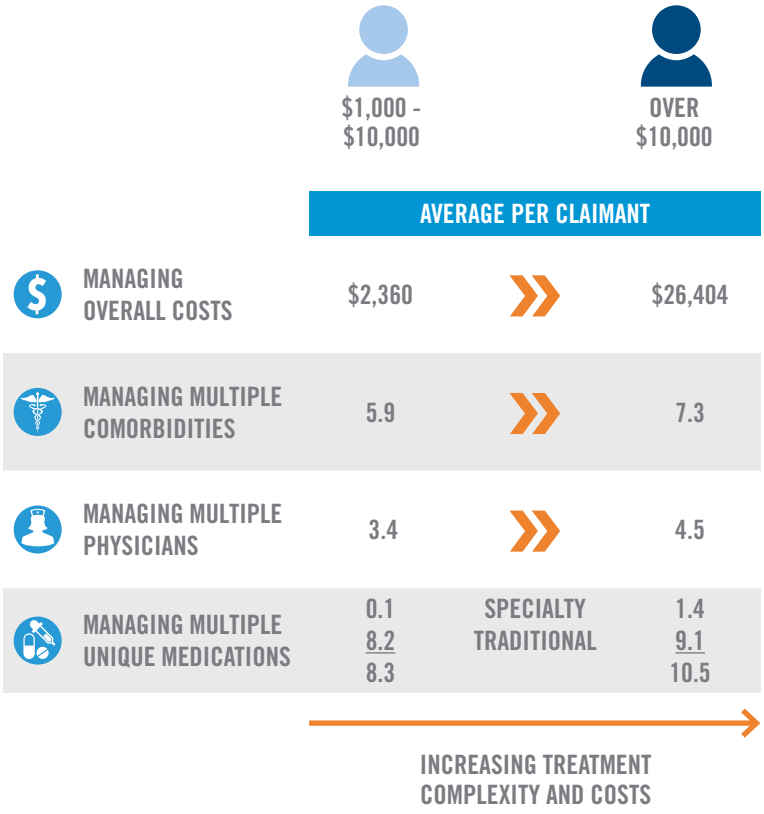
It is clear that members whose total claims are between $1,000 and $10,000 per year, as well as those whose claims are over $10,000 per year, need help:

- Making decisions that can help lower overall costs without lessening treatment effectiveness as their claims average $2,360 and $26,404 respectively;
- Managing their multiple chronic conditions, of which these members suffer from an average of 5.9 and 7.3 respectively;
- Managing the coordination of care provided by multiple physicians, as these patients use an average of 3.4 and 4.5 physicians respectively;
- Managing multiple medications, as they are taking an average of 8.3 and 10.5 medications respectively to manage their overall health. This includes a high number of traditional medications used by patients in both groups (8.2 and 9.1 respectively).

These members face multiple challenges, including disease progression, treatment complexity due to multiple conditions, gaps in care, and uncertainty about drug benefit decisions. Together, the regrettable impact of these challenges on the health of Canadian employees and their families, as well as on rising plan costs, demonstrate the critical need for innovative plan management solutions.

INNOVATIVE SOLUTIONS ARE REQUIRED TO DRIVE BETTER DECISIONS

Help claimants manage their overall costs as well as their care



CHALLENGE 4. MEMBERS LACK THE CLINICAL GUIDANCE THEY NEED.

Within a complex, rapidly changing pharmaceutical treatment landscape, typical Canadians do not have the clinical knowledge required to determine which drug is the most cost-effective, clinically appropriate option for their treatment. When a member suffers from multiple chronic conditions, these decisions become even more difficult as factors such as drug interactions and adverse event profiles must be considered. It is obvious that holistic, accessible clinical guidance—provided at the right time—is essential. This is evident through the following patient case studies, identified through our claims analyses.

PATIENT CASE STUDY 1. Tom suffers from six chronic conditions, including depression, high cholesterol, sleep issues, benign prostatic hyperplasia, high blood pressure, and diabetes. He requires 10 different medications in total. In 2016, Tom's annual drug claims totalled $8,084, including $7,169 in diabetes treatment alone. Through an analysis of his claims and a clinical pharmacist evaluation of his medication use, it becomes clear that Tom needs clinical guidance to optimize his therapies.

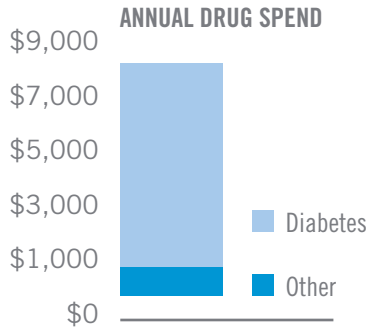
For example, Tom used five different diabetic medications in 2016, illustrating that his blood glucose (blood sugar) levels are not well controlled and that he requires education on both diabetes and drug management. Clinical guidance can help empower Tom to better manage his blood glucose and modify his lifestyle to slow the progression of his diabetes. Even more importantly, it can help him prevent diabetes-related complications such as kidney failure and nerve damage potentially leading to amputation.

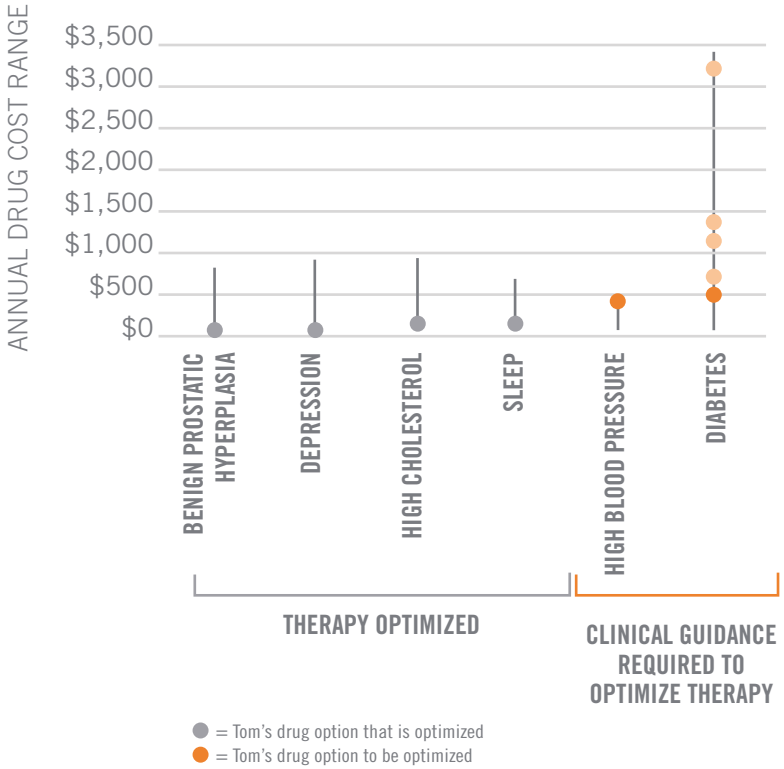
In addition, Tom needs help to optimize his high blood pressure therapy. He is using a relatively expensive blood pressure medication (Coversyl®) with an annual cost of $444.32. With the wide range of therapeutic alternatives available for blood pressure, cost savings may be possible while maintaining blood pressure targets.

CHRONIC CARE CLAIMANTS NEED HELP TO OPTIMIZE THERAPIES

Engaging and empowering patients with multiple conditions is essential

TOM FROM NOVA SCOTIA (MAINTENANCE)
6 chronic conditions
10 chronic drugs
6 physicians





PATIENT CASE STUDY 2. May is a 55-year-old patient from Ontario who suffers from four chronic conditions, including inflammatory bowel disease, for which she is prescribed the costly specialty drug Humira. Claims data revealed that she is taking nine maintenance medications, including Humira, and had prescriptions from three physicians in 2016. With many physicians and fragmented health records, it is unlikely that May is receiving consistent, holistic care.

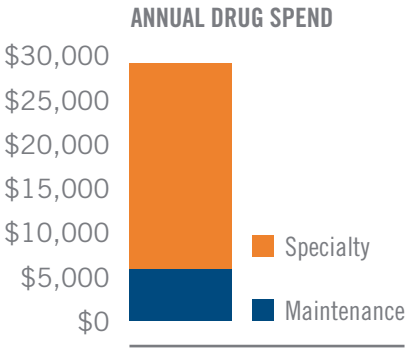
Clinical evaluation of May's claims data shows that her Humira use appears appropriate, but there are opportunities to provide clinical guidance to optimize her other therapies for depression, hormone replacement and bladder pain syndrome. For example, she is using three different medications for hormone replacement therapy (two of which are higher-cost brands) and there are opportunities to simplify her regimen.

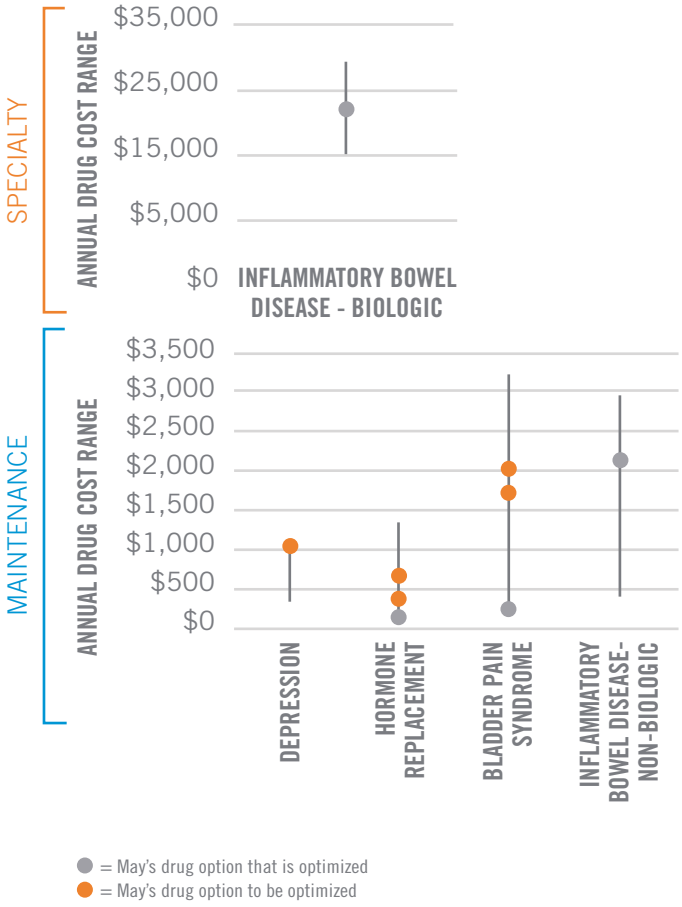
Through a collaboration with May and her prescribers, therapy optimization can lead to greater convenience for May while helping to protect her from adverse drug events, stay on track with her doctors' treatment instructions, lower overall costs for her and her plan, and achieve the best possible health outcomes.

SPECIALTY CLAIMANTS NEED HELP TO MANAGE COMORBIDITIES

Holistic care is critical to achieve optimal clinical outcomes

MAY FROM ONTARIO (SPECIALTY)
4 chronic conditions
9 chronic drugs
3 physicians





> “...14% OF CLAIMANTS ACCOUNT FOR 72% OF TOTAL SPENDING. PROVIDING TARGETED SUPPORT TO THESE PLAN MEMBERS PRESENTS THE GREATEST OPPORTUNITY TO CAPTURE COST SAVINGS WHILE ACHIEVING HEALTHIER OUTCOMES.”

SOLUTIONS: BENDING THE CURVE ON DRUG SPENDING AND SUBOPTIMAL TREATMENT

Balancing drug coverage access and costs is a challenge for every plan sponsor, given the increasing volume of therapeutic options available and the vast number of conditions those medications treat. This growing complexity demands a proactive response—plan sponsors can bend the curve on drug spending and suboptimal treatment by leveraging plan solutions that engage members to equip them to make informed, effective decisions. These solutions can ensure plan sustainability while contributing to optimum employee health and well-being.

LIGHTLY MANAGED PLANS will face the largest increase moving forward. These plans have some pricing and utilization controls in place, but tend to react to claims rather than driving better decisions. Many cover 100% of medication costs, meaning that members have no reason to pay attention to the cost of their treatments and may not even be aware of the value of their benefit.

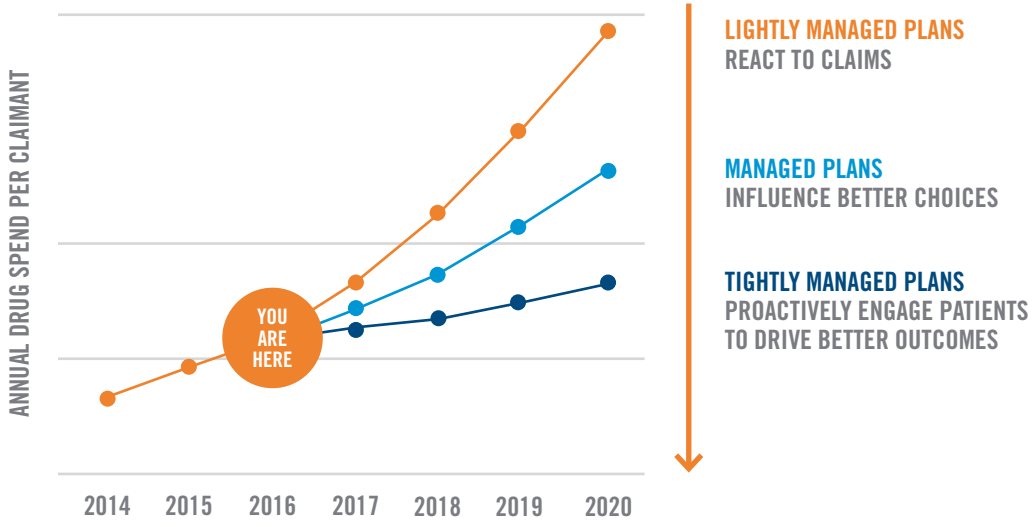
MANAGED PLANS will face a slightly lower increase moving forward. These plans attempt to influence better choices through benefit management tools such as dispensing fee caps and generic substitution rules. In addition, these plans create alignment by requiring the member to pay a portion of the cost of each prescription, in an attempt to create awareness of costs and influence better choices. However, this does not always result in action, as human beings are hard-wired for inattention and inertia.

TIGHTLY MANAGED PLANS that proactively engage members in order to drive optimum outcomes will be more successful at bending the curve on drug spending. These plans leverage clinical expertise and data analytics to identify opportunities at the patient level. In addition, these plans incorporate multiple plan management techniques, including formulary management tools, utilization management tools and clinical management tools, to provide the best possible patient care at the lowest possible cost. Tightly managed plans effectively engage patients and help them implement decisions that can ensure sustainability of the drug benefit. Multiple tools are available for plan sponsors to tightly manage their plans and drive better member decisions. Examples include:

- Ensuring drug utilization is aligned with clinical guidelines to achieve healthier outcomes and lower costs;
- Engaging members at critical decision points to optimize use of lower-cost, clinically effective treatment alternatives;
- Providing comprehensive care to members with multiple chronic conditions to drive better care and lower costs.

