EXPRESS SCRIPTS CANADA **2012 DRUG TREND REPORT**

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INTRODUCTION

It should come as no surprise to anyone that the Canadian health-care system is in crisis. Spiraling costs have compromised the ability of governments to provide sustainable, reliable, accessible, and affordable care for all Canadians.

The prescription drug benefit is a single, yet significantly large piece in this increasingly complex puzzle. The pharmacy landscape in 2012 remained dynamic and complex. The impact of patent expiries of multiple blockbuster drugs and the provincial generic price reforms notwithstanding, plan sponsors that provide health benefits to their employees must still deal with steadily rising costs related to the delivery and maintenance of the prescription drug benefit.

Clearly, one omnipresent reality remains for private plan sponsors – a huge amount of money continues to be wasted each year on the prescription drug spend. Although generic fill rates increased modestly in the past year, switches to lower-cost, clinically or therapeutically equivalent generics should, and must, increase. Waste caused by drug mix, channel mix and non-adherence continues to be an onerous weight on the shoulders of the Canadian health-care system.

Over the past few years, research by our parent, Express Scripts, has repeatedly demonstrated that better care and zero waste often go hand in hand: the most effective care often costs the least. Thus the challenge is not simply to make these goals compatible, but rather to do so in a manner that is acceptable to both plan members and plan sponsors. Express Scripts research has further revealed that the biggest gap is not between what plan sponsors want and what patients want, but rather between what patients want and patients do. So the real gap is between good intentions and observed behaviour.

It has become clear that Canada needs proven methods for providing quality health care at an affordable cost. Express Scripts Canada is committed to the development of innovative ways to further improve the quality of health care for millions of Canadians. Our core commitment to deliver benefits that achieve optimal health outcomes at the lowest cost is still at the centre of everything we do.

John Herbert
Director, Pharmacy & Clinical Services

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TREND OVERVIEW

TREND OVERVIEW

Plan sponsors that provide health benefits to their employees continue to deal with a vibrant pharmacy landscape that presents a myriad of challenges. Patients and payers often struggle to balance health-care needs and costs with other priorities. In particular, Specialty medications, while holding great promise for improved health, continue to increase in cost.

In 2012 – for the first time since 2002 when Express Scripts Canada first began to report on drug trend – a negative overall trend of 0.73% was recorded. This negative trend was driven by lower costs for Traditional drugs as a result of multiple patent expiries and provincial drug-price reforms. However, this flat trend will increase once again in the near future.

High-cost Specialty drugs now dominate both new drug approvals and pipelines. Express Scripts Canada predicts that the Specialty drug category will continue to experience double-digit growth in the near-term which, in turn, will likely result in an increase in the overall trend. To realize the goal of keeping prescription drug plans sustainable while optimizing patient health outcomes, all stakeholders – patients, health-care providers and private payers – must act now to reduce pharmacy-related waste.

TREND FOR DRUG SPEND FLATTENING… FOR THE TIME BEING

- The drug patent cliff and government pricing relief masked a significant increase in Specialty drug spend in 2012

POOR DECISIONS DRIVE MORE THAN $5 BILLION IN WASTE PER YEAR

- Waste = Spending More Without Improving Health Outcomes
- "Gaps in Care" create health-related waste for private payers

INNOVATIVE SOLUTIONS ARE AVAILABLE TO DRIVE BETTER DECISIONS

- Better decisions can lead to lower costs (reduce waste) and healthier outcomes (close gaps in care)

A NOTE ABOUT TREND:

ONE WORD, TWO APPROACHES…

Express Scripts Canada's drug-trend analysis is based on a retrospective methodology and, therefore, will differ from an insurance carrier's health-plan premium increase, which is based on a prospective methodology. An insurance carrier's prospective renewal calculation incorporates a drug plan's specific claims experience, changes in the proportion of eligible members with a claim, demographic changes, anticipated changes in the future mix of drugs, the erosion of member portion, a risk component, and 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 of an Extended Health Care (EHC) plan, of which prescription drugs are only one component.

In 2012 – for the first time since 2002 when Express Scripts Canada first began to report on drug trend – a negative overall trend of 0.73% was recorded

TERMINOLOGY USED IN THIS REPORT

- **Drug Trend:** Historical increase in cost allowable per claimant over the previous year
- **Cost Allowable:** Amount payable before member contribution
- **Claimant:** Each unique person who submits a prescription claim, including all dependents eligible for coverage under a plan member's health-benefits plan
- **Script:** Prescription or claim
- **Traditional Drugs:** Medications that are easy to self-administer, require less intensive clinical monitoring, and used to treat common medical conditions such as high cholesterol and high blood pressure
- **Specialty Drugs:** Injectable and non-injectable medications that are used to treat chronic, complex conditions such as rheumatoid arthritis, multiple sclerosis and cancer. These medications are usually costly, require special storage and handling, and need intensive clinical monitoring with frequent dosing adjustment

DRUG SPEND 2012

On a national basis, the average annual drug spend per claimant decreased 0.73% in 2012 to $755 per claimant, down $6 over the previous year. This modest decline is consistent with the flat trend of 0.5% recorded in 2011. It is a further reflection of the downward trend for Traditional drugs which, in part, is a result of the increased use of lower-cost generics. This downward trend was partially mitigated by the upward trend of Specialty drugs driven by the increased use of high-cost drugs, which will be thoroughly explored in this section.

FIGURE 1 | Increase in Drug Spend per Claimant
Trend Continues to Flatten...for the Time Being

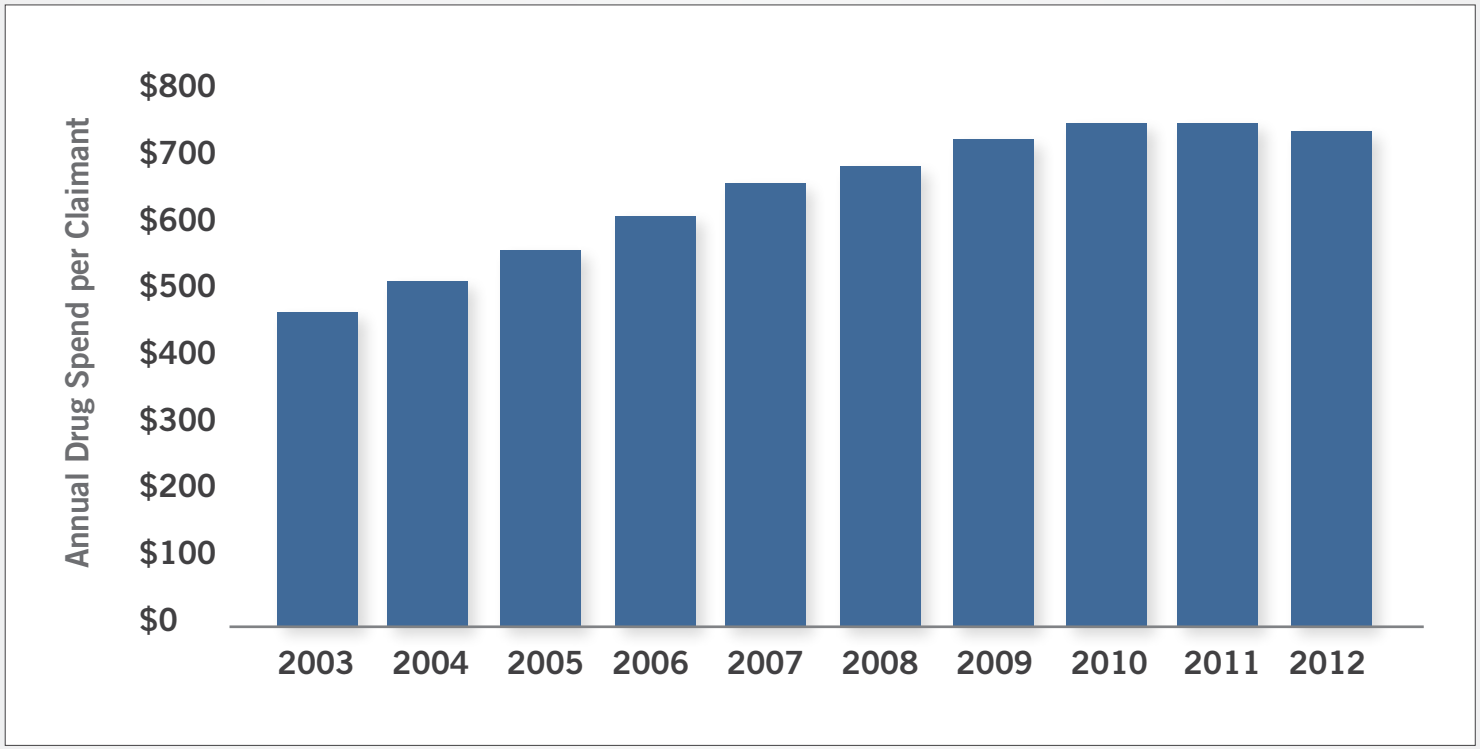
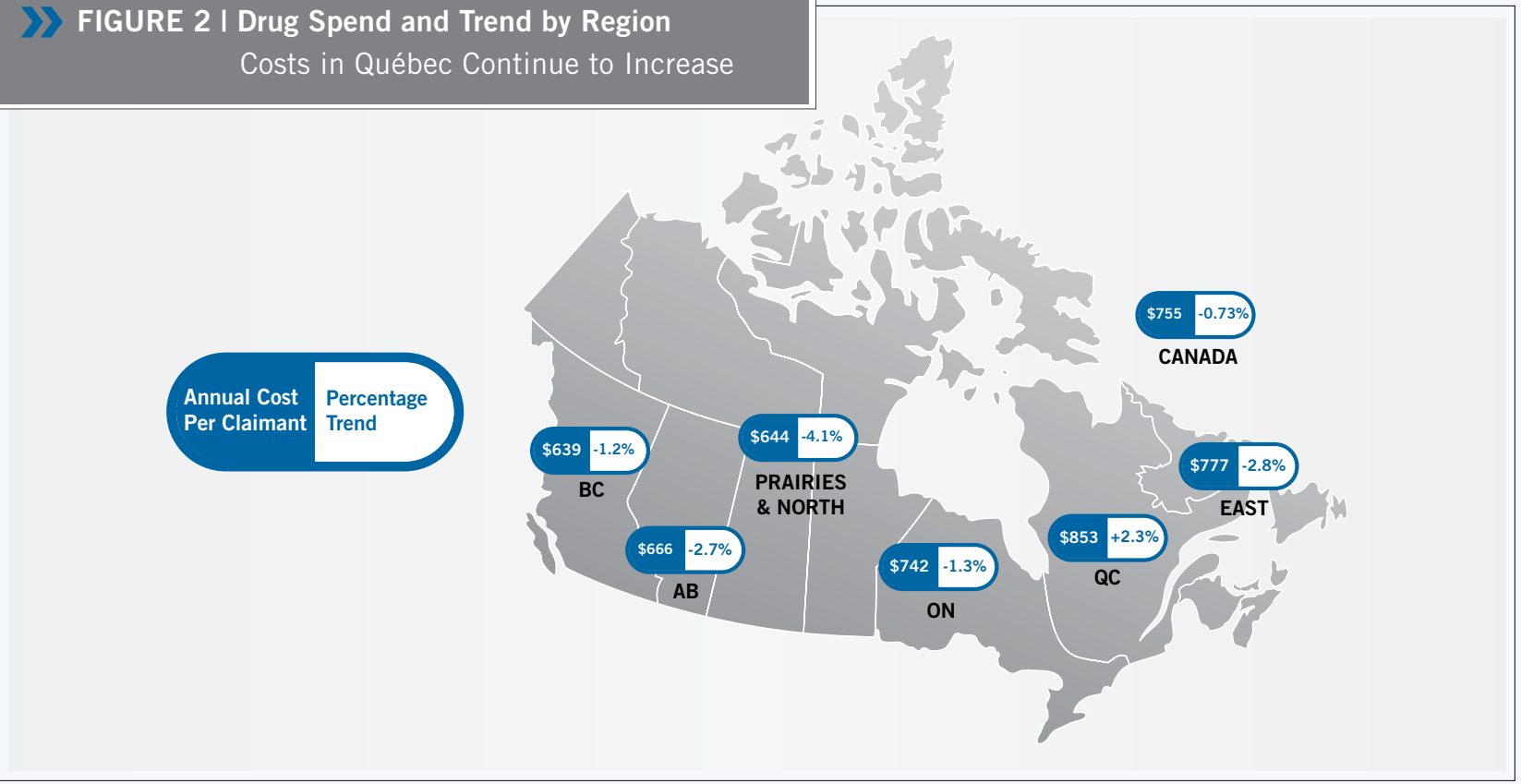


FIGURE 2 | Drug Spend and Trend by Region
Costs in Québec Continue to Increase



DRUG SPEND BY REGION

The patent expiries of multiple blockbuster drugs and generic price reforms initiated by many provinces were the drivers of the downward trend in drug spend across Canada. New Brunswick, Prince Edward Island, and Newfoundland & Labrador executed the first phase of their generic reforms in 2012; as such, these introductions had a sizeable impact on the decrease in trend of 2.8% for Atlantic Canada to $777. This compares with an upward trend of 1.9% to $799 in the preceding year. Similarly, in Ontario, the country's most populous province, the impact of generic price reforms led to a downward trend of 1.3% to $742, compared with $751 in 2011. Drug spend in the West (British Columbia, Alberta, and Prairies & North), at $639 to $666 per claimant, continued to be lower than in other provinces. This compared with $647 to $684 in 2011, and can be primarily attributed to the broader and more comprehensive public drug coverage available in the region. In Manitoba, for example, effective April 2012, the public plan provides coverage for all oral cancer medications. Conversely, although Québec lowered its generic prices to 25% of brand in April 2012, it was the only province to post an upward trend of 2.3% to $853. However, this was comparatively less than the trend of 5.2% in Québec during 2011. The difference in spend between the West and Québec has grown even wider over time. When comparing British Columbia and Québec, the difference increased from $165 per claimant in 2011 to $214 per claimant in 2012.

COMPONENTS OF DRUG TREND

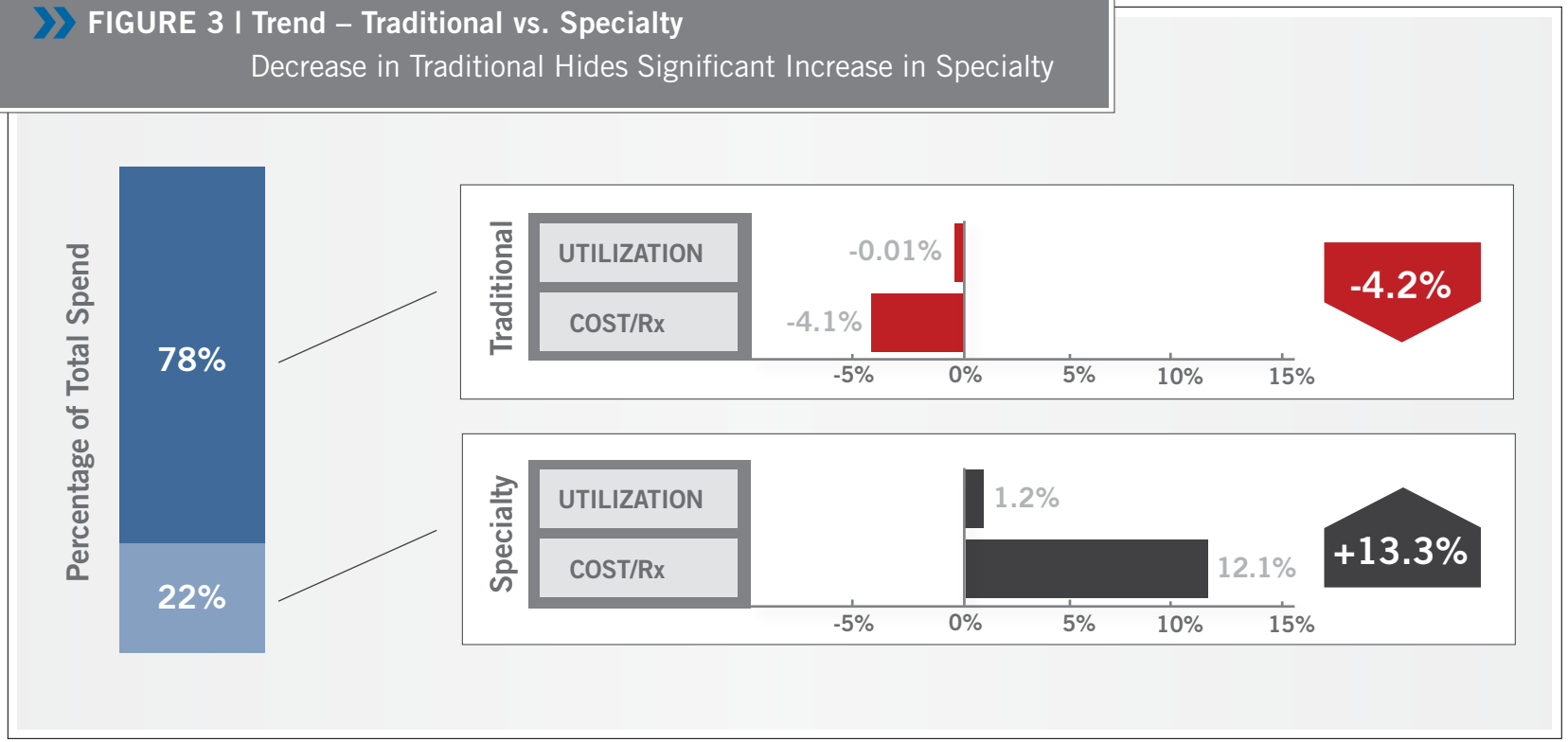
To get a better understanding on the drivers of the national drug trend, Express Scripts Canada has categorized and analyzed two groups of drugs – Traditional and Specialty.

Traditional drugs are defined as drugs used to treat common chronic medical conditions; they are relatively easy to administer and monitor, and often carry a relatively low cost. Examples include the 'statin' class for treating high cholesterol, to which Crestor® and Lipitor® belong, and 'water pills' for treating high blood pressure. Traditional drugs represent 98.8% of claims and 78% of spend.

Traditional drugs experienced a steeper downward trend of 4.2% in 2012, compared with 1.9% a year earlier. Over the past three years, the trend for Traditional drugs has been mitigated by a large number of patent expirations for blockbuster brand names. The precipice of this historic "patent cliff" was reached in 2012 when a number of generic alternatives to Crestor® (rosuvastatin) entered the marketplace. As a result, the cost per script has declined 4.1% in 2012, due not only to the availability of more generic medications, but also to continued lowering of generic drug costs due to provincial reforms. The use of Traditional drugs stayed relatively constant, with a very slight decrease of 0.01%, compared with a utilization increase of 1.9% in 2011.

FIGURE 3 | Trend – Traditional vs. Specialty

Decrease in Traditional Hides Significant Increase in Specialty



Specialty drugs are those used to treat chronic and complex conditions – regardless of dosage form. They are prescribed to treat myriad conditions, including such debilitating diseases as rheumatoid arthritis; complex diseases like cancer; rare conditions such as cystic fibrosis; and genetic diseases like Niemann–Pick disease. Complex and costly, Specialty drugs usually need special storage and handling. Therapies may require frequent dosing adjustments and intensive clinical monitoring.

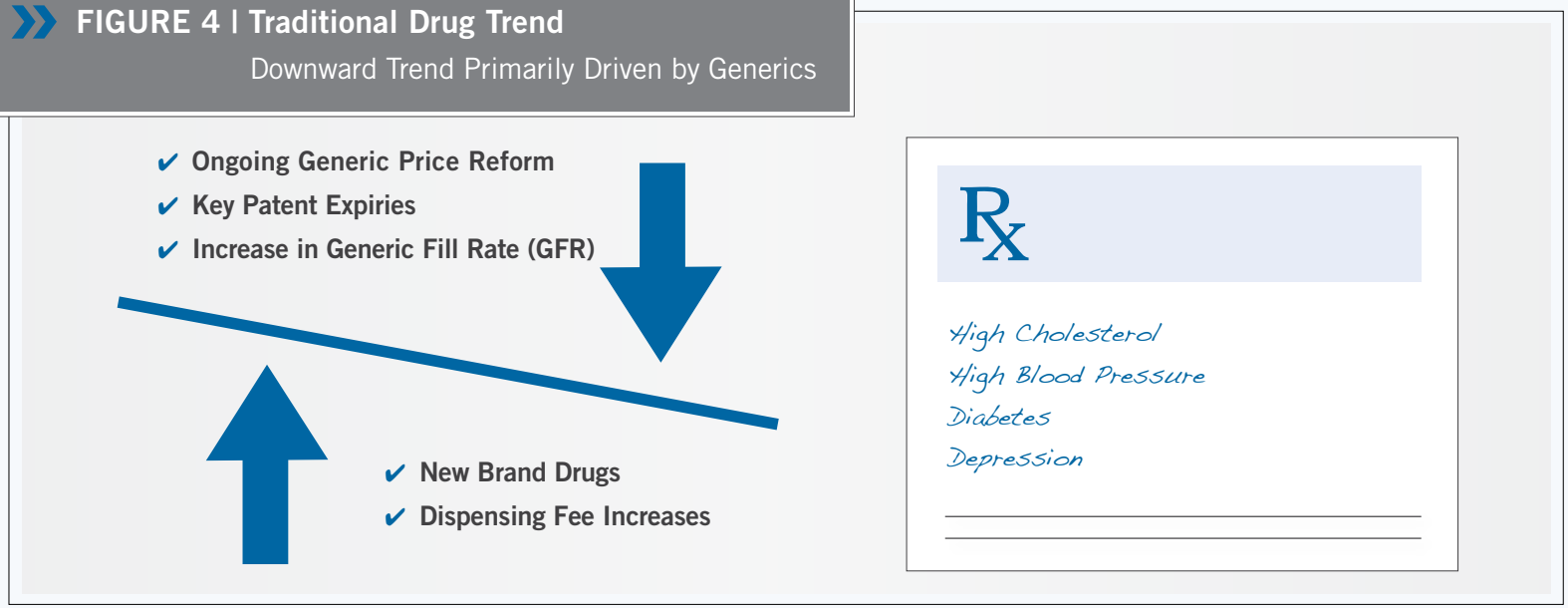
Specialty drugs represented 1.2% of claims in 2012, compared with 0.99% in the preceding year. In the past five years, for example, spend for Specialty drugs has grown from 13% of spend in 2007 to 22% of total spend in 2012.

Trend for Specialty drugs continues to climb; it has experienced double-digit growth since 2007. Most notably, Specialty drugs posted an increase in trend of 13.3% in 2012, compared with 12% in the year prior. Use of Specialty drugs increased 1.2% in 2012; by contrast, the cost per prescription (script) grew 12.1% in 2012, compared with 4.8% in 2011. The high cost per script and increase in utilization of Specialty drugs were the major driving forces in the increasing private drug spend over the past couple years.

TRADITIONAL DRUG TREND

In 2012, there were several factors that contributed to the downward trend for Traditional drugs. These included downward pressure on the cost per script due to a higher generic fill rate, as well as ongoing provincial generic price reforms. This downward pressure was partially offset by rising dispensing fees and approvals of new higher-cost brand-name drugs.

FIGURE 4 | Traditional Drug Trend
Downward Trend Primarily Driven by Generics



GENERIC FILL RATE

Generic fill rate (GFR) is defined as the percentage of total drug claims that are filled with generics; this continues to be a key metric for gauging the efficiency through which drug plans take advantage of the lowest-cost, clinically equivalent medications. All factors being equal, higher GFRs translate to lower costs and solid clinical outcomes. In 2012, a number of brand- name drugs went off patent, and generic alternatives were introduced to the market. Patent expiries of such highly used brands as Crestor®, Cozaar®, and Maxalt® helped drive up the national GFR by 2.6% to 53.4%. Although Québec has always had the lowest GFR in Canada, it had the greatest increase in GFR of 3.4% in 2012 and came closer to the national average. The abolishment of Québec's Best Available Price for 15 years (BAP-15 rule) – which stipulates that the province's public drug plan must reimburse brand-name drugs for 15 years after their listing on the formulary regardless of generic availability – is expected to further increase GFR in 2013 and beyond. A complete list of noteworthy first-time generics in 2012 appears in **Figure 6 | Noteworthy First-Time Generics in 2012**.