TIGHTLY MANAGED PLANS CAN BEND THE CURVE ON DRUG SPENDING

Engage patients and influence better choices to ensure sustainability



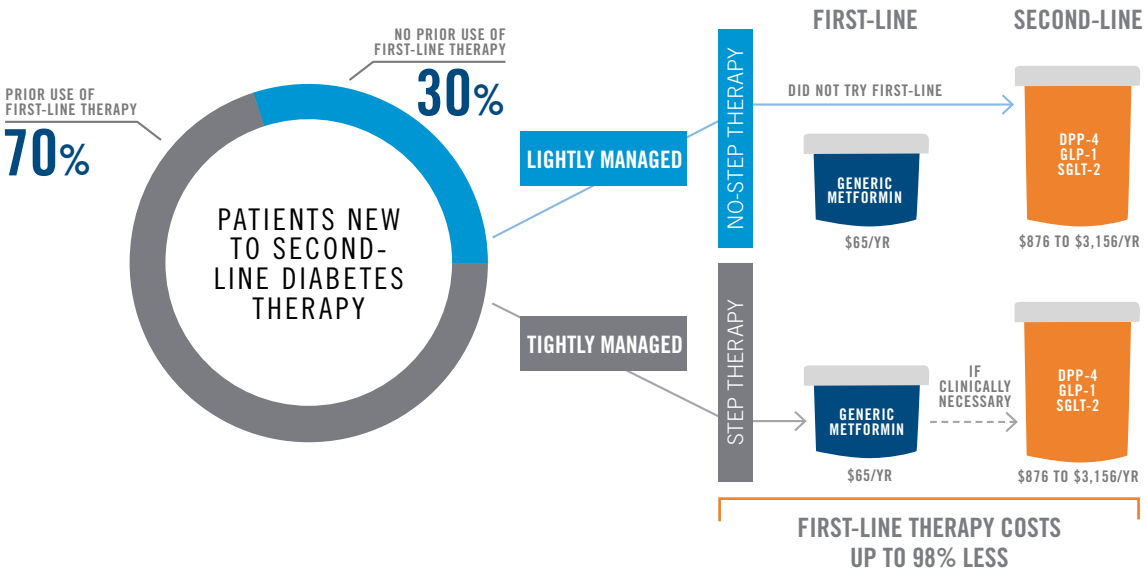
CASE STUDY 1. TIGHTLY MANAGED PLANS ALIGN DRUG UTILIZATION WITH CLINICAL GUIDELINES TO ACHIEVE HEALTHIER OUTCOMES AND LOWER COSTS.
Our retrospective claims analyses demonstrate that there are many instances when prescribing and dispensing practices do not appear to align with clinical guidelines. Taking treatment for diabetes as an example, our research showed that 30% of the patients who were new to a second-line therapy in 2015 had not first been prescribed metformin, the first-line treatment recommended by the Canadian Diabetes Association Clinical Practice Guidelines. According to the guidelines, second-line therapies such as dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like-peptide 1 (GLP-1) agonists, or sodium-glucose cotransporter 2 (SGLT-2) inhibitors may be beneficial if the glycemic target is not met by metformin alone.

A tightly managed plan that uses a step therapy approach can ensure patients begin diabetes treatment with first-line therapy while covering the use of second-line therapy, if clinically necessary. Patients are guided to first use metformin, which is highly effective, well tolerated, and has good long-term safety data. This can drive significant savings for both plan and patient, as the annual therapy cost of metformin is 92% to 98% less than these new second-line therapies.

For the many Canadians with diabetes who struggle to pay even their copayment on treatments and supplies, this approach also makes it more easy to keep them on track with their doctors' instructions, possibly preventing severe long-term complications such as cardiovascular diseases.

TIGHTLY MANAGED PLANS ENSURE PATIENTS BEGIN WITH FIRST-LINE THERAPY

Aligning with clinical guidelines lowers costs with healthier outcomes



> “...BEND THE CURVE ON DRUG SPENDING AND SUBOPTIMAL TREATMENT BY LEVERAGING PLAN SOLUTIONS THAT ENGAGE MEMBERS TO EQUIP THEM TO MAKE INFORMED, EFFECTIVE DECISIONS.”

CASE STUDY 2. TIGHTLY MANAGED PLANS ENGAGE MEMBERS AT CRITICAL DECISION POINTS TO OPTIMIZE USE OF LOWER-COST, CLINICALLY EFFECTIVE ALTERNATIVES.

With multiple drug options available for treatment of any given chronic condition, patients with a tightly managed plan benefit from a clinical expertise that guides them in making better drug choices and helps them implement those choices in collaboration with prescribers.

Jeremy is a 57-year-old man from Nova Scotia whose drug claims are adjudicated by Express Scripts Canada. Claims data reveals that he is currently using three medications to manage a gastric ulcer and high blood pressure. As part of a tightly managed plan, our claims analytics and clinical expertise would identify the opportunity to use lower-cost, effective alternatives that could result in annual cost savings of $824, 86% of Jeremy's annual drug spending.

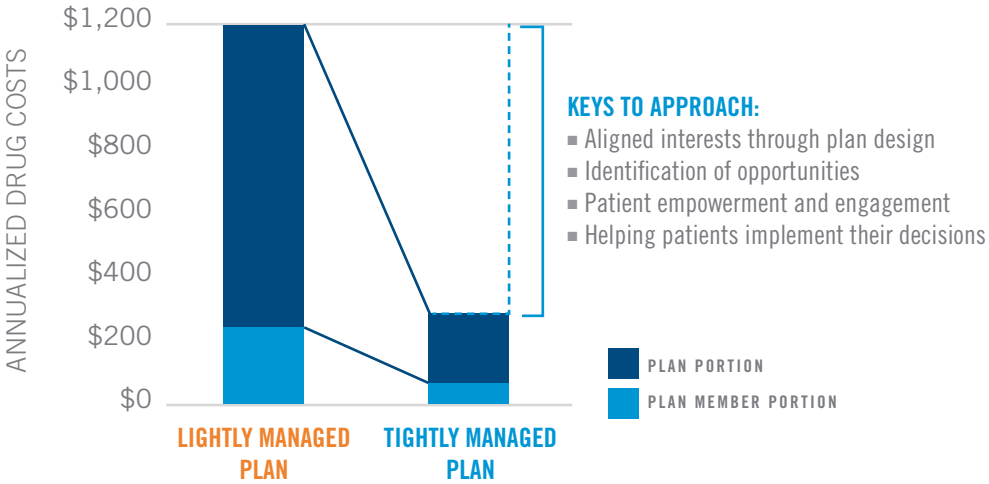
The dedicated pharmacy team would proactively engage Jeremy to advise him about the options and, with his permission, would then communicate the opportunity to Jeremy's prescribing physician. Once the physician agrees with the recommendation, the pharmacist would request the new prescription, successfully executing the best drug choice.

Through data analytics, clinical expertise and patient engagement, patients like Jeremy are empowered to make better treatment choices—and pharmacy solutions that assist in implementing these choices translate this empowerment into lower costs and healthier outcomes.

TIGHTLY MANAGED PLANS DRIVE BETTER DRUG CHOICES

Engage patients to optimize use of lower-cost, clinically effective alternatives

57-YEAR-OLD
FROM NOVA SCOTIA
WITH ULCER
AND HIGH BLOOD
PRESSURE MEDICATIONS



KEYS TO APPROACH:

- Aligned interests through plan design
- Identification of opportunities
- Patient empowerment and engagement
- Helping patients implement their decisions

CASE STUDY 3. TIGHTLY MANAGED PLANS PROVIDE COMPREHENSIVE CARE TO MEMBERS WITH MULTIPLE CHRONIC CONDITIONS, RESULTING IN BETTER CARE AS WELL AS LOWER COSTS.

Transitioning from a lightly managed plan to a tightly managed plan can lead to dramatic improvements in health and financial outcomes for a member with multiple chronic conditions. Tightly managed plans are much more effective at four key components of chronic care: utilization management, reimbursement navigation, dispensing, and ongoing counselling.

Darlene is a 41-year-old woman from Ontario who was recently diagnosed with Hepatitis c, for which she was prescribed a 12-week treatment with Epclusa. She is also taking medication for depression, insomnia and hypertension.

UTILIZATION MANAGEMENT APPROACH

Under a lightly managed plan, electronic adjudication controls simply react to claims. In the case of a prior authorization request, the plan would most likely approve the Epclusa claim based on the prescriber's request, without asking additional questions to validate Darlene's medical condition and medication status.

With a tightly managed plan, the plan manager would proactively reach out to Darlene to help her understand her drug coverage and pharmacy support. If her plan had a prior authorization program in place, it would include more robust clinical criteria that would look at her current and past medical and medication profile to ensure that Epclusa is the best drug for her individual care. The prior authorization manager would determine if Darlene could switch to a lower-cost alternative, such as an eight-week Harvoni treatment. If clinically appropriate, the prior authorization team would collaborate with her prescriber to discuss the options, potentially leading to savings of $18,000.

In addition, a comprehensive medication review would be done to assess therapy optimization opportunities for all Darlene's current therapies including her depression, insomnia, and hypertension medications.

INTRODUCE A REIMBURSEMENT NAVIGATION APPROACH

With a lightly managed plan, Darlene would not receive reimbursement guidance unless she voices her financial burden and cries for help.

A tightly managed plan, on the other hand, would offer proactive guidance to Darlene and would seek additional funding sources to lower the cost burden for both Darlene and her employer. Since both Harvoni and Epclusa are covered by the Ontario Drug Benefits Program, the reimbursement advisor would guide Darlene to apply for the provincial reimbursement, which could lead to overall savings of $27,000.

DISPENSING APPROACH

A lightly managed plan has no special protocol for dispensing specialty medications, so members receive only general medication counselling and there are few controls to help members and employers manage sometimes astronomical prescription costs.

With a tightly managed plan, a specialized pharmacist would provide holistic patient care and create a personalized health action plan to address Darlene's medical needs. Specialized clinical management would ensure she thoroughly understands how to manage her new Hepatitis c medication along with her other chronic drugs, and knows how to maximize the clinical benefits from this new, short-term, high-cost therapy to prevent relapse and the need for further treatment.

Further, a tightly managed plan would incorporate cost controls to avoid excessive pharmacy markup on such high-cost medications, which could generate another $4,000 in savings in Darlene's case.

ONGOING COUNSELLING APPROACH

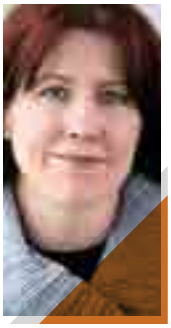
With the lightly managed plan, beyond the counselling provided by dispensing pharmacists, this passive approach means that clinical support may be provided only when Darlene makes a special request.

With a tightly managed plan, however, ongoing clinical monitoring and therapy-specific care would help Darlene manage her treatment for chronic and acute conditions. With her multiple medications, this holistic approach to care is critical to avoid drug interactions that could otherwise affect clinical outcomes as well as Darlene's quality of life today and in the future.

As the goal of Hepatitis c therapy is to reach a cure, a specialized pharmacist would provide proactive, ongoing clinical follow-ups to help Darlene manage her side effects and stay on track with her doctor's instructions, to achieve an optimum treatment outcome. This can also help ensure the drug is not wasted, requiring the patient to begin another costly course of treatment.

TIGHTLY MANAGED PLANS DRIVE BETTER CARE AND LOWER COSTS

Holistic specialty pharmacy program can optimize financial and health outcomes



41-YEAR-OLD FROM ONTARIO WITH HEPATITIS C (EPCLUSA 12 WKS = $65K) ALSO USING DEPRESSION, INSOMNIA, AND HYPERTENSION MEDICATIONS.

	LIGHTLY MANAGED	TIGHTLY MANAGED		BETTER CARE & LOWER COSTS
UTILIZATION MANAGEMENT	▪ React to claim ▪ Approve PA as per MD request	▪ Proactive outreach to patient ▪ Therapy optimization across all medications ▪ Robust PA criteria	»	Optimize therapy and reduce waste including switch to Harvoni 8 wks **($18K savings)**
REIMBURSEMENT NAVIGATION	▪ If/when patient requests it	▪ Help patient enroll with provincial program	»	Coordinate with Trillium **($27K savings)**
DISPENSING	▪ Fragmented care ▪ General counselling ▪ Few controls on cost	▪ Holistic approach to care ▪ Personalized health action plan ▪ Specialized clinical mgmt ▪ Cost controls on markup	»	More holistic patient care and tighter cost controls **($4K markup savings)**
ONGOING COUNSELLING	▪ Passive approach	▪ Ongoing clinical monitoring and therapy-specific care ▪ Side effect management to drive better adherence	»	**Healthier outcomes** Ensures drug is not wasted

SUMMARY

Given the number of challenges each plan member currently faces, it's clear that innovative solutions are required to maintain affordability and improve care. **Lightly managed plans that react to claims provide little value and are inadequate to control rising drug spending.** Tightly managed plans that leverage data analytics and clinical and behavioral expertise to empower members are critical to achieve optimal financial and health outcomes.

SECTION **II.**

A LOOK AT THE OVERALL **DRUG TREND FOR 2016**

PAGES 19 – 40

SECTION II.

A LOOK AT THE OVERALL DRUG TREND FOR 2016

A NOTE ABOUT TREND: ONE WORD, TWO APPROACHES…

Express Scripts Canada's drug trend analysis is based on a ***retrospective*** or historical methodology—a look back at the past. In this way, it differs from an insurance carrier's health plan premium increase, which is based on a ***prospective*** methodology—using data trends to anticipate future costs.

The Express Scripts Canada methodology also incorporates:

- A drug plan's specific claims experience;
- Changes in proportion of eligible members with a claim;
- Demographic changes;
- Anticipated changes in the future mix of drugs;
- Any erosion of member contributions;
- A risk component;
- Other health plan claims experience.

As a result, Express Scripts Canada's trend factor will typically be lower than an insurance carrier's predicted average increase for extended health care plans, of which prescription drugs are only one component.

TERMINOLOGY USED IN THIS REPORT

BIOSIMILARS: Health Canada defines a biosimilar as a biologic drug that enters the market after a version previously authorized in Canada, with demonstrated similarity to the original biologic drug.

COST ALLOWABLE: The amount of a prescription's total price that is allowable by the member's plan. The cost allowable does not exclude member cost share.

DRUG TREND: The historical increase in allowable cost per claimant over the previous year.

PLAN MEMBER, CLAIMANT: Each unique person who submits a prescription claim, including all dependents that are eligible for coverage.

SPECIALTY DRUGS: Medications used to treat chronic, complex conditions such as severe rheumatoid arthritis, multiple sclerosis and cancer. Specialty drugs are usually costly, require special storage and handling, need intensive clinical monitoring, and require frequent dosing adjustment.

SPENDING: Total payer cost allowable comprised of claims for a particular drug, category or therapy class during the year.