FIGURE 5 | Generic Fill Rate (GFR) on the Rise
All Regions Experience Increases

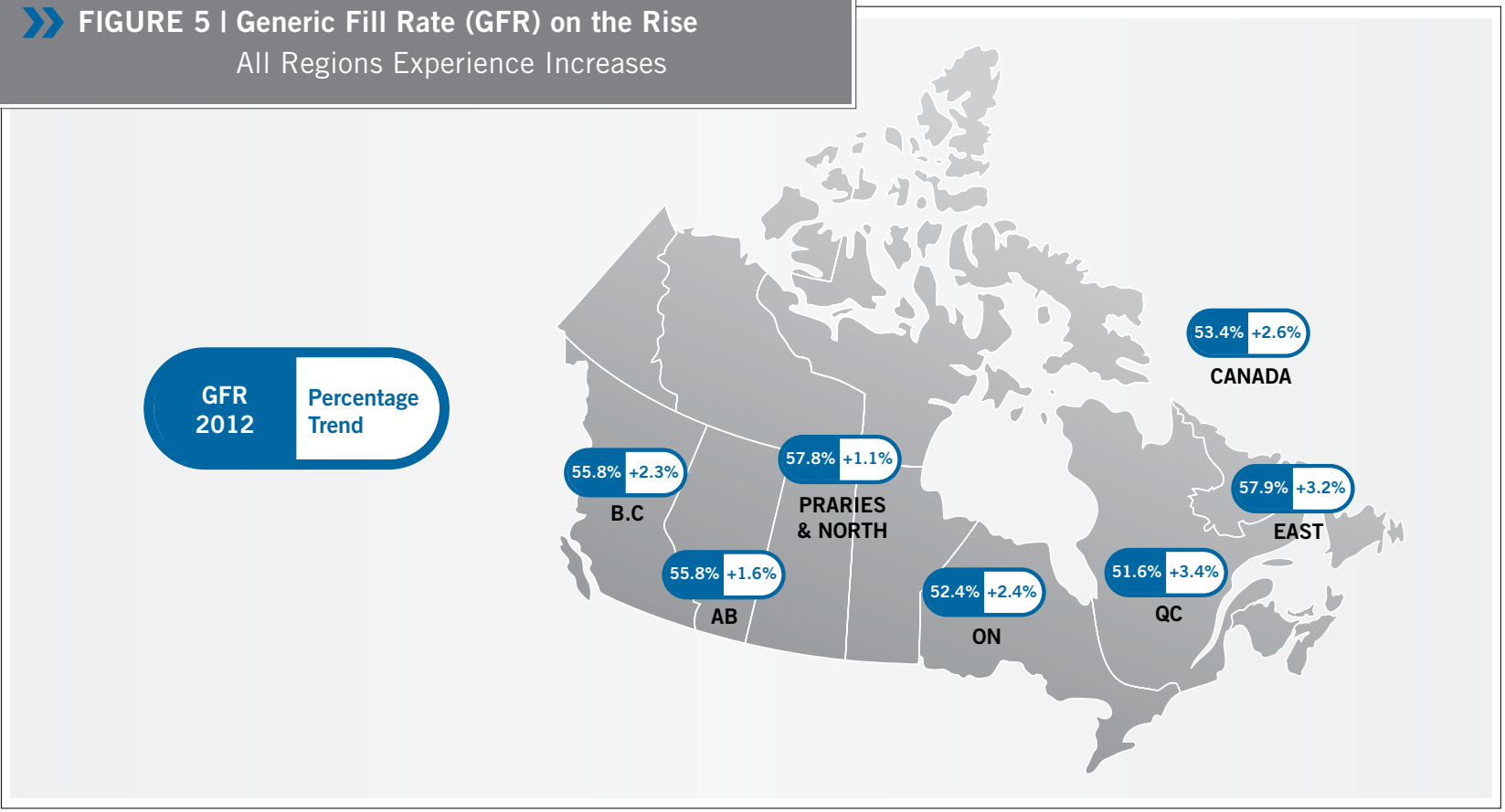


FIGURE 6 | Noteworthy First-Time Generics in 2012

Lower-Cost Alternatives for Plan Members

Brand Name	Generic Name	Route of Administration	Common Use(s)
Arimidex ®+	anastrozole	Oral	Breast Cancer
Malarone®	atovaquone-proguanil	Oral	Malaria Treatment And Prophylaxis
Bezalip ® SR	bezafibrate	Oral	High Cholesterol
Tracleer ®+	bosentan	Oral	Treatment Of Pulmonary Arterial Hypertension
Wellbutrin ® XL	bupropion	Oral	Antidepressant
Atacand ® Plus	candesartan/hydrochlorothiazide	Oral	High Blood Pressure
Aricept ®/Aricept RDT™	donepezil	Oral	Alzheimer's Disease
Baraclude™+	entecavir	Oral	Chronic Hepatitis B Infection
Lipidil EZ ®	fenofibrate [nanocrystal formulation]	Oral	High Cholesterol
3TC ®+	lamivudine	Oral	Treatment Of HIV Infection
Heptovir ®+	lamivudine hbv	Oral	Chronic Hepatitis B Infection
Combivir ®+	lamivudine-zidovudine	Oral	Treatment Of HIV Infection
Xalacom™	latanoprost/ timolol	Ophthalmic	Glaucoma
Cozaar®/Hyzaar ®	losartan/losartan and hydrochlorothiazide	Oral	High Blood Pressure
Merrem®	meropenem	Injection	Bacterial Infection
CellCept ®+	mycophenolate	Oral	Prevention Of Organ Rejection After Transplant
Patanol ®	olopatadine	Ophthalmic	Allergic Conjunctivitis
OxyContin ®	oxycodone	Oral	Chronic Pain
Rilutek ®+	riluzole	Oral	Amyotrophic Lateral Sclerosis
Maxalt®/Maxalt RPD ®	rizatriptan tablets/oral dissolving tablets	Oral	Migraines
Crestor ®	rosuvastatin	Oral	High Cholesterol
Viagra™	sildenafil	Oral	Erectile Dysfunction
Rapamune ®+	sirolimus	Oral	Prevention Of Renal Transplant Rejection
Micardis®/Micardis ® Plus	telmisartan/telmisartan and hydrochlorothiazide	Oral	High Blood Pressure
Temodal ®+	temozolomide	Oral	Cancer
Detrol®/Detrol LA™	tolterodine	Oral	Urinary Incontinence
Vfend™	voriconazole	Oral	Antifungal

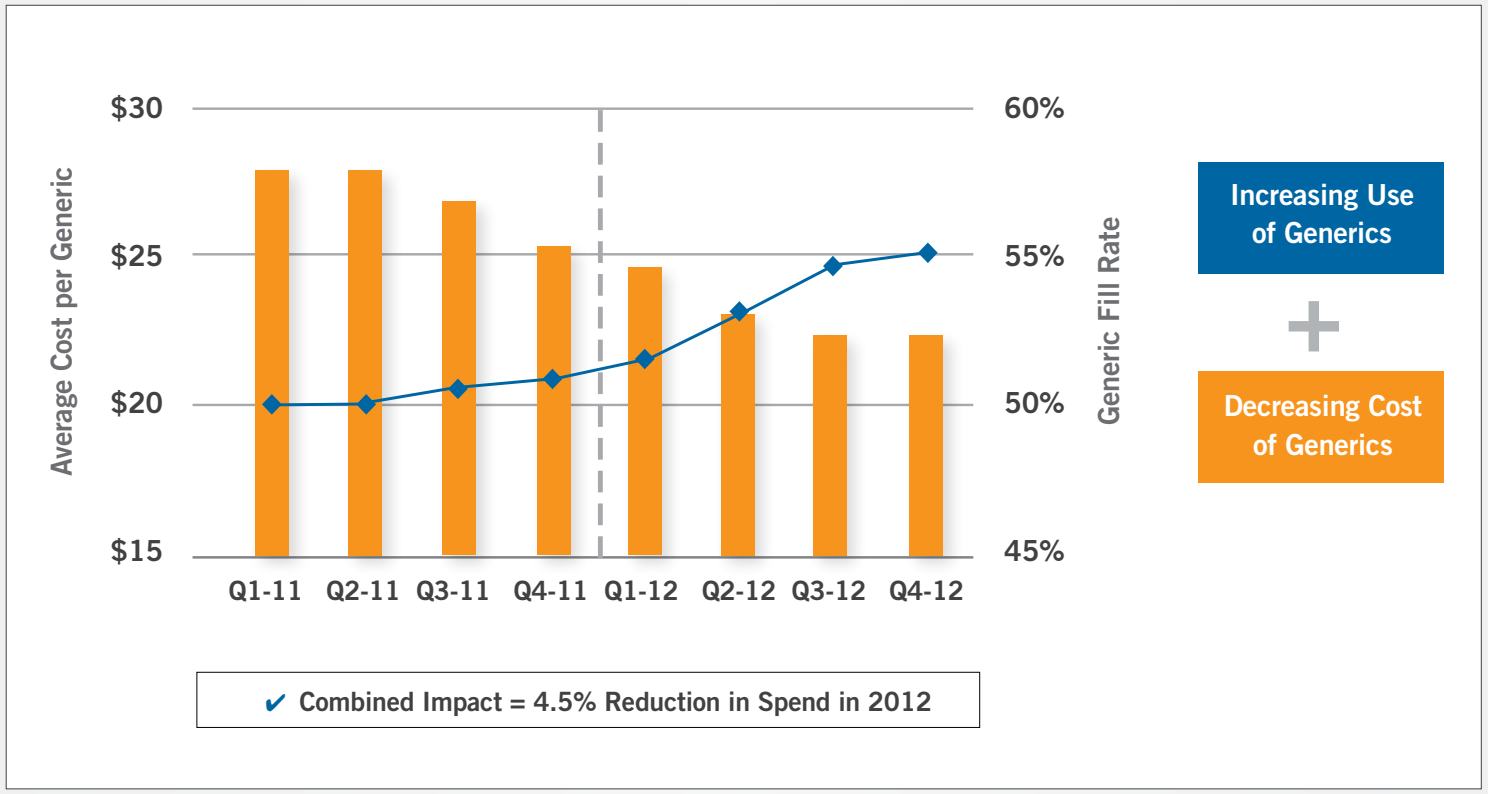
+ Denotes Specialty drug

PROVINCIAL GENERIC PRICE REFORMS

Since 2010, the provinces have taken a slightly different approach with respect to their implementation of drug-pricing reforms to reduce drug spend. Every province decreased generic drug prices in 2012. Ontario and Saskatchewan completed the last phase of their reforms, setting generic prices at 25% and 35% of brand respectively. New Brunswick, Prince Edward Island, and Newfoundland & Labrador, kicked off their first phase of reforms in the early part of the year – all of which expect to have their full programs in place by April 2013. Manitoba has lowered formulary generic prices to approximately 48% of brand, without a formal announcement and legislation of drug reform.

Provincial reforms have indeed lowered costs for generic drugs over time. Express Scripts Canada research showed that from the fourth quarter of 2010 to the first quarter of 2013, the average cost per generic prescription decreased 17.7% from $27 to $22. Clearly, the uses for generics, combined with the decreasing cost of generics, have led to a lower cost per script within the Traditional drug classes.

FIGURE 7 | Downward Pressure on Cost per Script
Impact of Patent Cliff and Government Pricing Relief



2013 and Beyond

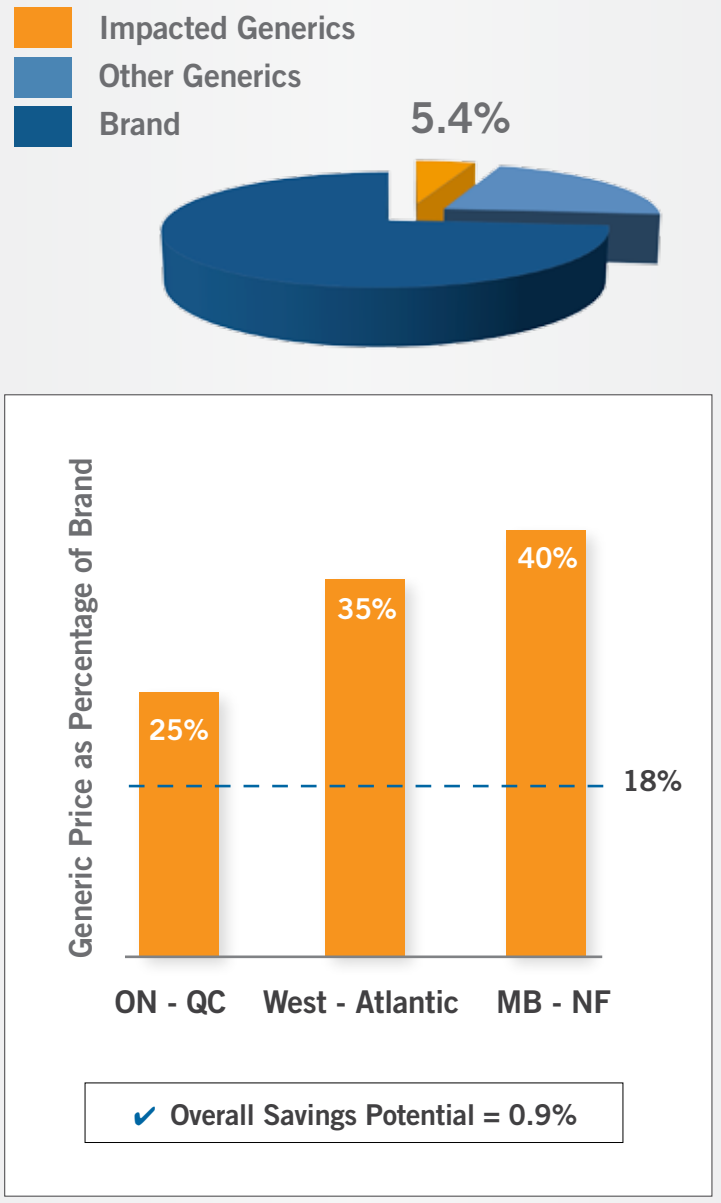
Express Scripts Canada anticipates that costs for generic drugs will continue to decrease throughout 2013. Express Scripts Canada further anticipates a more significant price drop after the decision by the Council of the Federation to set the price of six highly used generics at 18% of brand takes effect in April. Those six generics are:

- ✔ **Amlodipine** – indicated for the treatment of hypertension and other cardiovascular conditions
- ✔ **Atorvastatin** – indicated for the treatment of high cholesterol
- ✔ **Omeprazole** – indicated for the treatment of a variety of gastrointestinal conditions
- ✔ **Rabeprazole** – indicated for the treatment of a variety of gastrointestinal conditions
- ✔ **Ramipril** – indicated for the treatment of hypertension and other cardiovascular conditions
- ✔ **Venlafaxine** – indicated for the treatment of treating depression and other mental health conditions

It is also important to note that these six generics contributed 5.4% to overall spend in 2012. By lowering their prices from the current price points to 18%, Express Scripts Canada calculates an estimated savings of 0.9% for all private payers across Canada in 2013.

In March 2013, the Alberta government announced that effective May 1, 2013, prices for all generic drugs will be further reduced from 35% to 18% of brand prices. Express Scripts Canada's analysis shows that 37% of all drug claims from Alberta were filled with generics listed on its provincial formulary in 2012 and, as

FIGURE 8 | Further Price Cuts to Generics Expected
Impact in 2013 to Vary by Region

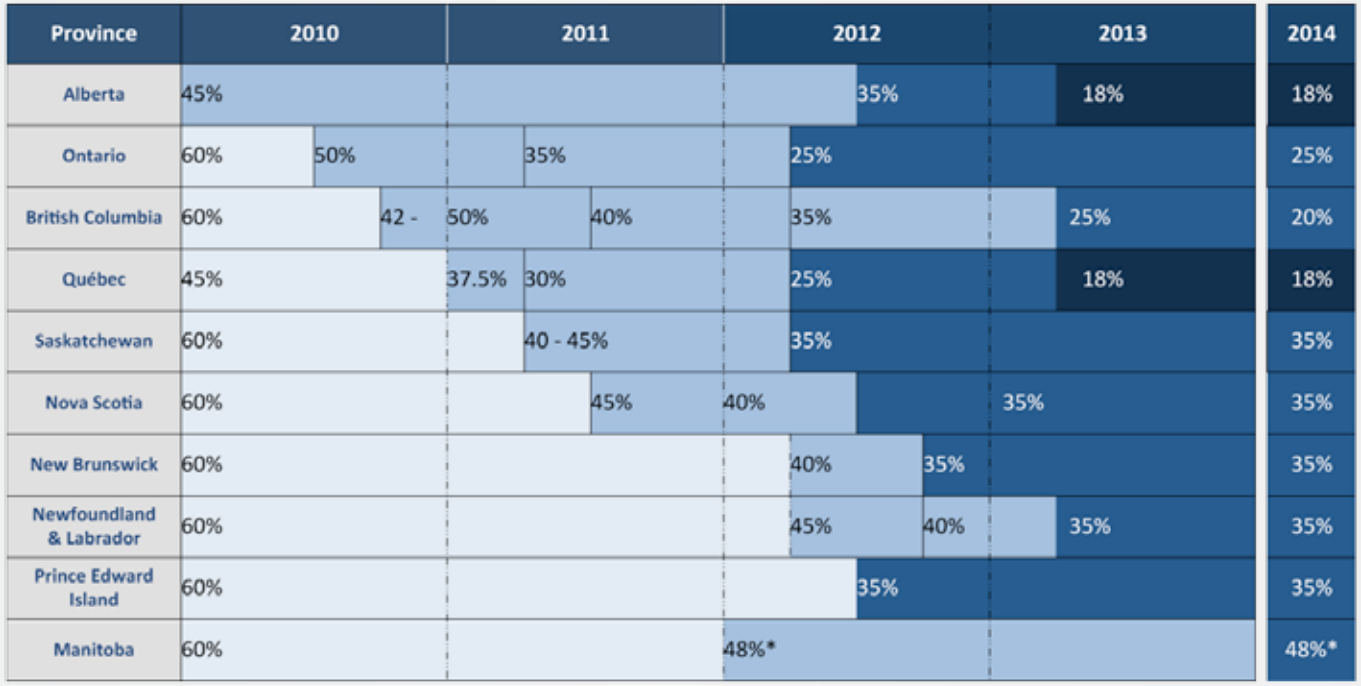


such, would be subject to the 35% pricing rule. With the assumption that these generics would be lowered from 35% to 18% of brand prices – and the allowable mark-up and dispensing fee stay unchanged – the potential savings for overall spend in Alberta in 2013 will be 5.6%. Given legislation in Québec that stipulates that drug prices in the province must match the lowest price on any provincial formulary, Québec should, therefore, also benefit from this change in pricing.