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

OVERALL TREND IN 2016

To empower private plan sponsors with the information they need to preserve treatment access while protecting plan sustainability, Express Scripts Canada analyzes traditional and specialty drug trends each year.

The overall drug trend reflects two factors: utilization (the number of prescriptions per plan member) and cost per prescription (the total cost allowable per claim).

Private plan spending increased again in 2016, continuing a trend that has seen overall drug spending in Canada double since 2000. Nationally, the average annual drug spending per member increased by 2.9% in 2016 to $840.52, slightly less than the 2015 spending increase of 3.9%. The 2016 increase was composed of a 2.8% increase in spending for traditional medications and an increase of 3.2% in spending for specialty medications.

Components of Trend

		TREND		
	COST PER CLAIMANT	UTILIZATION	COST	TOTAL
TRADITIONAL	$588.50	1.1%	1.7%	2.8%
SPECIALTY	$252.00	9.7%	-6.5%	3.2%
TOTAL OVERALL	$840.50	1.3%	1.6%	2.9%

January-December 2016 compared to the same period in 2015

> PRIVATE PLAN SPENDING INCREASED AGAIN IN 2016, CONTINUING A TREND THAT HAS SEEN OVERALL DRUG SPENDING IN CANADA DOUBLE SINCE 2000.

TRADITIONAL 2016 TREND OVERVIEW

Traditional drugs, defined as those used to treat common chronic medical conditions, made up 97.9% of the total number of claims in 2016. From a spending perspective, traditional drugs accounted for 69.9% of the 2016 total, down slightly from 70.1% in 2015.

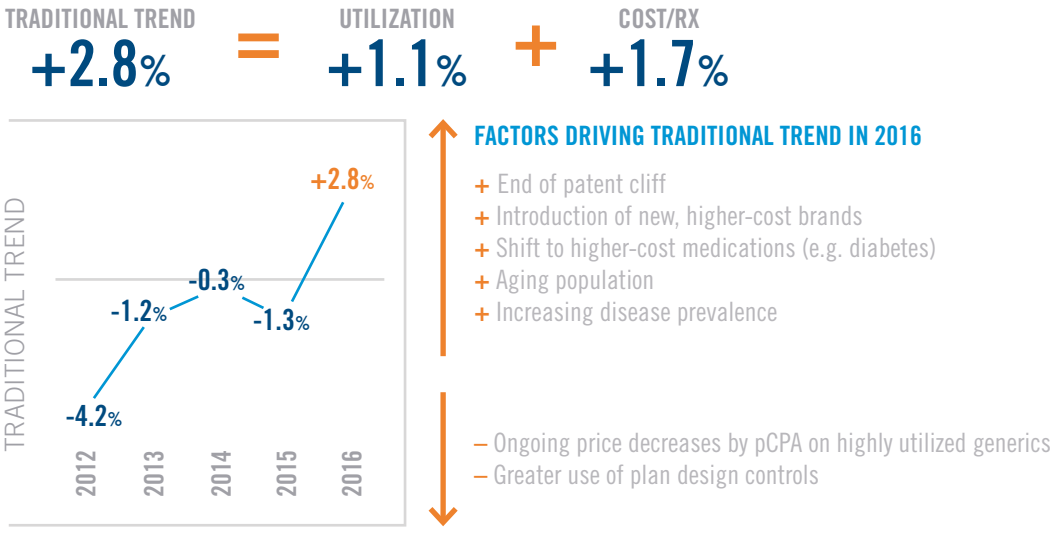
Over the past several years, the intensity of spending increases in this category has eased, primarily due to declining costs per prescription as patents expired on many widely used brand drugs. However, there is evidence that the cost benefits from the introduction of alternative lower-price generics have now been almost fully realized.

As the benefits of the "patent cliff" trend come to an end, new high-cost drugs for common conditions such as diabetes, epilepsy, schizophrenia, and high cholesterol have been introduced, resulting in a greater spending increase in this category in 2016. Despite lower generic prices resulting from the ongoing negotiations of the pan-Canadian Pharmaceutical Alliance (pCPA), and wider use of generics, the overall cost per traditional prescription increased by 1.7% in 2016. This compares to a decline of 1.3% in 2015, and this mounting price pressure is expected to continue over the next several years.

The utilization of traditional prescription medications increased by 1.1% in 2016, compared to an almost flat trend (0.03%) in 2015. Our analyses also revealed that the average number of claims per member increased to 13.12 in 2016 from 12.96 in 2015. Among the top 30 medications, year-over-year utilization has significantly increased for Vyvanse® in the treatment of attention-deficit disorder, Janumet® and Invokana® in the treatment of diabetes, Abilify® in the treatment of mental disorders, and Dexilant® in the treatment of gastric ulcers. Overall, increasing prescription drug use is driven by the introduction of new treatment options, increasing disease prevalence and disease progression among an aging population.

TRADITIONAL DRUG TREND ACCELERATES IN 2016

Upward factors outweigh downward pressure on traditional drug spend



SPECIALTY 2016 TREND OVERVIEW

Specialty drug spending has grown from 13% of total drug spending in 2007 to 30% of total spending in 2016. Specialty drugs are those used to treat complex, chronic conditions such as severe-stage rheumatoid arthritis, hepatitis C and cancer. Often costly and complex to administer, specialty drugs usually require special storage and handling and are less frequently prescribed. Patients treated with specialty drugs often require frequent dosing adjustments and intensive clinical monitoring. While specialty medications represented just 2.1% of total claims, they made up just over 30% of total drug spending.

Over the last couple of years, the alarming double-digit annual growth rate of specialty drug spending has created tremendous concern about the sustainability of benefit plans. A trend increase of a much more moderate 3.2% in 2016 was a welcome respite: while the use of specialty medications grew by 9.7%, the cost per specialty prescription declined by 6.5%. This decrease was caused by the adoption of multiple strategies implemented to combat specialty spending growth, including changes to the drug review process, increased provincial integration, product listing agreements, more robust prior authorization criteria, and specialty pharmacy preferred-provider networks.

The decrease in cost per specialty prescription was also heavily influenced by the completion of treatment of the initial wave of hepatitis C patients in 2016 as spending on hepatitis C medications fell dramatically.

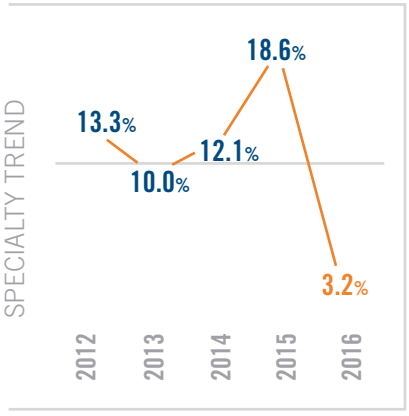
Excluding hepatitis C medications, the specialty category trend continued to grow by double digits, with a 10.7% increase in 2016. This trend was driven by an 11.1% increase in the utilization of other specialty medications, which was partially mitigated by a 0.4% decrease in the cost per prescription resulting from increased adoption of plan management controls. Increasing use of other specialty medications, along with rising disease prevalence and treatment availability, will continue to drive spending increases. This highlights the continued, urgent need to tightly manage plans to maintain sustainability.

	TREND		
	UTILIZATION	COST	TOTAL
SPECIALTY INCLUDING HEPATITIS C	9.7%	-6.5%	3.2%
SPECIALTY EXCLUDING HEPATITIS C	11.1%	-0.4%	10.7%

SPECIALTY TREND MITIGATED BY DECREASE IN COST PER SCRIPT

Dramatic decline in specialty growth rate driven by end of initial hepatitis C bubble

SPECIALTY TREND **+3.2%** = UTILIZATION **+9.7%** + COST/RX **-6.5%**



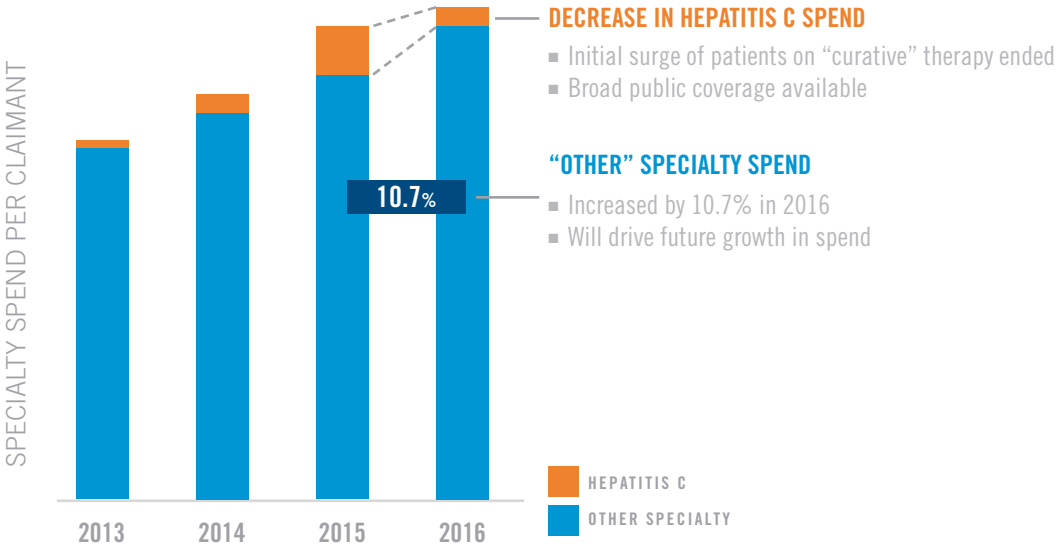
FACTORS MITIGATING SPECIALTY TREND IN 2016

+ Increasing prevalence
+ New high-cost specialty medications
+ New indication approvals

– Higher adoption of plan controls
  - Changes to drug review process
  - More robust PA criteria
  - Increased provincial integration
  - Product listing agreements
  - Specialty pharmacy PPNs
– End of initial hepatitis C bubble (accounted for a 5.3% reduction in overall cost per specialty rx)

DOUBLE-DIGIT SPECIALTY TREND CONTINUED OUTSIDE OF HEPATITIS C BUBBLE

"Other" chronic specialty medications will drive future increase in trend



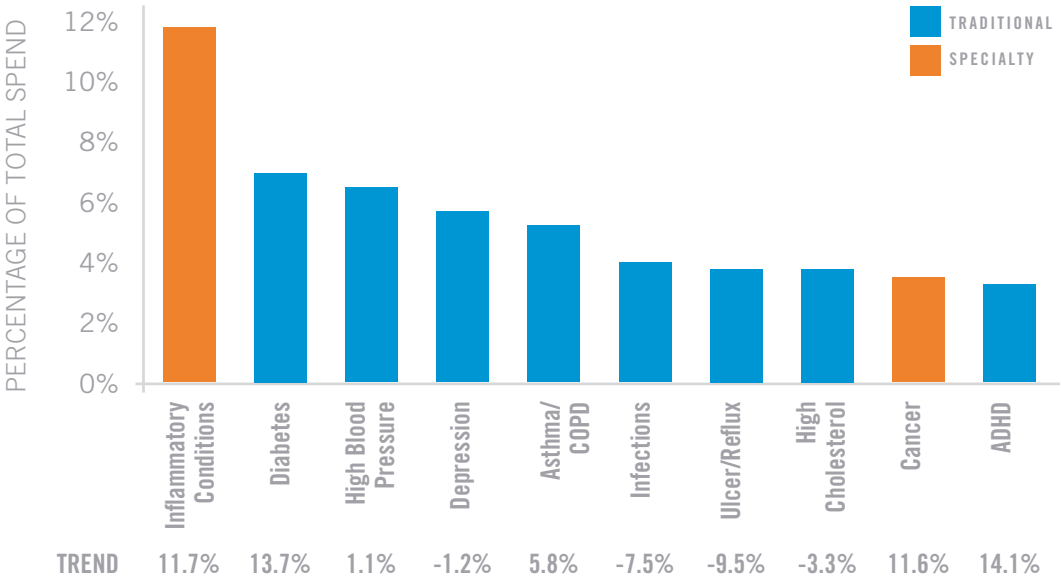
TOP 10 THERAPY CLASSES

One in every five dollars spent on prescription drugs in 2016 paid for medication for an inflammatory condition or diabetes. Spending on treatment for these two conditions increased in 2016 by 11.7% and 13.7% respectively. There was also double-digit growth in spending on cancer and attention-deficit hyperactive disorder medications during 2016.

Moving forward, a mix of traditional and specialty therapy classes will continue to put upward pressure on overall spending.

DOUBLE-DIGIT TREND SEEN AMONG TOP 10 CLASSES

Key traditional and specialty classes drive upward pressure on overall spending



TOP 10 MEDICATIONS BY SPENDING

Specialty medications that treat inflammatory conditions, including infliximab (Remicade®; Inflectra®) and adalimumab (Humira®), continue to make up the largest portion of overall spending. At the opposite end of the spectrum, Harvoni®, a specialty medication used to treat hepatitis C, ranked third in overall spending in 2015 and dropped to 50th in 2016.

Traditional medications that treat high cholesterol, ulcer/reflux, depression and diabetes continue to represent a significant portion of overall spending. In addition, it is interesting to note that the **attention-deficit disorder drug methylphenidate (Concerta, Biphentin) increased from number nine in terms of overall spending in 2015 to number four in 2016.**

FURTHER INSIGHTS ARE OUTLINED IN THE FOLLOWING THERAPY CLASS SECTION.

CHEMICAL	COMMON INDICATION	CATEGORY*	% OF TOTAL SCRIPTS	RANK BY SCRIPT	% OF TOTAL SPEND	RANK BY SPEND
Infliximab	Inflammatory Conditions	S	0.06%	303	4.48%	1
Adalimumab	Inflammatory Conditions	S	0.10%	216	3.33%	2
Rosuvastatin	High Cholesterol	T	2.80%	2	1.52%	3
Methylphenidate HCl	Attention-Deficit Disorder	T	1.01%	17	1.45%	4
Etanercept	Inflammatory Conditions	S	0.04%	335	1.36%	5
Atorvastatin	High Cholesterol	T	2.18%	3	1.29%	6
Esomeprazole	Ulcer / Reflux	T	0.72%	29	1.26%	7
Duloxetine	Depression & Pain	T	0.56%	38	1.01%	8
Escitalopram oxalate	Depression	T	1.15%	13	0.99%	9
Insulin glargine	Diabetes	T	0.36%	72	0.98%	10

*S = Specialty; T = Traditional

> MOVING FORWARD, A MIX OF TRADITIONAL AND SPECIALTY THERAPY CLASSES WILL CONTINUE TO PUT UPWARD PRESSURE ON OVERALL SPENDING.

TOP 10 THERAPY CLASSES AND INSIGHTS

1. INFLAMMATORY CONDITIONS

Drugs used to treat inflammatory conditions continue to account for the largest portion of spending. This specialty class includes medications used for a variety of diseases, including musculoskeletal diseases such as rheumatoid arthritis and ankylosing spondylitis, skin diseases such as psoriasis and psoriatic arthritis (which also has musculoskeletal symptoms), gastrointestinal diseases such as ulcerative colitis and Crohn's disease, and even eye diseases such as non-infectious uveitis. Many of these drugs have multiple indications for multiple inflammatory diseases, such as those listed above.

Given their anti-inflammatory effects, there has been a broadening of use for some of these drugs, which may increase overall utilization. In 2016, for example, Humira® (adalimumab) received approval for use for two new indications—hidradenitis suppurativa (an inflammatory skin condition) and non-infectious uveitis (inflammation of some of the tissues of the eye).

This therapy class, number one in drug spending in 2016, held the same place in 2015. The top three drugs in this class are:

- infliximab [Remicade®; Inflectra®];
- adalimumab [Humira®];
- etanercept [Enbrel®; Brenzys™].

Inflectra, which is a lower-cost alternative to Remicade, was the first biosimilar approved in this class. As the first such product available, its use has taken some time to develop. Initially approved in 2014, public plans did not regularly channel infliximab users to the biosimilar until 2016. More recently, provinces like Ontario and Quebec have moved to delist Remicade from its provincial formulary in favour of Inflectra.

The second biosimilar to be approved in this class in 2016 was Brenzys, the biosimilar for the reference biologic Enbrel.

Another possible reason the uptake of these lower-cost alternatives has been slower than expected is that, when these biosimilars are first approved, they have not been approved for all of the indications approved for the reference biologic. Inflectra received approval for the remaining indications to align with Remicade in 2016. Similarly, Brenzys was approved only for rheumatoid arthritis and ankylosing spondylitis, but not for polyarticular juvenile idiopathic arthritis, psoriatic arthritis or plaque psoriasis, for which Enbrel is indicated.

A new biologic, Taltz™ (ixekizumab), was approved in 2016 for use in plaque psoriasis. It has the same pharmacologic mechanism of action as Cosentyx® (secukinumab), as well as a similar cost, and is expected to occupy the same place in therapy.

While the majority of the drugs used in this category are biologics, two significant small-molecule (i.e., non-biologic) drugs were approved in 2014: Xeljanz™ (tofacitinib, ranked 11th by spending) and Otezla® (apremilast, 9th). They have limited indications, with Xeljanz indicated only for rheumatoid arthritis and Otezla indicated only for plaque psoriasis and psoriatic arthritis. Tumour necrosis factor alpha (TNF-α) inhibitors have a much longer history, and most physicians are familiar with their efficacy and safety compared to these relatively newer treatments. In spite of this, because they are small-molecule agents, they will eventually be eligible for generic substitution. Although biosimilars for Remicade and Enbrel have been approved, increases in utilization and expanding indications will continue to drive future increases in spending for inflammatory conditions.

Overall Trend	11.7%
Utilization Trend	11.45%
Cost Trend	0.23%
Average Cost per Rx	$2,349.90
2015 Rank	1
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	infliximab	Remicade® / Inflectra®	38.1%
2	adalimumab	Humira®	28.3%
3	etanercept	Enbrel® / Brenzys™	11.6%
4	ustekinumab	Stelara®	8.0%
5	golimumab	Simponi®	4.8%
	Others		9.2%

2. DIABETES

The group of drugs used to treat diabetes was the second highest by spending in 2016, driven by a steady trend of increased utilization. More recently, however, the cost per prescription trend for this group has become more prominent as new brand drugs entered the market. These newer drugs are seen as providing significant clinical improvements by delivering similar blood glucose lowering efficacy with fewer of the adverse effects associated with many older, lower-cost drug classes, such as lower risk of excessively low blood glucose (hypoglycemia), lesser tendency for weight gain, and potentially improved durability of the blood glucose lowering effect. Recently, new data has shown an additional potential benefit not seen in diabetes drugs in the past: improved cardiovascular safety unrelated to the blood glucose lowering effect. This has led to changes in clinical practice guidelines for high-risk patient groups.

Overall, four of the top 10 diabetes drugs are insulins: insulin glargine (Lantus®, #1), insulin aspart (NovoRapid®, #6), insulin detemir (Levemir®, #7), and insulin lispro (Humalog®, #9). Insulins are used for patients with type 1 and type 2 diabetes. Other diabetes drugs are almost all exclusively used for patients diagnosed with type 2.

Lantus was the top diabetes drug by spending in 2016. The first insulin biosimilar approved in Canada, Basaglar™, is a biosimilar for Lantus. Commercialized in December 2015, utilization of Basaglar started in 2016. While it provides only a 15% cost saving over the reference brand Lantus, the full impact of Basaglar has yet to be seen. However, given that insulin glargine is the top diabetes drug, significant savings could result. In its first year of availability, Basaglar accounts for just 0.23% of market share in the insulin glargine space. In an attempt to somewhat protect its market, the manufacturer of Lantus released Toujeo™ in 2015, which is a higher strength version of insulin glargine.

The second-highest diabetes drug by spending is Janumet, a fixed-dose combination of the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin with metformin. The single entity sitagliptin product, Januvia® (ranked 5th), was the first drug in the DPP-4 inhibitor class approved for use in 2007. As of 2016, there are four different DPP-4 inhibitors: Januvia® (sitagliptin), Onglyza® (saxagliptin), Trajenta® (linagliptin), and Nesina® (alogliptin). Each of these is also available in fixed-dose combinations with metformin: Janumet® (sitagliptin+metformin), Komboglyze® (saxagliptin+metformin), Jentadueto™ (linagliptin+metformin), and Kazano™ (alogliptin+metformin).

Victoza® (liraglutide, third in diabetes spending) was the first glucagon-like peptide-1 (GLP-1) receptor agonist approved in 2010. It was also the first non-insulin injectable diabetes drug, administered by subcutaneous injections once daily. In the last quarter of 2015, two once-weekly GLP-1 receptor agonists, Bydureon® (exenatide long-acting release) and Trulicity™ (dulaglutide), were approved in Canada, but these have not yet had a significant market impact. Market share continues to be dominated by Victoza®, which is one of the two drugs noted above that have demonstrated a reduction in the risk of cardiovascular events in individuals with diabetes who have experienced a prior cardiovascular event.

Metformin (fourth by diabetes spending) is the only older generic drug within the top 10 diabetes drugs. This is due to its long-standing use as a first-line pharmacologic therapy for type 2 diabetes, with very high utilization made up over one third of all diabetes drug prescriptions. It has the advantages seen in many new drugs: low risk of hypoglycemia and weight gain, while providing effective lowering of blood glucose.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors were first approved in 2014. There are currently three different molecules approved for use in Canada: Invokana® (canagliflozin, sixth in diabetes spend), Forxiga® (dapagliflozin) and Jardiance™ (empagliflozin). All are also available as fixed-dose combinations with metformin. Recently, two fixed-dose combinations of SGLT2 inhibitors with DPP-4 inhibitors were approved: Qtern® (dapagliflozin + saxagliptin) and Glyxambi™ (empagliflozin + linagliptin). DPP-4 inhibitors are another newer class of diabetes drugs that are currently only available as brand name products. This new combination signals the advent of the combination of two higher-cost drug classes, so an increase in spending is anticipated.

The diabetes drug spending trend will continue its double-digit growth in the next several years, reflecting a continued increase in the utilization of DPP-4 and SGLT2 inhibitors, along with increasing prevalence, disease progression, and cost per prescription.

Overall Trend	13.7%
Utilization Trend	3.96%
Cost Trend	9.70%
Average Cost per Rx	$80.10
2015 Rank	3
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	insulin glargine	Lantus® / Basaglar™	14.2%
2	sitagliptin-metformin	Janumet®	14.1%
3	liraglutide	Victoza®	10.2%
4	metformin	Glucophage®	9.7%
5	sitagliptin	Januvia®	8.7%
	Others		43.1%

3. HIGH BLOOD PRESSURE

High blood pressure, also known as hypertension, is a chronic medical condition that is a major risk factor for heart disease, stroke, chronic kidney disease and death. However, because it does not usually cause apparent symptoms, it is often left either untreated or undertreated until complications arise. High blood pressure affects approximately 23% of Canadian adults.

At the end of 2015, the results of a landmark hypertension trial known as SPRINT were released. This was a randomized controlled trial in which individuals at high risk for cardiovascular disease were randomly selected to receive either intensive treatment to a target systolic blood pressure (SBP) of less than 120 mm Hg or a standard treatment to a target SBP of less than 140 mm Hg. The trial was stopped early because there was a significant level of evidence of reduced cardiovascular events in the intensively treated group. The Canadian Hypertension Education Program Guidelines were updated in 2016 to incorporate this trial data, recommending an SPB target of ≤ 120 mm Hg to be considered for certain high-risk patients. During the trial, two to three different high blood pressure medications, used in combination, were required to reach this target, compared to one to two medications needed for the standard treatment target. This may change prescribing behaviour, leading to more combination therapies with the goal of improving clinical outcomes.

The majority of drugs used for high blood pressure are available as generics; however, two notable exceptions are the #1 and #3 ranked drugs in this group: Coversyl® and Coversyl® Plus. The patent for these products is not expected to expire until early 2018. Given the wide availability of generic options and opportunities for therapeutic optimization, a tightly managed plan could help curb spending in this therapy class. Market saturation and dominance of generic medications will likely result in a flat trend in this therapy class moving forward.

Overall Trend	1.1%
Utilization Trend	-1.40%
Cost Trend	2.54%
Average Cost per Rx	$29.50
2015 Rank	2
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	perindopril	Coversyl®	14.6%
2	amlodipine	Norvasc®	11.3%
3	perindopril – indapamide	Coversyl® Plus	6.5%
4	ramipril	Altace®	5.9%
5	nifedipine	Adalat®	4.8%
	Others		56.9%

4. DEPRESSION

Mental health, and depression in particular, remains a vital health concern for private plan sponsors. Effective treatment of depression is critical to reduce absenteeism and disability and maintain productivity.

The highest ranked drug for depression by spending, duloxetine (Cymbalta®), became available in a generic form in 2016. Along with this was the sublingual dosage form of escitalopram, Cipralex Meltz®, which also became available as a generic. Cipralex® (escitalopram oxalate) became available as a generic in 2014 and had a significant impact on depression drug spending due to its high utilization. Escitalopram oxalate remains in second place by spending, although its utilization is more than twice that of Cymbalta. With the dominance of generic medications and no potential blockbuster molecules in the pipeline, the spending trend in this category is expected to flatten moving forward.

Overall Trend	-1.2%
Utilization Trend	3.56%
Cost Trend	-4.72%
Average Cost per Rx	$41.20
2015 Rank	4
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	duloxetine	Cymbalta®	17.8%
2	escitalopram	Cipralex®	17.4%
3	venlafaxine	Effexor®	12.2%
4	desvenlafaxine	Pristiq®	9.8%
5	bupropion	Wellbutrin®	7.1%
	Others		35.7%

5. ASTHMA, COPD

Treatments for the common respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD) remain an important component of the drug trend. In 2016, two new specialty biologic drugs were approved for use in patients with uncontrolled severe asthma, Nucala™ (mepolizumab) and Cinqair™ (reslizumab). These drugs have similar modes of action (interleukin-5 [IL-5] inhibition) and are used for severe eosinophilic asthma, but are different from the existing specialty biologic agent used in severe allergic asthma patients, Xolair® (omalizumab, an anti-IgE agent). This means that they can be used in different subpopulations of asthma sufferers; the overlap between these populations is estimated to be between 25% and 35%. Xolair was the third-highest-ranking drug by spending in this therapy class in 2016. Also notable in this class is Nucala™, ranked 22nd by spending even after less than a year on the market.

While asthma and COPD are distinct medical conditions, many of the drugs used to treat them are used for both. The top two drugs by spending, Advair® (fluticasone – salmeterol) and Symbicort® (budesonide – formoterol), are prime examples. Both are combination inhaled corticosteroids and long-acting beta-agonist bronchodilators.

An important characteristic of the drugs in this therapy class is that most of them are only available as brand name products, including highly utilized brands such as Advair and Symbicort, as well as newer brands such as Breo® Ellipta®, Arnuity™ Ellipta®, Tudorza® Genuair® and Duaklir™ Genuair®. The generic fill rate (GFR) for this therapy class is only 35.1%, primarily due to salbutamol (Ventolin®), which was ranked first by utilization and sixth by spending. With the dominance of brand products and the emergence of biologic specialty drug options, spending in this therapy class is expected to continue to increase moving forward.

Overall Trend	5.8%
Utilization Trend	2.06%
Cost Trend	3.70%
Average Cost per Rx	$72.90
2015 Rank	5
Drug Type Classification	Primarily traditional with 3 specialty drugs

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	fluticasone – salmeterol	Advair®	18.0%
2	budesonide – formoterol	Symbicort®	17.5%
3	omalizumab*	Xolair®	14.3%
4	fluticasone	Flovent®	11.2%
5	montelukast	Singulair®	8.5%
	Others		30.5%

*Specialty biologic drug

6. INFECTIONS

This therapy class includes traditional antibiotics, antifungals and antivirals primarily used for treating acute infections. Drugs used for high-cost infectious diseases such as HIV/AIDS, hepatitis C and lung infection among cystic fibrosis patients are in distinct therapy classes. Drugs in this class are highly utilized and rank third by claims volume. The high generic fill rate of 88.8% helps to moderate spending in this therapy class, and it is expected that spending in this class will continue to decline as a percentage of overall drug spending in the future.

Overall Trend	-7.5%
Utilization Trend	0.93%
Cost Trend	-8.40%
Average Cost per Rx	$32.50
2015 Rank	6
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	amoxicillin	Amoxil	13.6%
2	valacyclovir	Valtrex	11.6%
3	clarithromycin	Biaxin	7.7%
4	azithromycin	Zithromax	5.5%
5	cephalexin	Keflex	4.7%
	Others		56.9%

> ONE IN EVERY FIVE DOLLARS SPENT ON PRESCRIPTION DRUGS IN 2016 PAID FOR MEDICATION FOR AN INFLAMMATORY CONDITION OR DIABETES.

7. ULCER, REFLUX

Drugs used to treat gastric ulcers and gastroesophageal reflux consist of two main types of drugs: proton-pump inhibitors (PPIs) and histamine H_2 receptor antagonists (H_2RAs). Of these, PPIs are the highest profile due to their generally higher unit costs and overall greater efficacy in suppressing acid secretion by the cells lining the stomach. Almost all drugs within PPIs and H_2RAs are available as generics, with the exception of Dexilant®(dexlansoprazole).

Until recently, ulcers and reflux were considered to be chronic conditions that required ongoing drug therapy to be managed. As a result of the high acid-suppression effect of PPIs, a number of long-term adverse effects have come to light, including increased risk of bone fractures, higher risk of C difficile infections in the bowel with associated diarrhea, higher risk of community-acquired pneumonia, vitamin B12 deficiency, low blood magnesium levels and increased risk of chronic kidney disease. This has led to reexamination of the need for ongoing therapy and the emergence of deprescribing efforts for this class of drugs. These efforts can consist of periodic use of PPIs "on demand", upon reemergence of reflux-related symptoms, or full discontinuation of PPIs when ulcer healing is complete in the absence of reflux-related symptoms.