Looking ahead, Express Scripts Canada believes that it will be interesting to see if other provinces choose to follow suit with similar price reductions. British Columbia, for example, is scheduled to lower its generic prices to 20%, effective April 1, 2014, and it is believed there is a good chance that it may adjust prices even further.

Scheduled price reforms for each province are summarized in **Figure 9 I Formulary Generic Prices as Percentage of Brand.**

FIGURE 9 I Formulary Generic Prices as Percentage of Brand
Costs Should Continue to Decrease in 2013



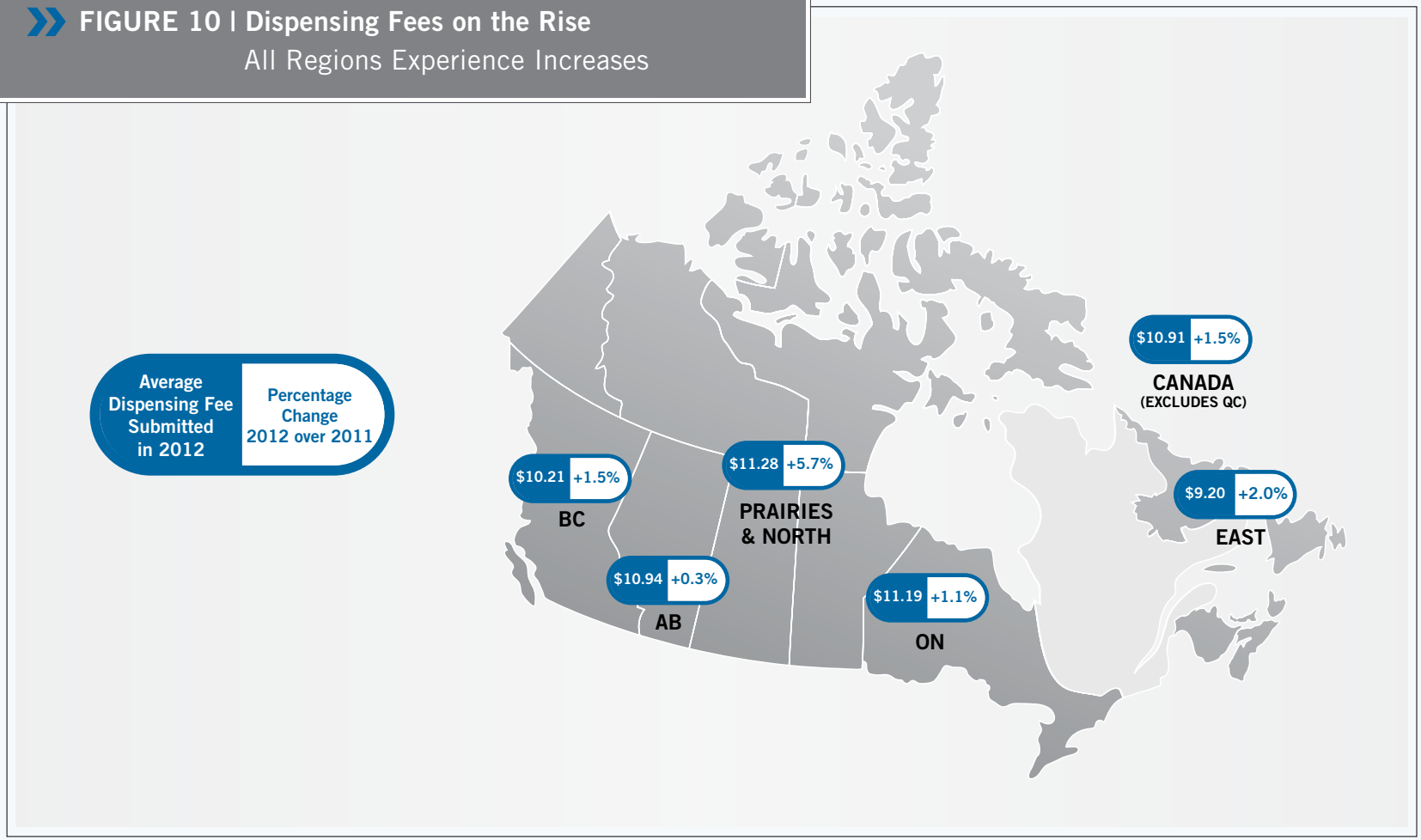
* Express Scripts Canada Analysis

DISPENSING FEE INFLATION

Increases to dispensing fees across Canada continued in 2012, which gently counterbalanced the downward trend that lowered the average cost per prescription. From a regional perspective, the Prairies & North again posted the highest increase of 5.7% for the average fee submitted; in doing so, the region also overtook Ontario for the highest average dispensing fee, at $11.28, in Canada.

Ontario, which now has the second-highest average dispensing fee at $11.19, had a greater fee inflation of 1.1% in 2012, compared with just 0.4% in 2011. The East, at $9.20 retained the distinction of having the lowest average dispensing fee, despite a moderate increase of 2% last year. By comparison, fee inflation in both British Columbia and Alberta slowed to 1.5% and 0.3% respectively in 2012, compared with 3.7% and 1.2% respectively in 2011.

FIGURE 10 | Dispensing Fees on the Rise
All Regions Experience Increases



TRADITIONAL DRUG APPROVALS

Although more of the drug-development activity in Canada has trended toward Specialty, a number of Traditional drugs received approval in 2012. Many of these new arrivals, however, are considered product-line extensions and/or "me-too" products. For example, Cipralex Meltz®, indicated for the treatment of mental-health conditions, is a new dosage form; it contains the same active ingredient and requires the same administration frequency of the existing brand, Cipralex®. Edarbi is considered a "me-too" product within the drug class of angiotensin receptor blockers (ARBs) for treating high blood pressure.

One of the noteworthy drugs to receive approval in 2012 is the anticoagulant, Eliquis™, which is indicated to prevent blood clotting in patients who have undergone elective total-hip or knee-replacement surgery, and to reduce the risk of stroke in patients with atrial fibrillation, the most common type of irregular heartbeat. The most widely used oral anticoagulant today is warfarin, but its use requires intensive blood monitoring to prevent a serious bleed. Other new drug alternatives similar to Eliquis™ are Xarelto® and Pradaxa™. Based on the pharmacology, ease of clinical monitoring, and clinical data of Eliquis™, it has the potential to be a best-in-class drug for conditions that affect thousands of Canadians.

Although more of the drug-development activity in Canada has trended toward Specialty, a number of new Traditional drugs received approval in 2012

FIGURE 11 | Traditional Drugs Approved in 2012

More Product-Line Extensions and "Me-Too" Products Entering Market

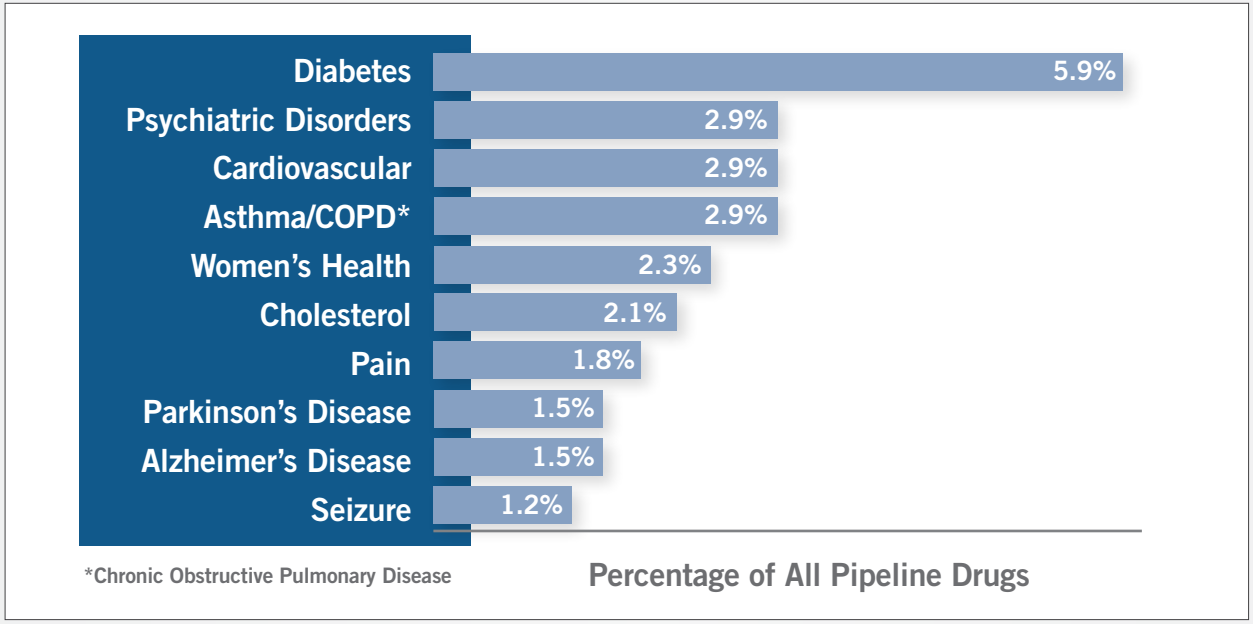
Brand Drug Name	Generic Name	Manufacturer	Indication(s)	Annual Ingredient Cost/Patient
Axiron®	testosterone	Eli Lilly Canada Inc.	Testosterone Deficiency	Pricing not available
Cambia®	diclofenac potassium	Takeda Pharmaceuticals America Inc.	Migraine	$270 - $540
Cipralex Meltz®	escitalopram	Lundbeck Canada Inc.	Depression/Anxiety/Obsessive Compulsive Behaviour	Pricing not available
Dificid™	fidaxomicin	Optimer Pharmaceuticals Inc.	Bacterial Infection	$2,240 (10-day treatment)
Divigel®	estradiol	Ferring Inc.	Hormonal Replacement for Menopause	$290
Edarbi	azilsartan	Takeda Pharmaceuticals America Inc.	Hypertension	$454
Edarbyclor	azilsartan/ chlorthalidone	Takeda Pharmaceuticals America Inc.	Hypertension	Pricing not available
Eliquis™	apixaban	Bristol Labs, division of Bristol-Myers Squibb	Thromboembolic Events Post-Surgery	$44 - $167 (post-surgery)
Epuris™	isotretinoin	Cipher Pharmaceuticals Limited	Acne	Pricing not available
Gelnique™	oxybutynin	Watson Laboratories Inc.	Overactive Bladder	$1,060
Komboglyze™	saxagliptin/metformin	Bristol Labs	Diabetes	Pricing not available
Latuda™	lurasidone	Sunovion Pharmaceuticals Canada Inc.	Schizophrenia	$1,400
Natazia®	estradiol/dienogest	Bayer Corporation	Birth Control	Pricing not available
Nucynta® IR	tapentadol	Janssen Ortho Inc.	Pain	$2,200 - $3,300
Onbrez® Breezhaler®	indacaterol	Novartis Canada Inc.	Chronic Obstructive Pulmonary Disease (COPD)	$800
Ondissolve™ ODF	ondansetron	Takeda Pharmaceuticals America Inc.	Nausea and Vomiting Due to Chemotherapy	Pricing not available
Opana® ER	oxymorphone	Valeant Canada limited	Pain	Pricing not available
Potiga™	retigabine (ezogabine)	Glaxosmithkline Inc.	Seizures	Pricing not available
Rapaflo™	silodosin	Watson Pharma Inc.	Benign Prostatic Hyperplasia	$670
Resotran™	prucalopride	Janssen	Constipation in Women	$780 - $1,260
Seebri® Breezhaler®	glycopyrronium bromide	Novartis Canada Inc.	COPD	Pricing not available
Toviaz™	fesoterodine	Genmed, a division of Pfizer Canada Inc.	Overactive Bladder	$940
Yaz® Plus	ethinyl estradiol/ drospirenone/ levomefolate calcium	Bayer Corporation	Birth Control	$220

TRADITIONAL DRUGS IN THE PIPELINE

Many industry insiders and researchers agree that while the pharmaceutical and biotechology sectors have numerous drugs under development, there is little chance that a new era of blockbuster drugs will arrive anytime soon to replace the blockbuster drugs that are currently losing patent protection in the Traditional drug category.

There is currently less focus on treating common Traditional conditions, such as cardiovascular disease, diabetes, psychiatric disorders, central nervous system disorders, and respiratory disease; and greater focus on Specialty conditions such as cancer, inflammatory conditions, and multiple sclerosis.

FIGURE 12 | Traditional Drug Pipeline
New Diabetes Medications Lead the Way

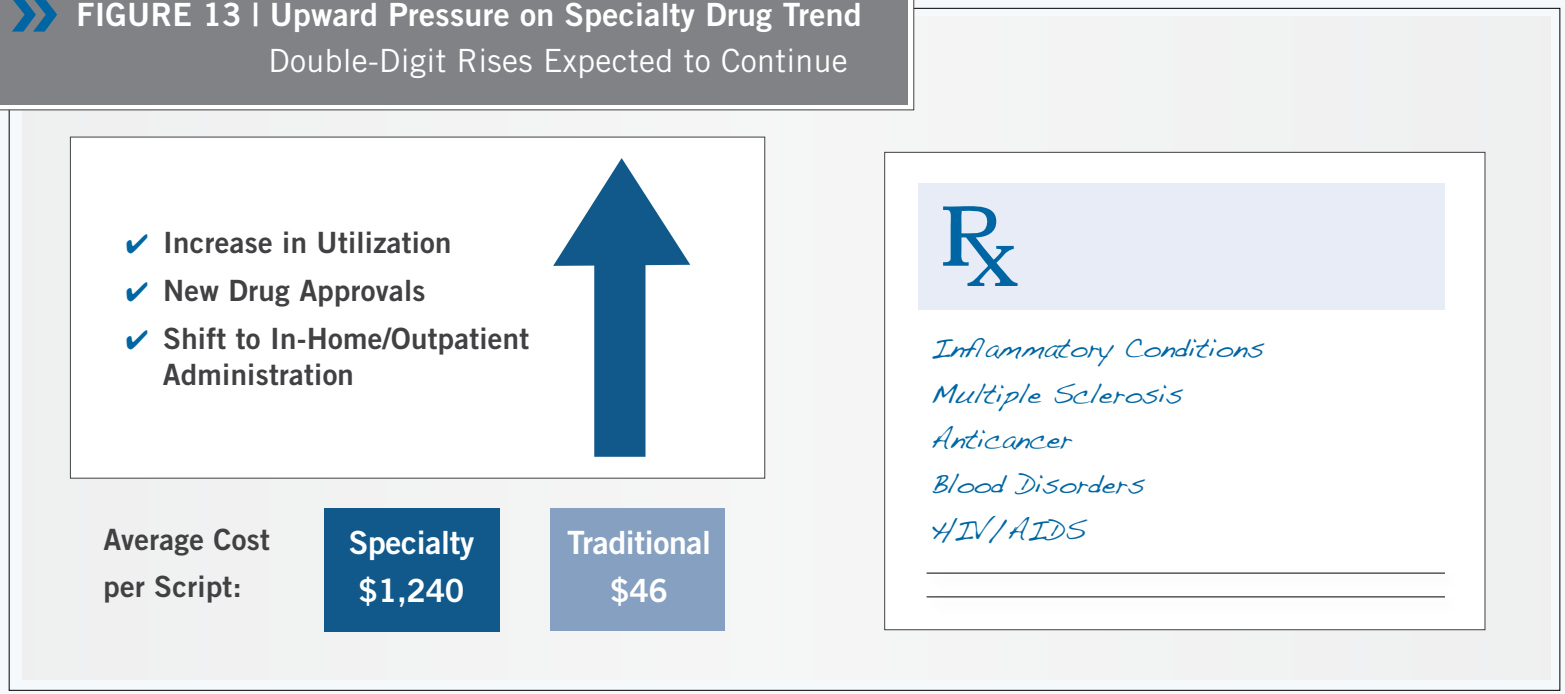


Traditional drugs only make up 36% of the pipeline. Within the Traditional category, drugs to treat diabetes account for the highest proportion (5.9%) of all pipeline drugs, while asthma/COPD (chronic obstructive pulmonary disease), psychiatric, and cardiovascular drugs each comprise approximately 2.9%. Investigational diabetes drugs that are being studied in late-stage clinical trials link to several drug classes including, but not limited to, sodium glucose co-transporter-2 (SGLT2) inhibitors, G-protein-coupled receptor 40 (GPR40) agonists, and glimins. SGLT2 inhibitors prevent the re-absorption of glucose in the kidneys, and would likely be the newest class to emerge on the market. With nine million Canadians being affected by diabetes or pre-diabetes today, Express Scripts Canada believes that any upcoming approvals for anti-diabetic medications with a unique mechanism of action have the potential to be highly used.

SPECIALTY DRUG TREND

Express Scripts Canada believes that the increasing use of Specialty drugs will change the future reimbursement landscape with the introduction of new Specialty drugs into the marketplace as well as a shift to in-home and outpatient administration.

FIGURE 13 | Upward Pressure on Specialty Drug Trend
Double-Digit Rises Expected to Continue



NEW SPECIALTY DRUG APPROVALS

While many Traditional blockbuster drugs are coming off patent, a growing number of drug manufacturers are devoting more research-and-development time and resources to Specialty treatments. Development of Specialty drugs requires a significant amount of investment; however, the patient population indicated for their use is typically small, and, as a result, Specialty drugs tend to be significantly more expensive than Traditional medications. Express Scripts Canada has found that Specialty drugs dispensed in 2012 were 27 times the price of Traditional medications.

Over the past couple of years, more Specialty drugs that provide clinically effective treatment – and sometimes the only drug-treatment option for complex diseases – have been approved. Specialty drugs contributed to 23% (10 out of 42) of all new drug approvals in 2010, and this percentage increased to more than 55% (29 out of 52) in 2012. Increasing treatment options for niche conditions provides good news for affected patients; however, the high drug cost has created financial concerns for both public and private payers.

Many notable Specialty drugs entered the market in 2012. Treatments for cancer were the most common of those approved – noteworthy examples include Caprelsa®, for thyroid cancer; Xalkori™, for non-small-cell lung cancer; and both Zelboraf™ and Yervoy™, for melanoma. These four cancer agents similarly have an estimated therapy cost of more than $100,000 per patient per year. Another notable drug is Kalydeco™, the first pharmacologic agent that targets and treats the G551D CFTR mutation in patients with cystic fibrosis; Kalydeco™ carries an annual cost of approximately $325,000 per patient.

Gene therapy, a technique used to correct defective genes that are responsible for disease development, is on Express Scripts Canada's radar. The first gene therapy for the treatment for lipoprotein lipase deficiency (LPLD), Glybera®, was approved in November 2012 by the European Commission under exceptional circumstances. Three Phase III clinical trials of Glybera® were conducted in Québec and The Netherlands, with 27 patients enrolled. This drug is estimated to cost about $1.6 million per patient, setting a new record for high-cost therapy. If approved in Canada, Glybera® would definitely contribute to the growing Specialty spend.

Specialty drugs contributed to 55% (29 out of 52) of all new drug approvals in 2012

FIGURE 14 | Specialty Drugs Dominated Approvals
New Treatments for Niche Conditions

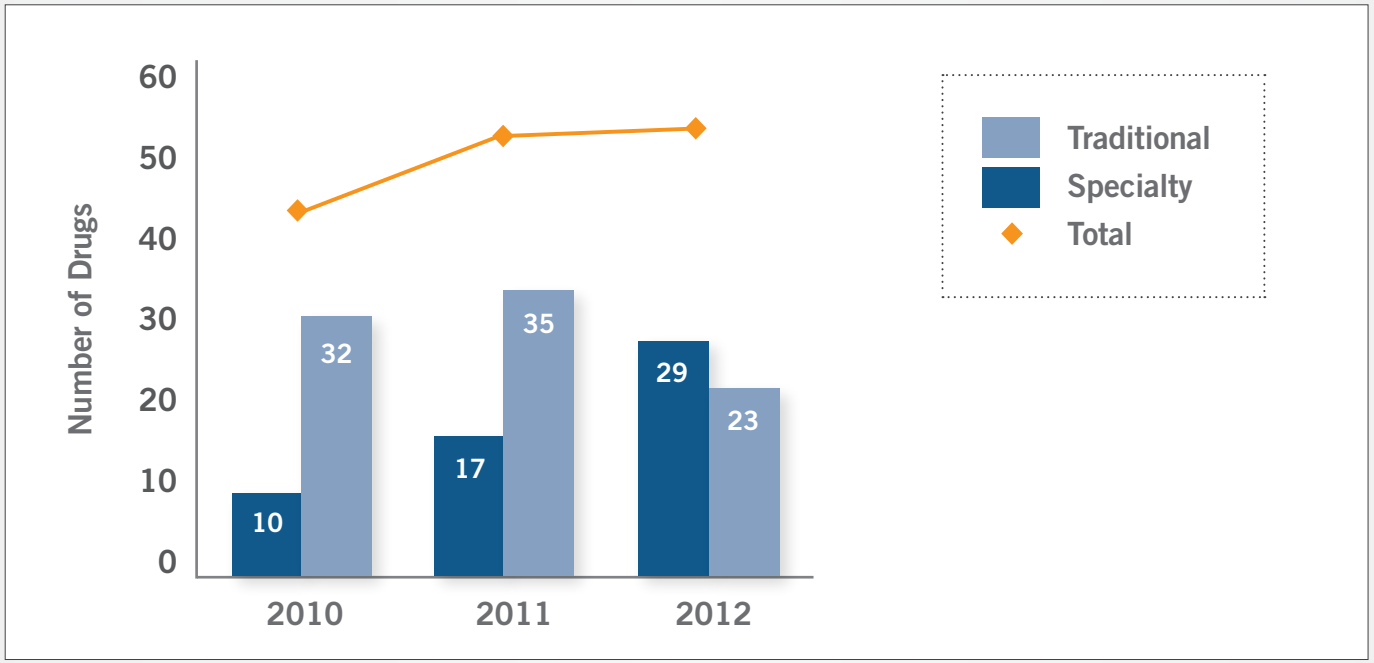


FIGURE 15 | Specialty Drugs Approved in 2012

High Price Tags Create Financial Burden for Many Patients Plan Sponsors

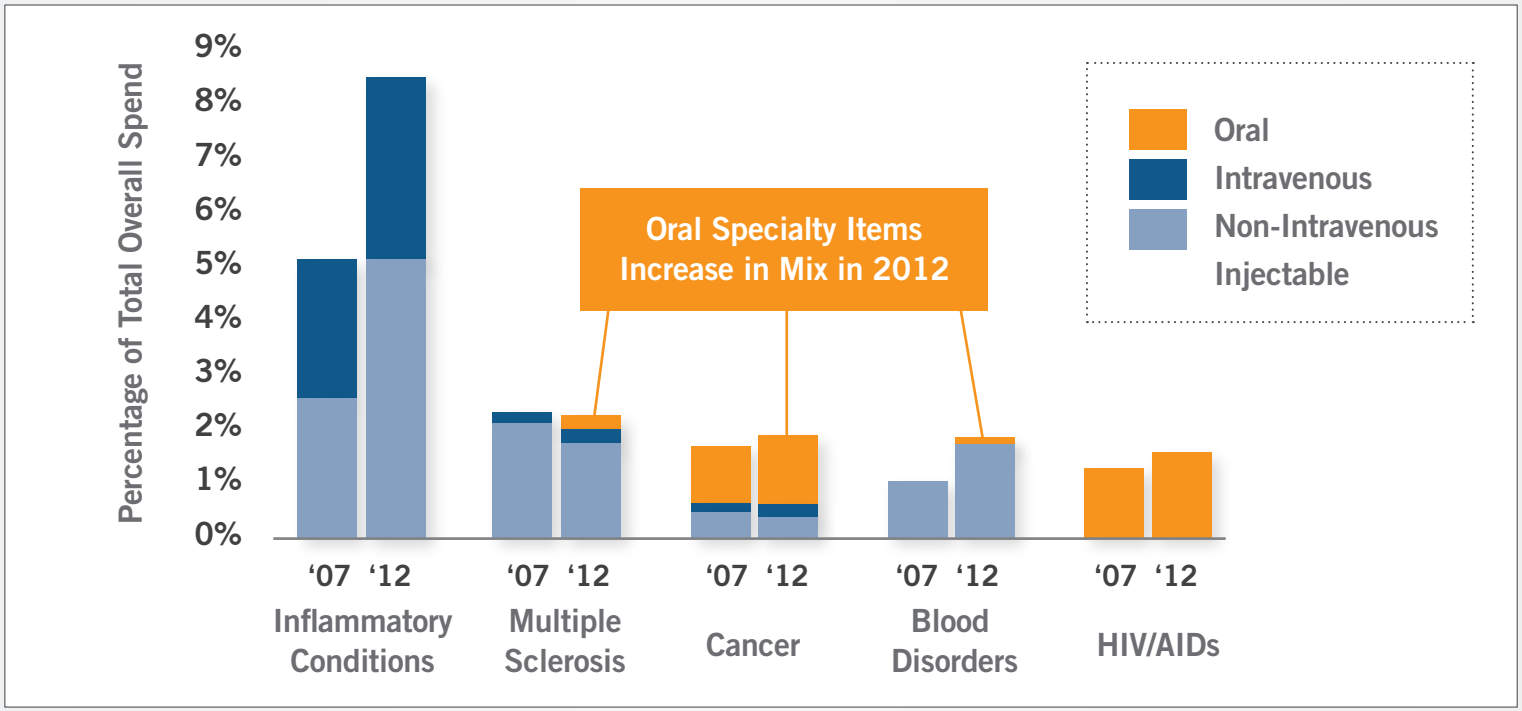
Brand Name	Generic Name	Manufacturer	Indication(s)	Annual Ingredient Cost/Patient
Aloxi®	palonosetron	Eisai Limited	Nausea and Vomitting Due to Chemotherapy	$69.30 (per course of chemotherapy)
Arzerra™	ofatumumab	Glaxosmithkline Inc.	Chronic Lymphocytic Leukemia	Pricing not available
BeneFIX®	coagulation factor ix (recombinant)	Wyeth Canada	Hemophilia B	Pricing not available
Caprelsa®	vandetanib	Astra Pharma Inc.	Thyroid Cancer	$696,000
Decapeptyl®	triptorelin acetate	Ferring Inc.	Fertility	Pricing not available
Dysport® (formerly Dysport Cosmetic)	botulinum toxin Type A (abobotulinumtoxina)	Ipsen Biopharm limited	Cosmetic	Pricing not available
Esbriet™	pirfenidone	Intermune Inc.	Idiopathic Pulmonary Fibrosis	$44,000
Fampyra™	fampridine	Biogen	Multiple Sclerosis	$4,950
Feraheme™	ferumoxytol	Takeda Pharmaceuticals America Inc	Chronic Kidney Disease	$8,900 - $23,750
Halaven®	eribulin mesylate	Eisai Limited	Breast Cancer	$2500 - $30,000
Inlyta™	axitinib	Pfizer Canada Inc.	Renal Cell Cancer	$5,900 - $70,800
Intelence®	etravirine	Janssen Ortho Inc.	HIV	$4,200
Jakavi®	ruxolitinib	Novartis Canada Inc.	Myelofibrosis	$60,000
Kalydeco™	ivacaftor	Vertex Pharmaceuticals (Canada) Inc.	Cystic Fibrosis	$325,000
Mozobil™	plerixafor	Genzyme Canada Inc.	Autologous Transplantation in Patients with Non-Hodgkin Lymphomas & Multiple Myeloma	$7,550 - $15,100