The comparable efficacy of the different individual PPIs has been recognized by public plans, leading to various measures designed to encourage therapeutic interchange to lower-cost drugs through mechanisms such as the Reference Drug Program in BC. The lowest cost PPI, rabeprazole (Pariet®), was not among the top five by spending and ranked fifth by prescription volume within its class—meaning that it is underutilized given its low cost and equivalent efficacy. Some public plans are also revisiting previously used initiatives to limit the duration of therapy with these drugs for both safety and cost reasons. For example, RAMQ in Quebec has implemented 90-day supply maximums for PPIs, with some exceptions provided depending upon individual clinical circumstances. Over time, these may impact prescribing habits for these drugs, resulting in an overall decrease in both utilization and spending. It is expected that spending in this therapy class will continue to decline as a percentage of overall drug spending.

Overall Trend	-9.5%
Utilization Trend	0.08%
Cost Trend	-9.58%
Average Cost per Rx	$44.80
2015 Rank	7
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	esomeprazole magnesium	Nexium®	32.4%
2	pantoprazole sodium	Pantoloc®	20.7%
3	dexlansoprazole	Dexilant®	13.0%
4	lansoprazole	Prevacid®	9.7%
5	pantoprazole magnesium	Tecta®	6.5%
	Others		17.7%

8. HIGH CHOLESTEROL

Research advances have led to the introduction of new specialty drugs to treat patients with severe, complex high cholesterol. Traditional drugs, including statins, continue to be the therapy mainstay and are listed as first-line therapies in most guidelines. Other drug classes, such as fibrates, cholesterol absorption inhibitors, bile-acid sequestrants, and niacin (nicotinic acid) derivatives, are also available as generics.

Recently, two specialty drug classes have been added to the group of drugs used to treat high cholesterol: microsomal triglyceride transfer protein inhibitors (e.g., Juxtapid™ [lomitapide]) and proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors (e.g., Repatha™ [evolocumab], Praluent™ [alirocumab]).

Juxtapid is only used for select patients with very high blood levels of cholesterol associated with a rare disorder called homozygous familial hypercholesterolemia. It was licensed in 2014 and an initial uptake in use was observed in these individuals; however, utilization for this drug is not expected to grow to any great extent.

The first PCSK9 inhibitor, Repatha, was brought to market in 2015 with the second one, Praluent, arriving in 2016. The uptake of these was not as high as initially anticipated; however, the prior authorization rejection rate for these drugs was higher than the usual rate for most other drugs. In Canada, these drugs are not indicated as alternatives to statins but are indicated as an adjunctive therapy with statins in certain high-risk individuals who are unable to achieve cholesterol targets.

Data from the first PCSK9 inhibitor cardiovascular outcome trial for Repatha, called FOURIER, was released in March 2017. This trial added Repatha to existing high- or moderate-intensity statin therapy. Patients in the Repatha™ group experienced a 15% reduced risk in the primary study end point (cardiovascular [CV] death, myocardial infarction [MI], stroke, hospitalization for unstable angina, or coronary revascularization) and a 20% reduction in the risk of the key secondary end point (CV death, MI or stroke). It should be noted, however, that the absolute event rate reductions were just -1.5%, meaning that Repatha did not eliminate the risk of cardiovascular events. The two composite end points were driven by decreases in the risk of MI, stroke and revascularization; the risks of CV death and all-cause mortality were unchanged in the two groups. Despite this, the results of FOURIER are likely to increase the utilization of PCSK9 inhibitors, particularly for higher-risk individuals.

The lower cost of generic atorvastatin as of April 2017 will slow the cost trend in the near term, while increasing utilization of PCSK9 would drive both cost and utilization trend slightly upward. Provided a tightly managed plan with a robust prior authorization program is in place, it is expected that the overall trend for this therapy class will stay flat or increase slightly.

Overall Trend	-3.3%
Utilization Trend	-1.45%
Cost Trend	-1.80%
Average Cost per Rx	$34.40
2015 Rank	8
Drug Type Classification	Primarily traditional with 3 specialty drugs (Praluent, Repatha, Juxtapid)

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	rosuvastatin	Crestor®	41.3%
2	atorvastatin	Lipitor®	35.0%
3	ezetimibe	Ezetrol®	7.6%
4	simvastatin	Zocor®	3.6%
5	fenofibrate	Lipidil®	3.4%
	Others		9.1%

9. CANCER

The most prolific area of drug development research is that aimed at the treatment of cancer. Research is ongoing in many areas that have only recently been developed, such as immunotherapy and various molecularly targeted agents. Developments also include non-drug platforms, such as gene-editing technology (e.g., CRISPR) and cell therapies (e.g., CAR-T), which could potentially transform personalized cancer treatments. Many of these newer therapies will extend the lives of people with cancer, potentially transforming cancer from a group of fatal diseases into chronic diseases that will require individualized long-term management.

Most of the recent developments in cancer therapies are molecularly targeted therapies. These are frequently highly individualized treatments designed for patients with specific molecular targets present in specific tumour types. Their development is still in relatively early stages, and there are hundreds more of these targeted therapies in even earlier stages of development. Also, second-generation versions of existing therapies that have fewer side effects and a lower propensity for resistance development will become available. Other recent developments include the use of immune checkpoint inhibitors to release the body's own immune response to cancer cell elimination, such as Yervoy™ (ipilimumab), Keytruda® (pembrolizumab) and Opdivo® (nivolumab). Since these immune checkpoint targets are present in many different types of cancer, new indications for some of these drugs were approved this year, while others are in development for potential future use.

Availability of generic oncology medications (e.g., temsirolimus and pemetrexed, approved in 2016) will not offset the high prices of branded treatments. It is anticipated that the increasing prevalence of self-administered oncology medications, sometimes as maintenance therapy, will result in higher utilization and costs moving forward.

Overall Trend	11.6%
Utilization Trend	3.24%
Cost Trend	8.39%
Average Cost per Rx	$502.89
2015 Rank	9
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	lenalidomide	Revlimid®	15.7%
2	imatinib	Gleevec®	5.7%
3	rituximab	Rituxan®	5.5%
4	methotrexate	-	4.7%
5	dasatinib	Sprycel®	4.7%
	Others		63.7%

10. ATTENTION DEFICIT HYPERACTIVITY DISORDER

There is a steady increase in the utilization of drugs for attention deficit hyperactivity disorder (ADHD), primarily due to higher rates of diagnosis in children and increased use among adults as the adolescent population ages and continues to require these drugs. Most of the drugs for this indication are available in generic forms with only a couple of exceptions (Biphentin®, Intuniv®); however, there is some controversy about the interchangeability of extended-release products. This has reduced the generic fill rate for many of these drugs, reducing the potential cost savings that could otherwise be achieved in this category.

Vyvanse® (lisdexamfetamine), an ADD treatment, was approved for a new condition: binge eating disorder (BED), becoming the only drug officially indicated for BED. Current BED treatment consists of psychotherapy (e.g., cognitive behavioural therapy [CBT]) or pharmacotherapy, or a combination of both. Current pharmacotherapy includes antidepressants (e.g., SSRIs), anticonvulsants (e.g., topiramate) and weight-loss medications (e.g., orlistat). (Use of pharmacotherapy may not be appropriate for all patients with BED.) While use of Vyvanse in BED is expected to be relatively low compared to its use in ADD, given that BED is the most common form of eating disorder and that there are no other treatments indicated for this, this new indication has led to increases in utilization of this drug in 2016.

While some generic options are available in this therapy class, it is anticipated that increases in utilization will continue to drive increases in spending in this category in the future.

Overall Trend	14.1%
Utilization Trend	13.57%
Cost Trend	0.52%
Average Cost per Rx	$96.10
2015 Rank	10
Drug Type Classification	Traditional

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF TOP 5 SPEND
1	Methylphenidate	Ritalin®/Concerta®/Biphentin®	45.6%
2	Lisdexamfetamine	Vyvanse®	27.2%
3	Amphetamine-Dextroamphetamine	Adderall®	8.5%
4	Atomoxetine	Strattera®	7.6%
5	Guanfacine	Intuniv®	7.3%
	Others		3.8%

> PRIVATE PLAN SPENDING INCREASED AGAIN IN 2016, CONTINUING A TREND THAT HAS SEEN OVERALL DRUG SPENDING IN CANADA DOUBLE SINCE 2000.

OTHER NOTEWORTHY THERAPY CLASSES

MULTIPLE SCLEROSIS (Ranked #11)

Multiple sclerosis (MS) is a chronic, immune-mediated inflammatory disease of the central nervous system (CNS). It involves the degeneration of myelin, the protective covering of nerve cells, which affects the transmission of impulses along nerve fibres. Canada has the highest rate of MS in the world, with an estimated 100,000 Canadians living with the disease. MS is most often diagnosed in young adults between 15 and 40 years of age; although younger children and older adults are also sometimes diagnosed with the disease.

First-line therapy for this condition includes interferon beta and glatiramer acetate, which are second and fourth among the top five drugs by spending prescribed for MS. In early 2017, Glatect™ became the first subsequent-entry, non-biological complex drug for Copaxone® (glatiramer acetate). This drug is unique in that it is not a substance produced by living cells and therefore is not a biologic; however, it is a complex drug consisting of many polymers formed by four different amino acids. As it is not fully characterized as a biologic, its approval pathway was like that of biosimilars. Glatect's cost is approximately 20% lower than that of Copaxone. In anticipation, the manufacturer of Copaxone released a three-times-weekly administered form of the drug (40 mg per dose)—currently, Copaxone and now Glatect are 20 mg per dose, administered once daily.

MS is generally categorized into relapsing and progressive forms. Within these, the relapsing-remitting form of MS (RRMS) is the most common, affecting 80% to 90% of patients. Over time, about half of the patients with RRMS will transition to secondary progressive MS (SPMS). All of the currently available drugs are indicated to treat RRMS. In 2016, a new, once-monthly administered monoclonal antibody became available to treat patients with relapsing forms of MS: Zinbryta™ (daclizumab beta). It will provide second- or third-line treatment for patients who have not had an adequate response to other therapies. Its cost will be in line with other similarly used therapies such as Gilenya® and Lemtrada®. It is administered subcutaneously and so can be administered at home, but will only be available through a controlled distribution system.

About 10% to 15% of MS patients will be initially diagnosed with primary progressive multiple sclerosis (PPMS). There are no drugs currently available to treat PPMS. However, in mid-2017, Ocrevus™ (ocrelizumab) is expected to become available; it will be the first drug approved in Canada for PPMS. It is anticipated that the expanding therapeutic options will continue to lead to increases in utilization and cost, driving future escalation in spending in this category.

Overall Trend	8.3%
Utilization Trend	4.70%
Cost Trend	3.58%
Average Cost per Rx	$1,846.90
Rank	2015: 12
Rank	2016: 11
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	fingolimod	Gilenya®	19.7%
2	interferon beta-1a	Avonex®	17.3%
3	dimethyl fumarate	Tecfidera™	16.7%
4	glatiramer acetate	Copaxone®	14.5%
5	teriflunomide	Aubagio®	11.8%
	Others		20.0%

HEPATITIS C (Ranked #26)

The treatment landscape for hepatitis C has changed considerably over the last few years. The greatest impact of these changes was seen in 2014 and 2015, with the availability of direct-acting antivirals (DAAs) for hepatitis C virus infection. These new antivirals are used in treatment regimens that do not require the use of pegylated interferon and ribavirin (PR), which were previously the mainstay of treatment. DAAs improved efficacy significantly, leading to higher cure rates. Shorter required duration of treatment, fewer adverse reactions and better tolerability led to improved treatment adherence. In addition, there were many patients who could not tolerate the older forms of treatment for hepatitis C who were without treatment options until DAAs became available. The result was very high levels of utilization of very high-cost treatments. This produced a drug trend growth of 232% from 2014 to 2015.

With the great efficacy of DAAs, patients have experienced cures from the disease. In terms of plan spending, these cures have translated into a significant decrease in drug trend of -63% in this therapy class, primarily driven by a significant fall in utilization of 59% in 2016.

Gaps in care for patients with hepatitis C continue to exist. Drug development continues to address these gaps, such as populations of patients with less common genotypes of hepatitis C virus infection that are harder to treat, like genotype 3, and patients with decompensated liver disease whose treatment has not been fully addressed with the first wave of DAAs.

Epclusa™ (sofosbuvir-velpatasvir) was approved in 2016. It is the first pan-genotypic DAA, meaning that it has been shown to be effective in treating hepatitis C infections with genotypes 1 through 6. It is also the first DAA to be approved for use in combination with ribavirin for patients with decompensated cirrhosis. With its simplicity in dosing schedule, Epclusa will be the treatment of choice for most patients. Zepatier® (elbasvir-grazoprevir) was another DAA approved in 2016. The advantages of this drug include its approval for use in patients who have failed prior therapy with a protease inhibitor combined with PR, and its ability to be used for patients who have significant renal disease. Epclusa and Zepatier were ranked third and fourth respectively among the top five hepatitis C drugs in 2016.

In early 2017, it was announced that the pan-Canadian Pharmaceutical Alliance (pCPA) had come to an agreement with some of the major hepatitis C DAA manufacturers regarding product listing agreements. Initially, this led to the easing of access for many DAAs through Ontario Drug Benefit coverage, including the top four drugs in 2016. It is anticipated that spending for hepatitis C will continue to decline, though not as sharply as in 2016.

Overall Trend	-63.3%
Utilization Trend	-59.31%
Cost Trend	-4.00%
Average Cost per Rx	$6,000.10
Rank	2015: 11
Rank	2016: 26
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF TOP 5 SPEND
1	ledipasvir-sofosbuvir	Harvoni®	43.0%
2	sofosbuvir	Sovaldi®	21.9%
3	sofosbuvir-velpatasvir	Epclusa™	9.9%
4	elbasvir-grazoprevir	Zepatier®	7.9%
5	ombitasvir-paritaprevir-ritonavir & dasabuvir	Holkira™ Pak	7.5%
	Others		9.8%

> WITH THE GREAT EFFICACY OF DAAs, [HEPATITIS C] PATIENTS HAVE EXPERIENCED CURES FROM THE DISEASE. IN TERMS OF PLAN SPENDING, THESE CURES HAVE TRANSLATED INTO A SIGNIFICANT DECREASE IN DRUG TREND OF -63% IN THIS THERAPY CLASS, PRIMARILY DRIVEN BY A SIGNIFICANT FALL IN UTILIZATION OF 59% IN 2016.

RARE DISEASE (Ranked #41)

The rare disease therapy class consists of many different diseases. The majority of recognized rare diseases are genetic in origin. Other causes, such as allergic, infectious, degenerative, proliferative, and environmental—or combinations of these—have been recognized as well. There is no single Canadian definition for a rare disease, sometimes called orphan disease. Common among the various definitions is that they are based on incidence or prevalence. There are currently three definitions widely used in Canada:

- Health Canada's draft definition of a rare disease is one that affects fewer than five in 10,000 persons in Canada.
- Alberta's public drug plan defines a rare disease as a genetic lysosomal storage disorder that occurs in fewer than one per 50,000 Canadians.
- Ontario's public drug plan's working definition of a rare disease is one that has an incidence rate of less than one in 150,000 live births or new diagnoses per year.