Brand Name	Generic Name	Manufacturer	Indication(s)	Annual Ingredient Cost/Patient
Prezista®	darunavir ethanolate	Janssen Ortho Inc.	HIV	$8,000 - $11,400
Prochymal®	remestemcel-l	Osiris Therapeutics Inc.	GVHD Treatment	Pricing not available
Removab®	catumaxomab	Fresenius Biotech	Cancer	Pricing not available
Riastap®	fibrinogen (human)	CSL Behring Canada Inc.	Acute Bleeding	Pricing not available
Stribild™	elvitegravir/cobicistat/ emtricitabine/ tenofovir disoproxil fumarate	Gilead Sciences Canada Inc.	HIV	Pricing not available
Treanda®	bendamustine hydrochloride	Lundbeck Canada Inc.	Non-Hodgkin Lymphoma	$30,000 to $50,000
Tretten®	catridecacog	Novo Nordisk	Congenital Factor 8 A-Subunit Deficiency	Pricing not available
Velcade®	bortezomib	Janssen Ortho Inc.	Multiple Myeloma	$59,000 - $118,400
Xalkori™	crizotinib	Genmed, a division of Pfizer Canada Inc.	Non-Small Cell Lung Cancer	$111,350
Xeomin® Cosmetic	botulinum neurotoxin type a	Mmerz Pharmaceuticals gmbh	Cosmetic	$330 - $3,900
Xiaflex®	collagenase clostridium histolyticum	Actelion Pharmaceuticals Ltd.	Dupuytren'S Contracture	Pricing not available
Yervoy™	ipilimumab	Bristol Labs, division of Bristol-Myers Squibb	Melanoma	$104,400
Zelboraf™	vemurafenib	Hoffmann-La Roche Limited	Melanoma	$141,000
Zyclara®	imiquimod	Medicis Canada Ltd.	Actinic Keratoses	$7,500

SHIFT TO MORE IN-HOME, OUTPATIENT PRODUCTS

Historically, drug treatments for complex conditions come in injectable formulations, but Express Scripts Canada sees an emerging trend with the increase in the proportion of Specialty drugs that are now available in oral dosage forms. Drugs indicated for the treatment of cancer clearly demonstrate this trend. To put this in perspective, in 2007, oral cancer drugs contributed 1.1% of the overall spend; by 2012, this increased to 1.3%, thanks largely to the increased use of new drugs like Sutent® and Revlimid®. Similarly, in 2007, the cornerstone therapy for the treatment of multiple sclerosis was subcutaneous interferon injections. Two new oral drugs – Gilenya® and Fampyra™ – were introduced after March 2011, and more oral drugs, with unique mechanism of actions, are in the pipeline. New, innovative oral and non-intravenous formulations that allow patients more convenient access to life-saving or life-sustaining treatments create a shift to more in-home and outpatient treatment, and contribute to the increasing Specialty spend by private payers.

FIGURE 16 | Use of Oral Specialty Drugs on Rise
More Access to Life-Sustaining and Life-Saving Treatments



SPECIALTY DRUGS IN THE PIPELINE

With the shift in focus by a growing number of pharmaceutical manufacturers to the development of Specialty drugs, Express Scripts Canada's 2012 analysis show that 64% of drugs in the pipeline belonged to the Specialty group. Cancer drugs, alone, account for 26.4% of the pipeline, followed by drugs for such inflammatory conditions as rheumatoid arthritis and psoriasis (7%), followed by Hepatitis C treatments (5%). Cancer drugs in the pipeline are expected to continue to follow the trend set in the past couple of years, as development focuses on biologic cancer treatments, oral cancer treatments, and targeted therapies that require specific genetic testing prior to the initiation of treatment.

Specialty Drugs and Genetic Testing

Rapid advancement in genomics is furthering our understanding of the genetic mutation responsible for a disease condition in a patient. As such, genetic testing is moving the medical world from individualized treatment to the front line of personalized medicine. Personalized medicine allows medical treatment to be tailored to the specific characteristics of each patient and their respective condition. For example, a commonly used cancer drug, Herceptin® (trastuzumab), is targeted therapy for HER2-positive breast cancer. Genetic tests are available to differentiate the HER2 variations in breast cancer to identify patients who are likely to respond and receive clinical benefits from the drug vs. potential non-responders. Another drug approved in 2012, Zelboraf™ (vemurafenib), requires genetic testing prior to being prescribed, as it is only effective in treating patients with metastatic melonoma with the BRAF*V600E mutation.

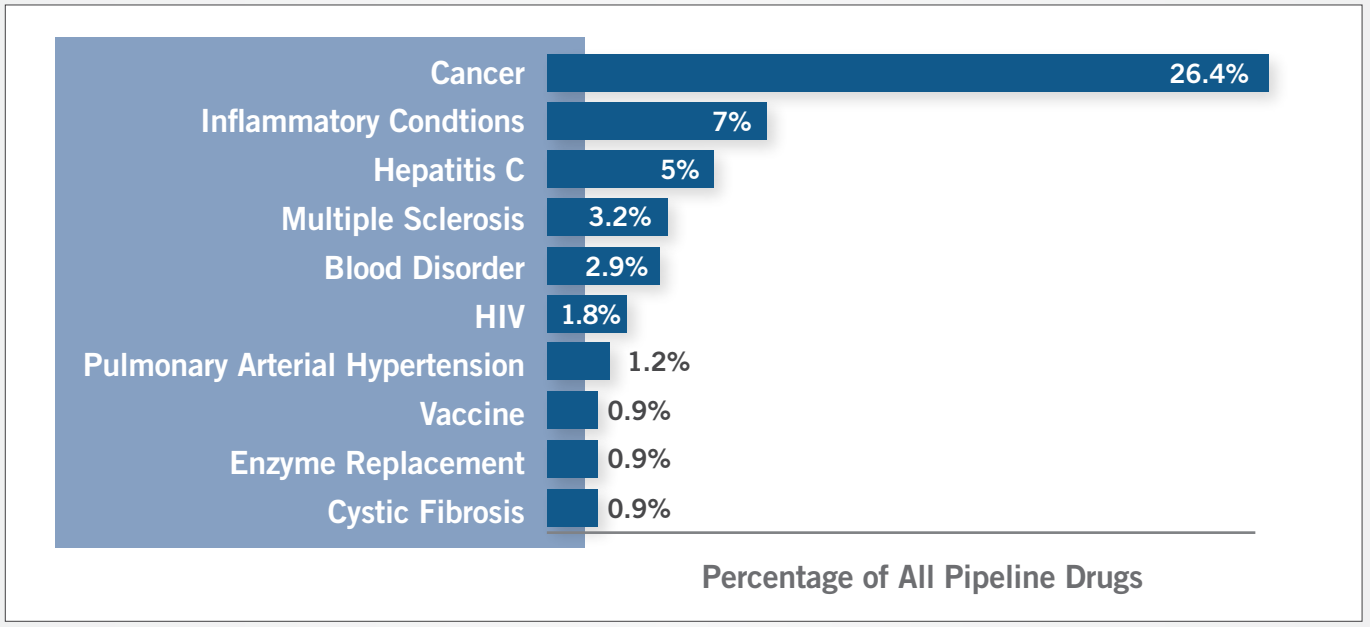
Development of Specialty Drugs to Treat Common Medical Conditions

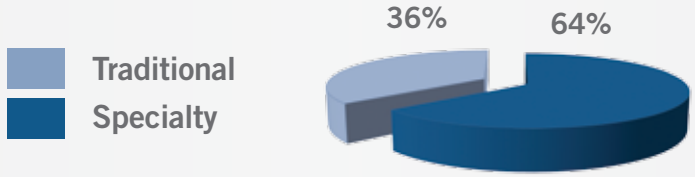
New Specialty drugs are also in development to provide treatments for a niche subset of common medical conditions. On January 29, 2013, a new Specialty drug, mipomersen (Kynamro™ in United States), was approved by the U.S. Food and Drug Administration (FDA) to be used as an adjunct to lipid-lowering medications and diet to treat patients with homozygous familial hypercholesterolemia (HoFH). HoFHis a rare, inherited disease that affects about one in one million people, which the low-density lipoprotein (LDL) or "bad" cholesterol reaches abnormally high levels and increases the risk for premature heart disease. Heart attacks and death often occur before patients reach age 30. Mipomersen is to be administered as a once-weekly, subcutaneous (SQ) injection, with an estimated annual cost of US$200,000-US$300,000 per patient in the U.S. Further down the pipeline, a new monoclonal antibody to proprotein convertase subtilisin/kexin 9 (PCSK9) that binds to LDL receptors is found to further reduce LDL-cholesterol in patients with primary hypercholesterolemia. Express Scripts Canada believes that the approval and probable use of this biologic in a wide population would create a high impact on drug spend.

Vaccine Treatments

Currently in development are vaccines to treat non-small-cell lung cancer (NSCLC), which is the leading cause of cancer-related death worldwide. Vaccines are developed to target different tumour markers, as well as to boost the patient's immune system to target the cancer cells. The idea behind the cancer vaccines seem to be potentially beneficial in advanced disease and in combination with other therapies. Two vaccines – anti-MUC-1vaccine (belagenpumatucel) and anti-TGF-2 vaccine (BPL-25) – have entered in Phase III trials as maintenance therapies after first-line chemotherapy, with promising results.

FIGURE 17 | Specialty Drug Pipeline
Heavy Focus on Cancer Therapies

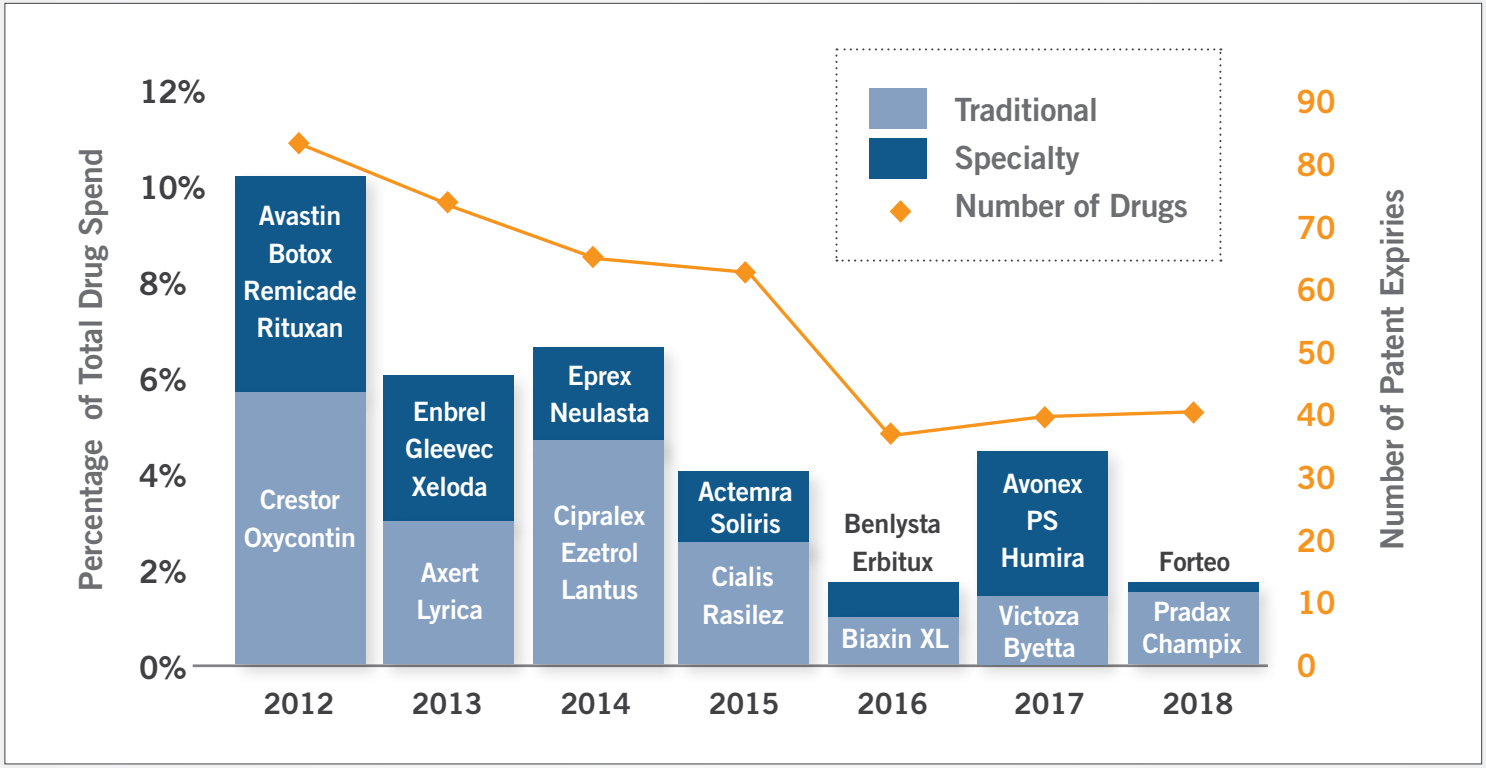




SPECIALTY DRUG PATENT EXPIRIES

Over the last three years, a number of blockbuster drugs in the Traditional group have gone off-patent. Two such drugs, Lipitor® and Crestor® – both of which are indicated for the treatment of high cholesterol – lost patent protection, which has helped to drive up the generic fill rate and lower the average prescription cost. In looking at the brand-patent cliff, Express Scripts Canada anticipates fewer drugs will experience patent expiries, but there is an emerging trend that more Specialty drugs will lose patent over the next five years. Some commonly used Specialty drugs like Avastin®, which is indicated for the treatment of brain and ovarian cancer, and Remicade®, which is indicated for the treatment of inflammatory conditions, lost patent in 2012; however, no subsequent entry biologics (SEBs) are available on the market yet. The primary uncertainty that private payers face today is how much plans can save following the patent expiries of Specialty drugs.

FIGURE 18 | Patent Cliff Slowing
Savings Remain Uncertain



To understand the potential impact of Specialty drug patent-expiries and potential availability of SEBs, it is necessary to first understand the differences between generics of Traditional drugs and SEBs:

✔ **Comparison to Innovator.** A generic is a copy of the brand as it contains the same medicinal ingredients and is considered bioequivalent to the reference product. On the other hand, a SEB is a biologic drug that enters the market subsequent to a version previously authorized in Canada. A SEB is similar to the innovator, but usually derived from a different living organism and manufactured by a different process.

✔ **Approval Process.** Generics follow the Abbreviated New Drug Submission pathway (ANDS) established by the Therapeutic Products Directorate of Health Canada. An ANDS requires less data and fewer supporting trials that focus on comparative bioavailability studies to show generics deliver the same amount of drug at the same rate as the reference brand. Conversely, SEBs follow the New Drug Submission (NDS) pathway, for which much more data is required to demonstrate comparability to innovator; clinical data to demonstrate efficacy is often required. These requirements necessitate a much larger scale of investment to bring a SEB to market.

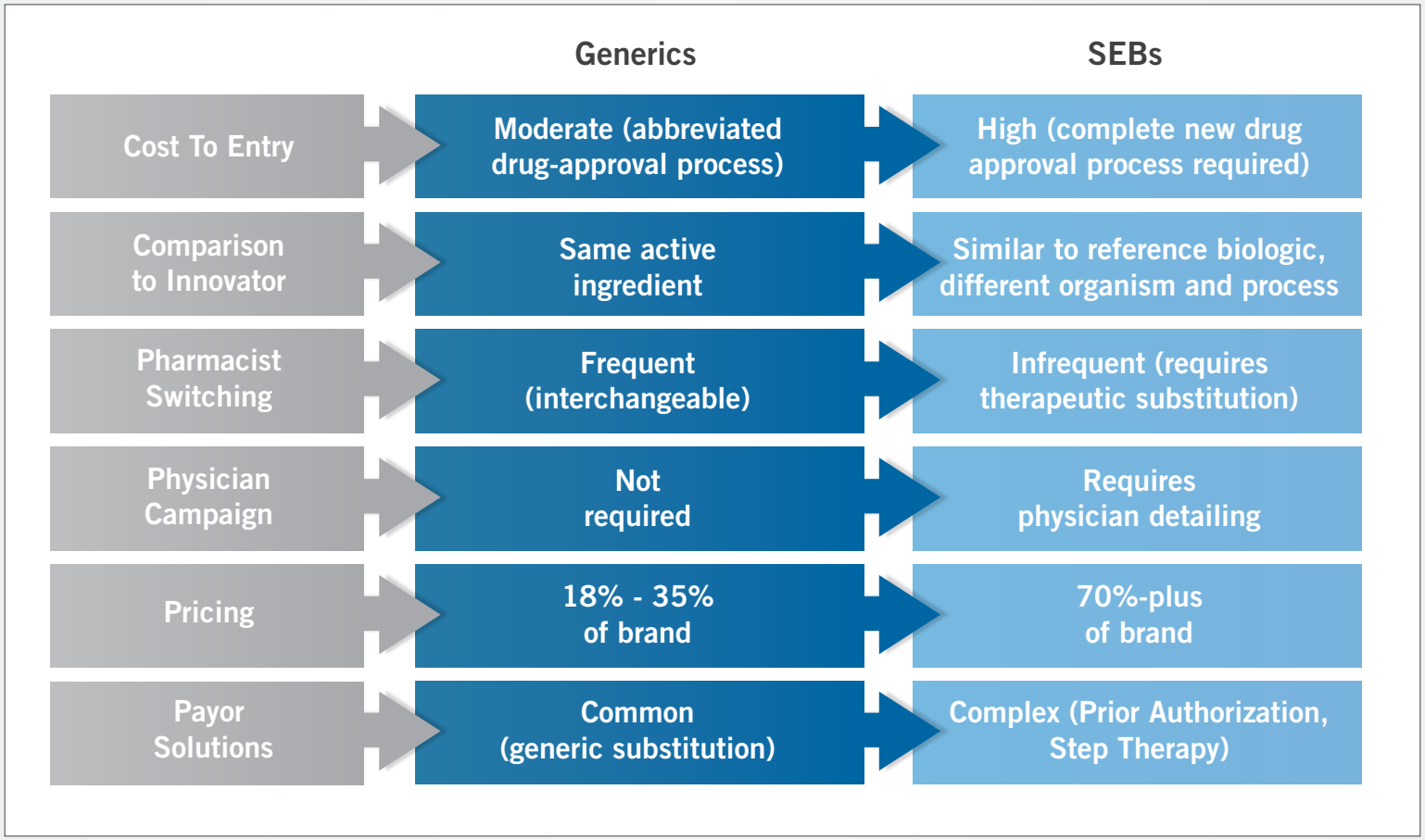
✔ **Product Availability.** There is a high likelihood of generics being available on market, based on the simpler approval process and less investment to launch the product. Generics are usually available soon after the brands come off patent, ranging from the next day to a few weeks. For SEBs, there is much variability about the timing and likelihood of product being available, based on the lengthy approval process and higher investment.

✔ **Switching.** Most generics are considered interchangeable with their brands across Canada. Switching occurs over 90% of the time, and can be done simply through generic substitution, with little intervention by pharmacists. Conversely, SEBs will not be automatically substituted with the innovator brand due to variations in the manufacturing process, which may lead to differences in efficacy and safety. Switching can only be done through therapeutic substitution; this is infrequent, and requires intervention by both the pharmacist and physician.

✔ **Pricing.** With ongoing provincial drug reform, formulary generics are typically priced between 18% and 40% of their reference brands. Express Scripts Canada anticipates SEBs will be only moderately less expensive than their reference brand, with expected price reductions of 20% to 30%. The only SEB in Canada, Omnitrope™, which is indicated for treating growth deficiency, is currently priced at 65% of the brand.

In anticipation of future launches of SEBs – and the need to manage these spends – Express Scripts Canada believes that feasible solutions include the use of a Prior Authorization program and/or Step Therapy program. These programs are successful in ensuring the right patient obtains reimbursement for the right drug, but they usually require both pharmacist and physician intervention, and may have higher member impact, when compared with using automatic generic substitution and a managed formulary to optimize the use of Traditional generic drugs.

FIGURE 19 | Specialty Patent Expiries Unlikely to Reduce Trend
Significant Barriers Exist for Subsequent Entry Biologics (SEBs)



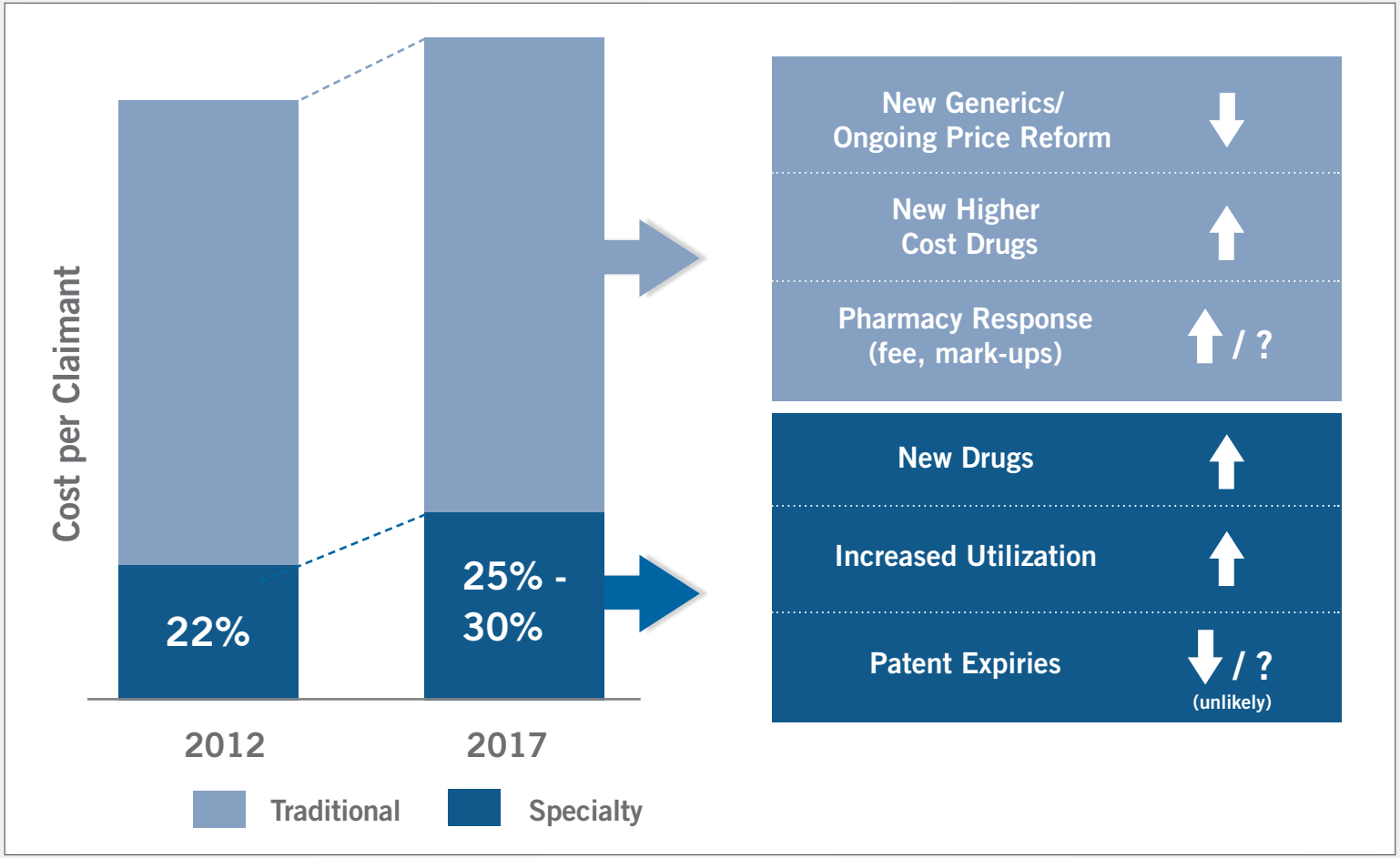
FORECAST

Traditional Drugs: Looking ahead, Express Scripts Canada expects utilization, which is influenced by prevalence and intensity, to remain relatively flat in 2013 and 2014. Once all provincial generic-reform activities have been implemented and the generic prices have settled in 2014, Express Scripts Canada anticipates the cost per script for Traditional drugs will eventually increase slightly because of brand inflation, which will offset the continued downward pressure from generics. Overall, Express Scripts Canada further predicts a relatively flat trend between 2013 and 2015 for the Traditional drug category.

Specialty Drugs: In contrast to the forecast for Traditional drugs, Express Scripts Canada anticipates double-digit growth, year over year, for the Specialty drug category. Both of the major trend components – cost per script and utilization – will contribute to positive trend. Over the next three years, cost per script will be the main factor, accounting for majority of the total growth. Brand inflation, and the introduction of novel, more-expensive therapies, will lead to annual increases in the range of 12%-15%. With the complexities around SEB development and approval, Express Scripts Canada predicts that the introduction of SEBs in key therapy classes – and their potential significant role in decelerating cost-per-script increases – remain uncertain.

Based on the assumptions that most pipeline drugs currently in Phase III clinical trials will enter the market, and that Specialty drugs will continue to have double-digit growth, Express Scripts Canada believes that Specialty medications will represent an increasingly larger component of overall drug expenditure. By 2017, Express Scripts Canada further believes that Specialty medications will account for approximately 25%-30% of the total drug spend for private payer plans in Canada.

FIGURE 20 | Drug Benefit Costs Will Rise in Future
Specialty Increases to Drive Drug Trend



TREND OVERVIEW 2

THERAPY CLASS REVIEW

DRIVING BETTER DECISIONS 54

THERAPY CLASS REVIEW

THERAPY CLASS REVIEW

Over the last five years, the drug benefit landscape in Canada has undergone significant changes. In 2012, the Top 10 Therapy Classes represented 58.9% of total spend and 56.6% of total prescription volume. For the first time since 2002 when Express Scripts Canada began to report on drug trend, a Specialty therapy class occupied the number-one ranking among all therapy classes by total spend. Inflammatory Conditions took over the top spot from High Blood Pressure, which was ranked first by spend in 2010 and 2011; prescriptions for Inflammatory Conditions contributed to 9.48% of the total spend, while only accounting for 0.25% of the total claims (see **Figure 21 | Top 10 Therapy Classes by Spend**).