Although the prevalence or incidence rate of rare diseases, regardless of the definition used, is very low, there are over 7,000 currently recognized rare diseases. This means that one in 12 Canadians is estimated to have a rare disease, approximately 2.8 million in total.

Due to the low number of patients and resulting low market size, drugs used to treat these diseases tend to be ultra-high cost. Most rare diseases, 65% to 75%, have their onset in childhood and therefore require ongoing use, another reason this is a high-profile therapy class.

In 2016, a number of new drugs and expanded indications for rare diseases were approved:

- Ravicti™ (glycerol phenylbutyrate) is a treatment for urea cycle disorders that reduce the ability of patients to manage ammonia, which is produced as a result of the breakdown of proteins and amino acids. This is a potential alternative to Pheburane® (sodium phenylbutyrate), which is also used for this disorder. Dosing is based on body surface area, making cost estimates somewhat unpredictable. However, annual treatment costs can be as high as $270,000.
- Zemaira® (human alpha-1 proteinase inhibitor, alpha-1 antitrypsin) is a replacement preparation used for patients with severe alpha-1 proteinase inhibitor deficiency, which manifests as an early and progressive emphysema form of chronic obstructive pulmonary disease (COPD). Cost information for Zemaira is currently not available; however, it is an alternative to currently available Prolastin®-C, which has an estimated average annual treatment cost of $115,000.
- Nitisinone is used to treat patients with hereditary tyrosinemia type-1 (HT-1), an inherited inability to break down the amino acid tyrosine. This results in liver, kidney and central nervous system dysfunction and usually manifests early in life. Three different brands (MDK-Nitisione, Nitisinone Tablets, Orfadin) of this drug were approved in late 2016 and early 2017.
- Sandoz Miglustat is the first generic form of Zavesca®, which is used for the treatment of type 1 Gaucher disease. The difference between this new generic and the reference brand is that Zavesca is also indicated for use in patients with Niemann-Pick type C disease, while Sandoz Miglustat is not. Pricing for the Sandoz generic version is not yet available, while the Zavesca treatment cost is approximately $120,000 per year.
- In early 2017, Ilaris® (canakinumab), which is used to treat patients with Cryopyrin-Associated Periodic Syndromes (CAPS), received approvals for three other rare diseases: Familial Mediterranean Fever (FMF), Tumor Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS), and Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD). These are all forms of autoinflammatory, periodic fever syndromes, of which there are dozens of others. Dosing is similar for all of the different indications. The treatment costs are substantial, exceeding $200,000 per year.

With three new rare disease medications approved in 2016, along with more in the pipeline, it is anticipated that increases in utilization and cost will continue to drive future increases in spending in this category.

Overall Trend	42.1%
Utilization Trend	19.20%
Cost Trend	22.94%
Average Cost per Rx	$4,685.70
Rank	2015: 45
Rank	2016: 41
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	elosulfase alfa	Vimizim®	25.2%
2	sapropterin dihydrochloride	Kuvan™	19.9%
3	alpha1-proteinase inhibitor (human)	Prolastin® / Zemaira®	16.2%
4	canakinumab	Ilaris®	8.7%
5	velaglucerase alfa	Vpriv®	6.5%
	Others		23.5%

CYSTIC FIBROSIS (Rank #48)

Cystic fibrosis (CF) is the most common fatal genetic disease affecting Canadian children and young adults. It affects the secretory cells that produce mucus, sweat, and digestive juices. In people with CF, a defective gene that encodes the cystic fibrosis transmembrane conductance regulator (CFTR) protein causes these secretions to become thick and sticky. This leads to severe problems with breathing (the most prominent and life-threatening symptom), digestive problems, endocrine disorders (including diabetes), and others. It is estimated that one in every 3,600 children born in Canada has CF. More than 4,100 Canadian children, adolescents, and adults with cystic fibrosis currently attend specialized CF clinics.

There are over 240 genetic mutations that have been confirmed to cause CF. In the past, most treatments for CF were supportive and included drugs to treat its symptoms, such as bronchodilators and mucolytics. These therapies were also used for the treatment of other conditions. Pulmozyme®, the second-leading CF drug by spending, is used as supportive therapy for maintaining lung function, specifically for patients with CF. Two others in the top five in this therapy class, Kalydeco® and Orkambi™, have been approved to actually modify the function of the CFTR protein and only work for individuals with specific genetic defects.

The F508del mutation is the most common found in individuals with CF, with 85% to 90% carrying at least one copy of this mutation. In 2016, Orkambi™, a combination of ivacaftor (Kalydeco®) and lumacaftor, was approved for patients 12 years of age and older who are homozygous[1] for the F508del mutation. It is estimated that this mutation could be present in up to half of the Canadian CF population, with a staggering estimated annual treatment cost of $260,000 per person. Its availability drove the overall trend from 12.98% in 2015 to 48.3% in 2016. With additional indication expansion of Orkambi™ expected in the near term, it is anticipated that spending in this therapy class will continue to increase moving forward.

Overall Trend	48.3%
Utilization Trend	24.72%
Cost Trend	18.60%
Average Cost per Rx	$3,216.10
Rank	2015: 48
Rank	2016: 48
Drug Type Classification	Specialty

RANK BY SPEND	DRUG NAME	COMMON (REFERENCE) BRAND	% OF SPEND
1	ivacaftor	Kalydeco®	51.5%
2	dornase alfa	Pulmozyme®	32.6%
3	lumacaftor-ivacaftor	Orkambi	15.9%

[1] Alternative forms of a gene are called alleles. When someone has two of the same allele, they are homozygous.

SECTION **III.**

PROVINCIAL & MARKET FACTORS

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SECTION III.

PROVINCIAL & MARKET FACTORS

PROVINCIAL DEVELOPMENTS

In 2016, Canadian provinces showed increasing spending trends of varying magnitude. In this section, we dissect the trends in private drug spending within each province, and review major provincial legislative and reimbursement changes that have had an impact on them. As this analysis revealed, most provincial drug programs are undergoing significant change. It is therefore critical for private plans to leverage cost controls to avoid or minimize cost increases due to these provincial changes as well as other market factors.

BRITISH COLUMBIA

Private plans in British Columbia had a trend growth of 3.8% in 2016, driven mostly by a 2.6% increase in utilization.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN BRITISH COLUMBIA

- **THERAPEUTIC OPTIMIZATION.** BC PharmaCare has made the Reference Drug Program (RDP) a cornerstone of its program since 1995. In December 2016, the RDP was modernized to include three new therapeutic categories, targeting eight highly utilized drug classes for five traditional therapy classes:

DRUG CLASSES	THERAPY CLASSES
Angiotensin Receptor Blockers (ARBs)	High blood pressure
Histamine$_2$ Receptor Blockers (H_2 Blockers)	Gastric ulcers/Reflux
Nitrates	Cardiovascular health
Proton Pump Inhibitors (PPIs)	Gastric ulcers/Reflux
Dihydropyridine Calcium Channel Blockers (CCBs)	High blood pressure
HMG-CoA Reductase Inhibitors (statins)	High cholesterol
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)	Pain and fever
Angiotensin Converting Enzyme Inhibitors (ACEI)	High blood pressure

For each drug class, a drug is selected as the reference and is used to determine the maximum daily amount payable for non-reference drugs in this category. This applies to drugs that may have different active ingredients but are in the same therapeutic class, and are equally safe and effective. As an example, atorvastatin and rosuvastatin are the reference drugs in their drug class, while fluvastatin, lovastatin, pravastatin and simvastatin are partially covered. This aligns with the philosophy of Express Scripts Canada's therapeutic substitution plan management, designed to control spending increases in the traditional drug category.

- **PHARMACY PRACTICE.** The College of Pharmacists of British Columbia (CPBC) recently amended its Professional Practice Policy to allow pharmacists to make therapeutic interchanges in these RDP categories. Our analytics found these eight drug classes represented 19.55% of claims and 12.89% of spending in BC last year. Reduced reimbursement under the RDP will result in slower accumulation of the member's deductible if they continue to use the higher-cost drug options, with subsequent prescription costs passed onto their private plan. This will lead to a likely increase in private plan spending for these drugs in 2017 and onwards.
- **BIOSIMILARS.** New biosimilar drugs made an appearance on the BC PharmaCare formulary in February 2016. Since then, the BC PharmaCare Special Authority (SA) requests new patients requiring infliximab to be approved for the biosimilar brand Inflectra only—first for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis indications, subsequently adding Crohn's disease and ulcerative colitis to its formulary in November of the same year. Patients whose initial approval was received before the effective change date are still eligible for coverage of brand name Remicade. More recently, the province has added Grastofil (biosimilar of Neupogen, used in patients with low white blood cells) as the preferred filgrastim product to its formulary.
- **OPIOID CONTROL.** The inappropriate use, abuse, and diversion of prescription narcotics have emerged as a significant public health and safety issue in Canada and other jurisdictions around the world. The opioid crisis hit British Columbia in 2016, with an alarmingly high number of overdoses and deaths. The province became one of the first in Canada to make naloxone—a life-saving drug used to reverse the effects of an opioid overdose—available without a prescription. This change allowed wider access to naloxone with the intent of saving lives.

ALBERTA

The overall drug trend for private plans in Alberta was 3.0% in 2016, with utilization up 1.9% and costs up 1.1%.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN ALBERTA

- **THERAPEUTIC OPTIMIZATION.** In October 2016, Alberta modified its coverage of acid reflux medications (proton pump inhibitors – PPIs), limiting coverage to lower-cost medications rabeprazole (Pariet®) and Tecta® (pantoprazole magnesium). In 2017, choosing to continue with other drugs in this therapy class will result in the cost difference being billed to patients or private payers, leading to higher private drug spending.
- **BIOSIMILARS.** Alberta also moved forward with changes to special authorization for infliximab patients. For patients prescribed infliximab for the first time, authorization for the biosimilar Inflectra will be considered. Remicade will not be approved for new infliximab patients with ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis, Crohn's disease or ulcerative colitis. However, coverage for Remicade will continue for patients who are currently well maintained on the medication.

SASKATCHEWAN

The overall drug trend for private plans in Saskatchewan was 2.9% in 2016, mainly due to a utilization hike of 6.5% accompanied by a cost trend reduction of 3.6%.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN SASKATCHEWAN

- **POLICY CHANGE.** Since June 1, 2016, the cost of a prescription listed on the Saskatchewan Formulary or approved under Exception Drug Status was increased from $20 to $25 for the Seniors' Drug Plan and Children's Drug Plan. Since the public plan is the first payer, this means higher spending will be passed along to private plans. However, the impact is expected to be minimal, as the population affected by this increase represents a relatively small portion of private plan members.

MANITOBA

The overall drug trend for private plans in Manitoba was 1.1% in 2016, with a slight utilization growth of 0.4% and a cost trend growth of 0.7%.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN MANITOBA

- **DRUG SCHEDULE.** In 2016, Manitoba made a step forward in limiting access to codeine-containing products, as a prescription is now necessary for the purchase of any codeine-containing product. Previously, exempted codeine products such as Tylenol® #1 and Robaxacet®-8 could be purchased from a pharmacist without a prescription. Under the new rules, a physician, authorized nurse practitioner, dentist or pharmacist must assess each patient before issuing a prescription for an exempted codeine product, which will then be entered in the patient's profile. While this regulatory change aims to reduce the incidence of misuse, changing non-prescription drugs that are typically not covered by drug plans to prescription status will lead to increases in private drug spending.

ONTARIO

The overall drug trend for private plans in Ontario was 3.1% in 2016, with utilization up 1.0% and costs up 2.1%.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN ONTARIO

- **OHIP+: CHILDREN AND YOUTH PHARMACARE.** The province of Ontario has announced expanded drug coverage for individuals aged under 25 years old as part of the 2017 annual budget. This new provincial pharmacare program, called "OHIP+: Children and Youth Pharmacare", is proposed to come into effect on January 2018. If approved, this new program would fully cover 4,400 drugs for the province's four million children and young adults.
- **FEE LIMITS.** In 2016, the province adapted the Health Network System (HNS) for the pharmacy dispensing fee limitation initiative initially announced in 2015. The Ontario Drug Benefit (ODB) allows five fees per 365-day limit for specific chronic-use medications such as high blood pressure and high cholesterol therapies, regardless of dispensing pharmacy. When claims are processed, pharmacies are informed of how many allowable fees are remaining. If no fees are available, the pharmacy is advised of the next fee availability date, and only drug costs and markups are paid. Some exceptions are permitted for eligible patients requiring more frequent dispensing.
- **BIOSIMILARS.** Ontario also facilitated patient access to biosimilars. Since February 2016, Inflectra (infliximab) is a Limited Use Benefit in Ontario for the following four indications: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and severe plaque psoriasis. In December 2016, the ODB added three new indications to the list: ulcerative colitis, Crohn's disease and fistulising Crohn's. Existing approvals for Remicade under the Exceptional Access Program (EAP) will continue to be honoured. New EAP requests for Remicade for the indications above (RA, AS, PsA, Plaque Psoriasis) will not be considered, nor will requests due to Inflectra intolerance or non-response.

- **OPIOID CONTROL.** Several initiatives have emerged in Ontario in response to this severe global challenge.
  - Since October 1, 2016, patients are required to return all used fentanyl patches to their pharmacist prior to receiving their next supply of patches.
  - A number of high-strength, long-acting opioids were delisted from its formulary starting in January 2017. (Examples include 200-mg tablets of morphine, and 75-mcg/hr and 100-mcg/hr patches of fentanyl.) No exemptions will be considered.
  - The health ministry is now reimbursing pharmacies for providing Naloxone Emergency Kits to eligible individuals, such as current or past opioid users who may be at risk of overdose, and family members or friends of at-risk individuals.
- **WIDER GENERIC SUBSTITUTION.** Since November 1, 2016, if an EAP drug has an interchangeable generic product designated through the Off-Formulary Interchangeable (OFI) mechanism, the ministry will only approve the funding of the generic product.
- **PHARMACY PRACTICE.** Since December 15, 2016, pharmacists, pharmacy students and interns are permitted to administer vaccines to any patient older than five years old for 13 vaccine-preventable diseases. The vaccines on this list are not being reimbursed by the Ontario government for pharmacist administration, so private payers may expect claims, as patients are more comfortable receiving vaccines in pharmacies.

QUEBEC

The overall drug trend for private plans in Quebec was 1.6% in 2016. Costs increased by 2.4% while utilization diminished by 0.8%.

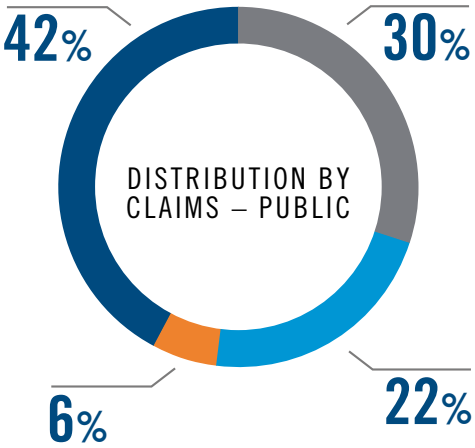
NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN QUEBEC

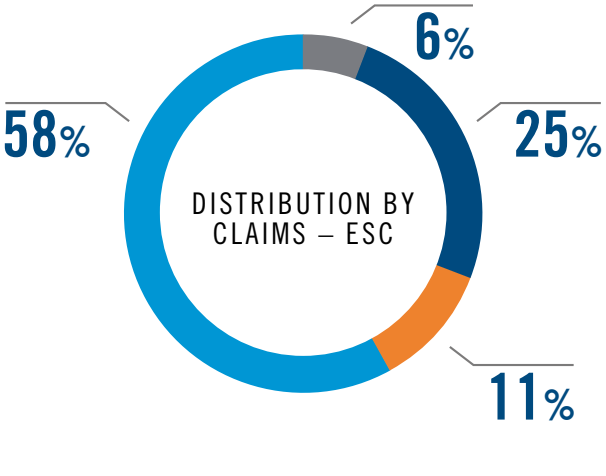
- **PHARMACY PRACTICE.** Since June 2015, Law 41 allows pharmacists to deliver billable professional services to the population of Quebec. These services include:
  - Prescribing when no diagnosis is required;
  - Prescribing for minor conditions;
  - Extending prescription over 30 days;
  - Adjusting a prescription according to a therapeutic target.

The RAMQ published its statistics for the first year of the new Law 41 billable professional services, and our researchers compared the distribution of these four types of claims between public and private payers.

Differences can be explained as follows:

- Members with private coverage are younger and working; they are active and travel more. Also, multiple chronic conditions are more prevalent among seniors insured by the public plan. Both factors lead to more private plan claims under categories “Prescribing for minor ailments” and “Prescribing when no diagnosis is required”.
- More prescription extension services are required among the senior population, which has a higher number of chronic medications and is covered by the public plan.





1. PRESCRIBING A DRUG TO TREAT A MINOR CONDITION
2. PRESCRIBING A DRUG WHEN NO DIAGNOSIS IS REQUIRED
3. EXTENDING A PRESCRIPTION BEYOND 30 DAYS
4. ADJUSTING PRESCRIPTION TO REACH THERAPEUTIC TARGETS

- "Adjusting a prescription according to therapeutic target" relates primarily to chronic therapies such as antihypertensives and anticoagulants, which are most commonly prescribed to patients in the senior population insured by the public plan.

- **BIOSIMILARS.** The province of Quebec completely delisted Remicade from its formulary in early 2017. Individuals starting infliximab therapy will only be candidates for therapy with Inflectra (with the exception of pediatric indications). Preexisting patients on Remicade will continue to receive coverage.
- **ADDITIONAL PHARMACY PRACTICE CHANGES.** On December 7, 2016, Bill no. 92 was adopted. This bill includes an amendment which leads to the obligation for pharmacists to provide a detailed receipt for all patients with a private insurance, disclosing dispensing fees, drug costs, and markups for all drugs or supplies covered by the public plan. Detailed receipts will be required from Quebec pharmacists as of September 2017. This change will enhance transparency of prescription charges to patients, enabling patients to make better pharmacy choices.

NEW BRUNSWICK

The overall drug trend for private plans in New Brunswick was stagnant at 0.1% in 2016. Utilization growth of 3.3% was offset by a cost trend decrease of 3.1%.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN NEW BRUNSWICK

- **DRUG INFORMATION SYSTEM.** The New Brunswick Department of Health implemented the Drug Information System (DIS)/Prescription Monitoring Program (PMP). The DIS is part of the Electronic Health Record (EHR), which will display real-time medication history for patients who have a prescription filled in any community pharmacy in New Brunswick.
- **BIOSIMILARS.** In 2016, Inflectra was added to the provincial formulary for the treatment of ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis, ulcerative colitis and Crohn's disease. Requests for coverage for new infliximab patients with these indications will be approved for Inflectra only. Patients who received approval for Remicade before this change will continue to receive coverage.

PRINCE EDWARD ISLAND

The overall drug trend for private plans in Prince Edward Island was 2.9% in 2016, with a cost trend of 3.8% and a utilization trend of -0.8%. There were no noteworthy legislative or pharmacy practice changes identified.

NOVA SCOTIA

The overall drug trend for private plans in Nova Scotia was strikingly high in 2016, at 10.1%. This results from a utilization trend growth of 5.3% and a cost trend growth of 4.8%, with a net increase of $92.70 in cost per plan member compared to 2015. This spending hike was primarily driven by increased prescription volume for three therapy classes—inflammatory conditions, cancer and diabetes.

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN NOVA SCOTIA

- **DRUG INFORMATION SYSTEM.** In November 2016, the province announced that all 305 community pharmacies in Nova Scotia were connected to the Drug Information System, allowing pharmacists, doctors and other authorized healthcare providers to access information about patients' medication history. This information includes filled prescriptions as well as medication-related allergies, adverse reactions and medical conditions. The Drug Information System also helps to prevent prescription drug diversion by providing information to the Nova Scotia Prescription Monitoring Program. The system was introduced in 2011 and the first pharmacy was connected in November 2013. Since then, the system has collected data on more than 17 million records for more than 700,000 Nova Scotians.
- **BIOSIMILARS.** Patients who will receive prescriptions for infliximab for the first time after June 1, 2016 will be candidates for the biosimilar Inflectra for the following indications: ankylosing spondylitis, plaque psoriasis and rheumatoid arthritis. As of December 1, 2016, ulcerative colitis, Crohn's disease and psoriatic arthritis indications were added to follow the same criteria. Candidates who were already receiving Remicade will be exempted from this measure.

NEWFOUNDLAND

The overall drug trend in Newfoundland was 4.6% in 2016, mainly due to an increase in cost per prescription of 3.9% along with a slight increase in utilization (0.7%).

NOTEWORTHY DEVELOPMENTS WITHIN THE PHARMACY LANDSCAPE IN NEWFOUNDLAND

- **OPIOID CONTROL.** The province has tackled this problem by facilitating access to Suboxone® (buprenorphine/naloxone). Under the Newfoundland and Labrador Prescription Drug Program, this drug no longer requires special authorization for those undergoing opioid addiction treatment. Additionally, the province has announced distribution of more than 1,200 naloxone take-home kits for those at risk of opioid overdose.

PAN-CANADIAN PHARMACEUTICAL ALLIANCE

Provincial health authorities continued to work together through the pan-Canadian Pharmaceutical Alliance (pCPA) to achieve greater value for drugs for publicly funded programs and patients. Established in August 2010, the pCPA conducts joint provincial and territorial negotiations for generic and brand name drugs. All brand name drugs put forward for funding through the national review processes—the Common Drug Review (CDR)—are now considered for negotiation through the pCPA. As of April 1, 2016, completed negotiations on brand and generic drugs have resulted in an estimated $712 million in annual savings.

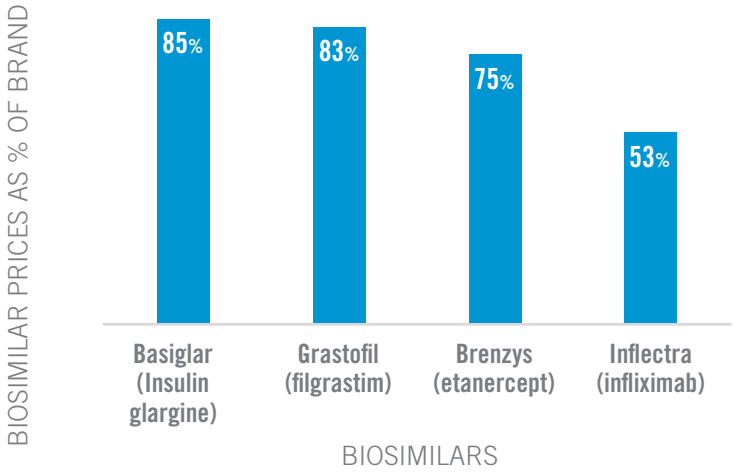
SUBSEQUENT ENTRY BIOLOGICS (SEBS) FIRST PRINCIPLES

Biosimilars were previously known in Canada as Subsequent Entry Biologics. In April 2016, the pCPA published *First Principles for Subsequent Entry Biologics (SEBs)* to guide negotiations on biosimilars and reference biologics. It includes the following:

- All biosimilars and reference biologic manufacturer proposals will be considered only through the national pCPA negotiation process rather than through individual or selected jurisdictions. Negotiations with requesting manufacturers will proceed at the discretion of the pCPA.
- Consistent with its mandate, which includes increasing patient access to clinically effective and cost-effective drug treatment options, the pCPA will encourage a competitive environment that includes biosimilar market growth and is conducive to long-term cost reductions and sustainability for public drug plans.
- The introduction of a biosimilar must provide a reduction in price (compared to the reference drug) to benefit all Canadians.

More biosimilars became available in 2016. Provincial coverage varies, with pricing differential likely being a key factor:

- The biosimilar of etanercept (Brenzys) and insulin glargine (Basaglar) have yet to appear on provincial formularies;
- Grastofil, the biosimilar of Neupogen, priced at 83% of the brand price, is now listed on British Columbia and Ontario formularies;
- For patients who have not been prescribed Remicade prior to the change, the biosimilar Inflectra has been adopted as the preferred infliximab product in all provinces. Inflectra is priced at 53% of the brand price.



GENERICS INITIATIVES

The pCPA announced the Value Price Initiative in 2013. On April 1st of each year since the announcement, it reduces the cost of some highly utilized generics to 18% of the equivalent brand name product. As of 2016, 18 products were targeted by the pCPA. Our analytics revealed that these products accounted for 6.7% of claims and 3.5% of private plan drug costs in 2016.

A one-year bridging period for the pCPA Generics Initiative has been effective since April 1, 2017. The bridging arrangement will result in additional savings and allow time for the evaluation of the current Generics Initiative, as well as explore next steps. Under the bridging arrangement, the cost of six generic chemicals—amlodipine, atorvastatin, clopidogrel, pantoprazole, ramipril, and simvastatin—has been further reduced from 18% to 15% of brand prices since April 1, 2017.

CHEMICAL NAME	COMMON INDICATION	GENERIC PRICES AS PERCENTAGE OF BRAND
Amlodipine	High blood pressure	15%
Atorvastatin	High cholesterol	15%
Citalopram	Depression	18%
Clopidogrel	High blood pressure	15%
Donepezil	Alzheimer's disease	18%
Ezetimibe	High cholesterol	18%
Gabapentin	Neurological disorders	18%
Metformin	Diabetes	18%
Olanzapine, olanzapine ODT	Mental disorders	18%
Omeprazole	Ulcer/Reflux	18%
Pantoprazole sodium	Ulcer/Reflux	15%
Quetiapine	Mental disorders	18%
Rabeprazole	Ulcer/Reflux	18%
Ramipril	High blood pressure	15%
Rosuvastatin	High cholesterol	18%
Simvastatin	High cholesterol	15%
Venlafaxine	Depression	18%
Zopiclone	Sleep	18%

BRAND NAME DRUG NEGOTIATIONS

In 2016, negotiations were completed for 31 new brand name drugs. Of these, 20 were for specialty medications such as Xolair® (for chronic idiopathic urticaria), Simponi® SC (for ulcerative colitis), Grastofil™ (for blood disorders), Cosentyx® (for plaque psoriasis), and Revlimid® (for multiple myeloma).

Lack of transparency in regard to these negotiation outcomes could lead to price reductions or financial benefits not being extended to patients insured by private plans. As a result, these patients and plan sponsors may continue to pay higher prices, and Express Scripts Canada anticipates an increase in utilization due to broader coverage on a provincial level. This issue is even more urgent in Quebec, as drug listing on the RAMQ formulary following these agreements obliges private plans to provide similar reimbursement. **Without parallel negotiated price reductions, the unavoidable result is spending increases for private plans.**

EXAMPLE: HEPATITIS C DRUGS

In February 2017, pCPA announced it had reached agreements with three manufacturers of hepatitis C drugs Harvoni®, Sovaldi®, Daklinza™, Epclusa™, Sunvepra™, and Zepatier®. The pCPA's approach to hepatitis C treatment negotiations was guided by:

- The goal of providing treatment for patients regardless of genotype and disease severity;
- Financial affordability and sustainability;
- A fair approach in negotiating value among multiple drugs and manufacturers.

These agreements have led to changes in provincial coverage:

- Ontario eased access to these high-cost therapies, including Epclusa and Harvoni, through Limited Use (LU) coverage. By changing coverage from Exceptional Access Program (requiring a tedious, lengthy approval process) to LU (immediate online adjudication, as long as the physician writes the LU code on the prescription), this improved access by eliminating the reimbursement administration process, and shortened time to treatment. The published Drug Benefit Prices (DBP) represent a discount of approximately 5% over previous pricing. This reduction, though welcome, is relatively insignificant in overall spending terms given the typical therapy cost of close to $67,000 per patient.
- British Columbia expanded its criteria in March 2017 to provide coverage to more patients living with hepatitis C. Starting in 2018-2019, PharmaCare will provide coverage for any British Columbian living with chronic hepatitis C, regardless of the type or severity of their disease.

More provinces are expected to announce expanded coverage for these medications throughout 2017.

Facilitated access to provincial coverage could result in lower spending for private plans if claims are well integrated. On the other hand, easier prescribing could influence prescribing behaviour, resulting in a hike in prescription volume that drives utilization growth and spending increases.

MARKET FACTORS

2016 FIRST-TIME GENERIC AND BIOSIMILAR INTRODUCTIONS

The brand name drugs for which patents expired in 2016 represent only 3.4% of overall spending, further evidence we have reached the end of the "patent cliff" that has mitigated spending increases in recent years.

Tightly managed plans can capture savings on the introduction of new generics within the traditional drug space, as these are generally interchangeable. To do so, plans should ensure they are using a mandatory generic substitution plan that reimburses only the lower-cost, clinically effective generic alternative.

Compared to prior years, 2016 also saw a high number of specialty drugs come off patent. Copies of nonbiologic specialty medications such as Ziagen® are generics that are typically interchangeable with the reference brand. However, copies of biologic specialty medications such as Enbrel® are biosimilars that are not interchangeable with the reference brand. A new prescription for the biosimilar is required in order to dispense this lower-cost alternative. Overall, increasing availability of biosimilars can generate savings through a combination of product listing agreements on the reference product and the uptake of the lower-cost biosimilar.

CATEGORY	CHEMICAL NAME	REFERENCE BRAND NAME DRUG	COMMON INDICATION	% OF TOTAL SPEND IN 2016
TRADITIONAL	escitalopram	Cipralex Meltz®	Depression	0.01%
	darifenacin	Enablex®	Kidney/Bladder disease	0.01%
	gatifloxacin	Zymar™	Eye disease, Misc.	0.02%
	tadalafil	Cialis®	Erectile dysfunction	0.35%
	anidulafungin	Eraxis®	Infections	N/A
	nitric oxide	Inomax®	Respiratory disease	N/A
	duloxetine	Cymbalta®	Depression	1.35%
	paliperidone	Invega®	Mental disorders	0.02%
	oseltamivir	Tamiflu®	Infections	0.03%
SPECIALTY	abacavir	Ziagen®	HIV/AIDS	0.01%
	abacavir/lamivudine	Kivexa®	HIV/AIDS	0.16%
	etanercept	Brenzys™ (biosimilar of Enbrel)	Inflammatory conditions	1.44%
	temsirolimus	Torisel™	Cancer	N/A
	pemetrexed	Alimta®	Cancer	0.00%
	miglustat	Zavesca®	Rare disease	0.00%
	zidovudine	Retrovir® (AZT)	HIV/AIDS	0.00%

2016 NEW BRAND APPROVALS
(In alphabetical order of common indications)

Newly approved medications will continue to drive increases in traditional and specialty drug spending. Medical advancements have made new therapeutic options available for chronic conditions, such as biologic Cinqair™ for treatment of asthma and biologic Praluent™ for high cholesterol.

CATEGORY	CHEMICAL NAME	BRAND NAME	COMMON INDICATION
TRADITIONAL	bepotastine	Bepreve™	Allergy
	bilastine	Blexten™	Allergy
	olopatadine	Pazeo®	Allergy
	rupatadine	RupaII™	Allergy
	levonorgestrel releasing IUS	Kyleena®	Birth control
	edoxaban tosylate	Lixiana®	Cardiovascular disease
	vorapaxar	Zontivity™	Cardiovascular disease
	canagliflozin / metformin	Invokamet®	Diabetes
	empagliflozin/metformin	Synjardy™	Diabetes
	linagliptin-empagliflozin	Glyxambi™	Diabetes
	saxagliptin-dapagliflozin	Qtern®	Diabetes
	gadoterate meglumine	Dotarem	Diagnostic agents
	ciprofloxacin-fluocinolone acetonide	Otixal™	Ear, nose, throat disorders
	latanoprost	Monoprost®	Eye disease (glaucoma)
	travoprost	Izba™	Eye disease (glaucoma)
	apomorphine	Movapo™	High blood pressure
	perindopril arginine/amlodipine	Viacoram®	High blood pressure
	budenoside	Cortiment®	Inflammatory bowel disease
	finafloxacin	Xtoro™	Inflammatory bowel disease
	betamethasone-calciprotriol	Enstilar™	Narcotic antagonists
	naloxone HCl	S.O.S. Naloxone Hydrochloride	Narcotic antagonists
	brivaracetam	Brivlera™	Neurological disorders
	human normal immune globulin	Panzyga®	Preventative vaccines
	vitamin A (all-trans-retinyl palmitate) and vitamin E (all-rac-alpha-tocopheryl acetat)	Vitamin A and Vitamin E Oral Liquid Preparation	Skin conditions
	eszopiclone	Lunesta™	Sleep
SPECIALTY	botulism antitoxin heptavalent	BAT™	Antidotes/Chelating agents
	deferasirox	Jadenu®	Antidotes/Chelating agents
	idarucizumab	Praxbind™	Antidotes Chelating agents
	sugammadex sodium	Bridion™	Antidotes/Chelating agents
	reslizumab	Cinqair™	Asthma/COPD
	albutrepenonacog alfa	Idelvion™	Blood disorders
	antihemophilic factor (recombinant), (octocog alfa)	Kovaltry™	Blood disorders
	antihemophilic factor (recombinant), pegylated	Adynovate	Blood disorders
	alectinib	Alecensaro™	Cancer
	cobimetinib	Cotellic®	Cancer
	daratumumab	Darzalex™	Cancer
	elotuzumab	Empliciti™	Cancer
	ixazomib citrate	Ninlaro™	Cancer
	olaparib	Lynparza™	Cancer
	osimertinib mesylate	Tagrisso™	Cancer
	palbociclib	Ibrance™	Cancer
	venetoclax	Venclexta™	Cancer
	ivacaftor / lumacaftor	Orkambi™	Cystic fibrosis
	asunaprevir	Sunvepra™	Hepatitis C
	elbasvir / grazoprevir	Zepatier®	Hepatitis C
	sofosbuvir-velpatasvir	Epclusa™	Hepatitis C
	alirocumab	Praluent™	High cholesterol
	emtricitabine/tenofovir alafenamide	Descovy™	HIV/AIDS
	zidovudine/lamivudine/nevirapine	Apo-Zidovudine-Lamivudine-Nevirapine	HIV/AIDS
	ixekizumab	Taltz™	Inflammatory conditions
	daclizumab beta	Zinbryta™	Multiple sclerosis
	selexipag	Uptravi®	Pulmonary hypertension
	alpha-1 proteinase inhibitor	Zemaira®	Rare disease
	glycerol phenylbutyrate	Ravicti™	Rare disease
	nitisinone	Orfadin/MDK-Nitisinone	Rare disease

> TIGHTLY MANAGED PLANS CAN CAPTURE SAVINGS ON THE INTRODUCTION OF NEW GENERICS WITHIN THE TRADITIONAL DRUG SPACE, AS THESE ARE GENERALLY INTERCHANGEABLE.

2016 NEW INDICATION APPROVALS
(In alphabetical order of common indications)

Expanding indication approvals in 2016, particularly with specialty medications, means continued increases in utilization and spending.

CATEGORY	BRAND NAME	CHEMICAL NAME	COMMON INDICATION
TRADITIONAL	Octagam®10%	immune globulin (human)	Blood disorders
	Brilinta®	ticagrelor	Cardiovascular disease
	Xigduo®	dapagliflozin/metformin	Diabetes
	Jardiance™	empagliflozin	Diabetes
	Vyvanse®	lisdexamfetamine dimesylate	Eating disorder
	Ciloxan®	ciprofloxacin	Eye disease, Misc.
	Visanne®	dienogest	Hormone replacement
	Arepanrix™ H5N1	influenza H5H1 vaccine	Preventative vaccines
	Synflorix®	pneumococcal 10-valent conjugate vaccine	Preventative vaccines
SPECIALTY	Alprolix®	coagulation factor IX (recombinant), Fc fusion protein	Blood disorders
	Rixubis	nonacog gamma	Blood disorders
	Keytruda®	pembrolizumab	Cancer
	Revlimid®	lenalidomide	Cancer
	Opdivo®	nivolumab	Cancer
	Afinitor®	everolimus	Cancer
	Dysport™	abobotulinumtoxinA	Cosmetic agents
	Somavert™	pegvisomant	Endocrine/Metabolic disorders
	Daklinza™	daclatasvir	Hepatitis C
	Harvoni®	sofosbuvir-ledipasvir	Hepatitis C
	Galexos®	simeprevir	Hepatitis C
	Truvada®	emtricitabine/tenofovir disoproxil fumarate	HIV/AIDS
	Entyvio™	vedolizumab	Inflammatory bowel disease
	Humira®	adalimumab	Inflammatory conditions
	Stelara®	ustekinumab	Inflammatory conditions
	Cosentyx®	secukinumab	Inflammatory conditions
	Inflectra®	infliximab	Inflammatory conditions
	Simponi®	golimumab	Inflammatory conditions
	Remsima™	infliximab	Inflammatory conditions
	Volibris®	ambrisentan	Pulmonary hypertension
	Esbriet®	pirfenidone	Respiratory disease

POSSIBLE NEAR-TERM APPROVALS OF NEW BRANDS UNDER HEALTH CANADA REVIEW (In alphabetical order of common indications)

If they are approved, these brands will mean further increases in future spending.

CATEGORY	CHEMICAL NAME	COMMON INDICATION
TRADITIONAL	dermatophagoides farinae extract - dermatophagoides pteronyssinus extract	Allergies
	fluticasone propionate	Asthma/COPD
	fluticasone proprionate - salmeterol xinafoate	Asthma/COPD
	salbutamol sulfate	Asthma/COPD
	defibrotide	Cardiovascular disease
	vernakalant hydrochloride	Cardiovascular disease
	fluoxetine hydrochloride	Depression
	human insulin (recombinant)	Diabetes
	insulin degludec	Diabetes
	insulin lispro	Diabetes
	lixisenatide	Diabetes
	iodine	Diagnostic agents
	florbetaben (18f)	Diagnostic agents
	cyclosporin	Eye disease, Misc.
	lifitegrast	Eye disease, Misc.
	netupitant, palonosetron hydrochloride	Gastrointestinal
	alvimopan	Gastrointestinal
	eluxadoline	Gastrointestinal
	glycopyrrolate	Gastrointestinal
	cinnarizine, dimenhydrinate	Gastrointestinal
	flibanserin	Gynecologic misc.
	prasterone	Hormone replacement
	cefixime	Infections
	ozenoxacin	Infections
	mesalazine	Inflammatory bowel disease
	brexpiprazole	Mental disorders
	buprenorphine hydrochloride	Pain, narcotic analgesics
	oxycodone	Pain, narcotic analgesics
	neisseria meningitidis group b recombinant lipidated protein 2086 subfamilies a, b	Preventative vaccines
	varicella-zoster virus glycoprotein e (ge)	Preventative vaccines
	nusinersen	Rare disease
	suvorexant	Sedative/Hypnotic
	lorcaserin hydrochloride	Weight loss

CATEGORY	CHEMICAL NAME	COMMON INDICATION
SPECIALTY	ferric derisomaltose	Blood disorders
	iron dextran	Blood disorders
	fibrinogen (human)	Blood disorders
	von willebrand factor (human)	Blood disorders
	C1 esterase inhibitor (human)	Blood disorders
	atezolizumab	Cancer
	midostaurin	Cancer
	necitumumab	Cancer
	pegaspargase	Cancer
	tenofovir alafenamide hemifumarate	HIV/AIDs
	peramivir	Infections
	follitropin delta	Infertility
	baricitinib	Inflammatory conditions
	brodalumab	Inflammatory conditions
	etanercept	Inflammatory conditions
	guselkumab	Inflammatory conditions
	mercaptamine bitartrate	Kidney/Bladder disease
	obeticholic acid	Liver disease
	ocrelizumab	Multiple sclerosis
	romosozumab	Osteoporosis/Skeletal disorder
	anthrax immunoglobulin (human)	Preventative vaccines
	immune globulin (human)	Preventative vaccines
	eliglustat tartrate	Rare disease
	migalastat hydrochloride	Rare disease

Reference: Government of Canada, Drug and health product submissions under review (SUR), website.

POSSIBLE NEAR-TERM APPROVALS OF NEW INDICATIONS UNDER HEALTH CANADA REVIEW
(In alphabetical order of common indications)

If approved, new indications for existing medications will increase utilization of the following drugs.

CATEGORY	CHEMICAL NAME	BRAND NAME	COMMON INDICATION
TRADITIONAL	glycopyrronium bromide - indacaterol maleate	Seebri® Breezhaler®	Asthma/COPD
	nadroparin calcium	Fraxiparine®	Cardiovascular disease
	tinzaparin sodium	Innohep®	Cardiovascular disease
	canagliflozin	Invokana®	Diabetes
	empagliflozin	Jardiance™	Diabetes
	linagliptin	Trajenta®	Diabetes
	linagliptin - metformin	Jentadueto™	Diabetes
	liraglutide	Victoza®	Diabetes
	mifepristone - misoprostol	Mifegymiso	Gynecologic misc.
	aripiprazole	Abilify®	Mental disorders
	lurasidone	Latuda®	Mental disorders
	lacosamide	Vimpat®	Neurological disorders
	rufinamide	Banzel®	Neurological disorders
	haemagglutinin-strain a(h1n1) - haemagglutinin-strain a(h3n2)	Fluviral®	Preventative vaccines
	pneumococcal polysaccharide	Prevnar®	Preventative vaccines

> EXPANDING INDICATION APPROVALS IN 2016, PARTICULARLY WITH SPECIALTY MEDICATIONS, MEANS CONTINUED INCREASES IN UTILIZATION AND SPENDING.

CATEGORY	CHEMICAL NAME	BRAND NAME	COMMON INDICATION
SPECIALTY	omalizumab	Xolair®	Asthma/COPD
	eltrombopag olamine	Revolade®	Blood disorders
	eptacog alfa	Niastase®	Blood disorders
	C1 esterase inhibitor (human)	Cinryze®	Blood disorders
	blinatumomab	Blincyto™	Cancer
	crizotinib	Xalkori®	Cancer
	dabrafenib	Tafinlar®	Cancer
	daratumumab	Darzalex™	Cancer
	eribulin mesylate	Halaven®	Cancer
	erlotinib hydrochloride	Tarceva®	Cancer
	lenvatinib mesylate	Lenvima™	Cancer
	nivolumab	Opdivo®	Cancer
	palbociclib	Ibrance™	Cancer
	panitumumab	Vectibix®	Cancer
	pembrolizumab	Keytruda®	Cancer
	thioguanine	Lanvis®	Cancer
	trametinib	Mekinist®	Cancer
	fulvestrant	Faslodex®	Cancer
	leuprolide acetate	Lupron®	Cancer
	apixaban	Eliquis®	Cardiovascular disease
	ivacaftor - lumacaftor	Orkambi™	Cystic fibrosis
	ranibizumab	Lucentis®	Eye disease, Macular degeneration
	ledipasvir, sofosbuvir	Harvoni®	Hepatitis C
	ombitasvir, paritaprevir, ritonavir	Norvir®	Hepatitis C
	simeprevir	Galexos®	Hepatitis C
	sofosbuvir- velpatasvir	Epclusa™	Hepatitis C
	cobicistat- elvitegravir- emtricitabine-tenofovir alafenamide hemifumarate	Tybost®/Vitekta™/ Emtriva®/Viread®	HIV/AIDS
	adalimumab	Humira®	Inflammatory conditions
	anakinra	Kineret®	Inflammatory conditions
	etanercept	Enbrel®	Inflammatory conditions
	golimumab	Simponi®	Inflammatory conditions
	immune globulin (human)	Iveegam	Preventative vaccines
	haemagglutinin-strain b	Agriflu®	Preventative vaccines

Reference: Government of Canada, Drug and health product submissions under review (SUR), website.

ABOUT EXPRESS SCRIPTS CANADA®

Express Scripts Canada transforms the way organizations and employees think about and participate in their drug benefit plan. Express Scripts Canada provides pharmacy services to thousands of Canadian patients. Through its proprietary consumer intelligence, clinical expertise, and patients-first approach, Express Scripts Canada promotes better health decisions for plan members, while managing and reducing drug benefit costs for plan sponsors. Express Scripts Canada is indirectly owned by Express Scripts Holding Company.

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EXPRESS SCRIPTS CANADA is committed to following, promoting and implementing sustainable practices. We apply global sustainability principles to the way we do business, and to the ways we fulfill the needs of clients, patients and employees. Express Scripts Canada is committed to proactively balancing economic development with environmental stewardship and social development, and operates its business in a manner that respects the environment and conserves natural resources.

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