Inflammatory Conditions, Cancer and Multiple Sclerosis represent a growing portion of the Specialty therapy classes. In 2007, these three therapy classes contributed only 5% of total drug spend, but by 2012, they had trebled to approximately 15% due to greater utilization of drugs used to treat these conditions. On the other hand, Traditional therapy classes – specifically High Cholesterol and High Blood Pressure – now contribute to a smaller proportion of the overall drug spend, compared to five years ago, due to a decrease in the cost per script caused by key patent expiries in these classes, and drug price reforms.

There were some notable movements among Specialty drugs in the 2012 ranking. Remicade®, a Specialty drug indicated for the treatment of Inflammatory Conditions, ranked seventh by spend in 2007, rose to number one in 2012. Conversely, the Traditional drug, Lipitor®, which is indicated for the treatment of high cholesterol, was ranked number one by spend in 2007, has now dropped to fifth. This was primarily due to a decrease in the average cost per script for Lipitor® with the uptake of generics that began in April 2011, along with lower generic prices over time due to provincial drug reforms. High Cholesterol drugs, such as Crestor® and Lipitor®, are still highly used; they were ranked second and third respectively in prescription volume in 2012.

Express Scripts Canada believes that Specialty therapy classes will continue to grow in spend and claims, (see **Figure 22 | Top 30 Therapy Classes 2012 – Ranked by Total Cost** and **Figure 23 | Top 30 Therapy Classes 2012 – Ranked by Total Claims**), driven by the growing additions of new high-cost drugs for treating complex chronic, niche or rare diseases. Express Scripts Canada further believes that the arrival of subsequent-entry biologics, which could provide cost-savings opportunities, will not have the same level of impact as have generic Traditional drug products due to multiple influencing factors discussed in **Section 1 – Trend Overview**.

In 2012, the **Top 10 Therapy Classes** represented **58.9%** of total spend and **56.6%** of total prescription volume

FIGURE 21 | Top 10 Therapy Classes by Spend

Inflammatory Conditions Overtakes High Blood Pressure

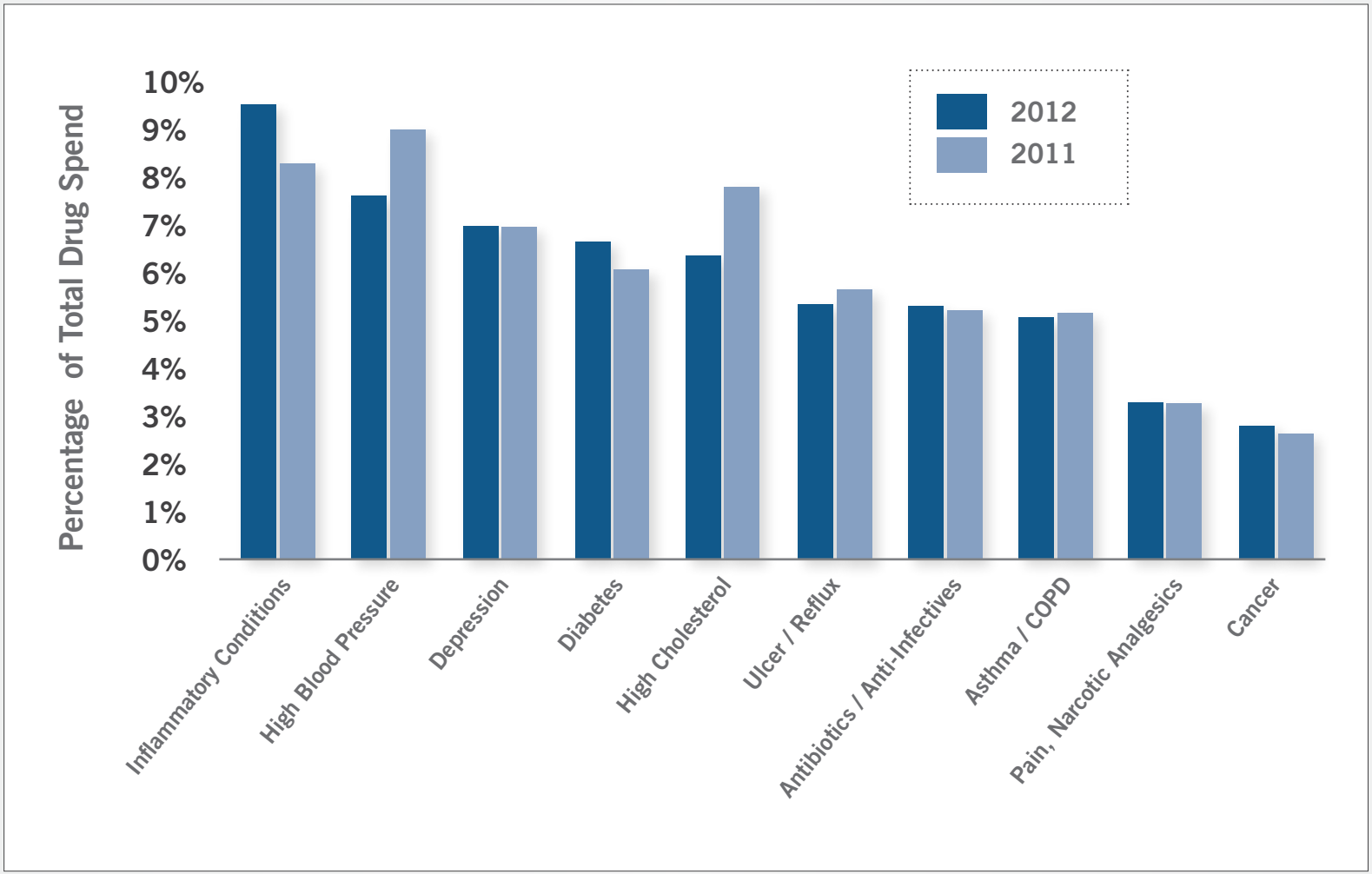


FIGURE 22 | Top 30 Therapy Classes 2012 – Ranked by Total Cost

Accounted for 98% of Total Prescription Drug Spend in Canada

Rank by Total Cost	THERAPY CLASSES	Percentage of Total Cost		Rank by Total Cost	Percentage of Total Claims		Rank by Claims		Trend
2012		2011	2012	2011	2011	2012	2011	2012	
1	Inflammatory Conditions	8.30%	9.48%	2	0.23%	0.25%	44	41	13.79%
2	High Blood Pressure	8.98%	7.63%	1	13.18%	13.02%	1	1	-15.36%
3	Depression	6.93%	7.02%	4	7.72%	7.86%	3	3	0.88%
4	Diabetes	6.12%	6.63%	5	5.41%	5.54%	6	6	8.00%
5	High Cholesterol	7.80%	6.40%	3	6.16%	6.17%	4	4	-18.37%
6	Ulcer / Reflux	5.67%	5.33%	6	4.61%	4.73%	8	7	-6.37%
7	Antibiotics / Anti-Infectives	5.21%	5.25%	7	8.62%	8.33%	2	2	0.29%
8	Asthma / COPD	5.15%	5.06%	8	4.43%	4.40%	9	9	-2.11%
9	Pain, Narcotic Analgesics	3.28%	3.28%	9	5.70%	5.68%	5	5	-0.22%
10	Anticancer	2.68%	2.81%	11	0.59%	0.60%	35	35	4.66%
11	Neurological Disorders	2.76%	2.81%	10	2.67%	2.75%	13	13	1.37%
12	Birth Control	2.52%	2.56%	12	3.81%	3.66%	10	10	1.16%
13	Multiple Sclerosis	2.39%	2.53%	13	0.08%	0.08%	51	51	5.78%
14	Allergy	2.25%	2.33%	15	2.74%	2.77%	12	12	2.86%
15	NSAIDs - Pain and Inflammation	2.33%	2.30%	14	4.66%	4.53%	7	8	-1.66%
16	Blood Disorders	1.81%	2.05%	18	0.59%	0.67%	34	32	12.78%
17	Attention Deficit Disorder	1.90%	2.01%	17	1.11%	1.17%	22	21	5.59%
18	HIV / AIDS	1.60%	1.77%	21	0.12%	0.13%	48	47	9.83%
19	Hormone Replacement	1.62%	1.76%	19	1.90%	1.91%	15	15	7.77%
20	Skin Conditions	1.62%	1.66%	20	2.48%	2.46%	14	14	2.01%
21	Cardiovascular Disease	2.01%	1.50%	16	1.49%	1.41%	18	18	-25.76%
22	Antipsychotic	1.27%	1.35%	23	1.32%	1.39%	19	19	6.00%
23	Migraine	1.42%	1.31%	22	0.63%	0.63%	31	34	-8.22%
24	Diabetic Supplies	0.92%	0.97%	25	0.78%	0.80%	27	27	4.04%
25	Osteoporosis	0.96%	0.88%	24	1.16%	1.07%	21	22	-9.03%
26	Preventative Vaccines	0.70%	0.86%	31	0.60%	0.64%	33	33	22.66%
27	Erectile Dysfunction	0.71%	0.83%	29	0.38%	0.41%	38	37	17.09%
28	Gastrointestinal	0.87%	0.80%	26	0.93%	0.89%	24	26	-7.94%
29	Kidney / Bladder Disease	0.73%	0.76%	28	0.90%	0.92%	25	24	4.89%
30	Muscle Relaxant	0.69%	0.72%	32	0.70%	0.71%	30	31	3.65%

FIGURE 23 | Top 30 Therapy Classes – Ranked by Total Claims

Dominated by Drugs Used to Treat Chronic Medical Conditions

Rank by Claims	THERAPY CLASSES	Percentage of Total Claims		Rank by Claims	Percentage of Total Cost		Rank by Total Cost		Trend
2012		2011	2012	2011	2011	2012	2011	2012	
1	High Blood Pressure	13.18%	13.02%	1	8.98%	7.63%	1	2	-15.36%
2	Antibiotics / Anti-Infectives	8.62%	8.33%	2	5.21%	5.25%	7	7	0.29%
3	Depression	7.72%	7.86%	3	6.93%	7.02%	4	3	0.88%
4	High Cholesterol	6.16%	6.17%	4	7.80%	6.40%	3	5	-18.37%
5	Pain, Narcotic Analgesics	5.70%	5.68%	5	3.28%	3.28%	9	9	-0.22%
6	Diabetes	5.41%	5.54%	6	6.12%	6.63%	5	4	8.00%
7	Ulcer / Reflux	4.61%	4.73%	8	5.67%	5.33%	6	6	-6.37%
8	NSAIDs - Pain and Inflammation	4.66%	4.53%	7	2.33%	2.30%	14	15	-1.66%
9	Asthma / COPD	4.43%	4.40%	9	5.15%	5.06%	8	8	-2.11%
10	Birth Control	3.81%	3.66%	10	2.52%	2.56%	12	12	1.16%
11	Thyroid Disorders	2.77%	2.85%	11	0.62%	0.65%	35	35	4.69%
12	Allergy	2.74%	2.77%	12	2.25%	2.33%	15	14	2.86%
13	Neurological Disorders	2.67%	2.75%	13	2.76%	2.81%	10	11	1.37%
14	Skin Conditions	2.48%	2.46%	14	1.62%	1.66%	20	20	2.01%
15	Hormone Replacement	1.90%	1.91%	15	1.62%	1.76%	19	19	7.77%
16	Anti-Anxiety	1.84%	1.75%	16	0.40%	0.39%	41	42	-4.90%
17	Sedative / Hypnotic	1.53%	1.57%	17	0.69%	0.72%	33	31	4.55%
18	Cardiovascular Disease	1.49%	1.41%	18	2.01%	1.50%	16	21	-25.76%
19	Antipsychotic	1.32%	1.39%	19	1.27%	1.35%	23	22	6.00%
20	Topical Antibiotics / Anti-Infectives	1.19%	1.18%	20	0.70%	0.72%	30	33	1.87%
21	Attention Deficit Disorder	1.11%	1.17%	22	1.90%	2.01%	17	17	5.59%
22	Osteoporosis	1.16%	1.07%	21	0.96%	0.88%	24	25	-9.03%
23	Eye Disease, Misc	1.05%	1.05%	23	0.38%	0.42%	43	41	10.42%
24	Kidney / Bladder Disease	0.90%	0.92%	25	0.73%	0.76%	28	29	4.89%
25	Steroids Anti-Inflammatory	0.86%	0.89%	26	0.24%	0.25%	46	46	3.17%
26	Gastrointestinal	0.93%	0.89%	24	0.87%	0.80%	26	28	-7.94%
27	Diabetic Supplies	0.78%	0.80%	27	0.92%	0.97%	25	24	4.04%
28	Benign Prostatic Hyperplasia	0.77%	0.78%	28	0.52%	0.49%	39	40	-6.90%
29	Acne	0.76%	0.74%	29	0.66%	0.72%	34	32	8.22%
30	Nutritional Products	0.62%	0.73%	32	0.29%	0.31%	44	45	8.76%

THERAPY CLASSES TO WATCH

In-depth reviews of selected therapy classes offer insight from Express Scripts Canada with respect to the key influencing factors of utilization and cost per prescription, along with what may lie ahead in the future.

TRADITIONAL THERAPY CLASSES

- **Diabetes** – The prevalence of the disease continues to increase worldwide and within Canada, a direction reflected by the 2.4% increase in utilization in 2012. New drugs with novel mechanisms of action are being developed which work by addressing some of the pathologic defects causing diabetes. Express Scripts Canada expects these combinations of factors will likely lead to increased drug spend in this therapy class.
- **High Cholesterol** – This therapy class continues to show a declining trend, despite continuing to show high utilization with the generic availability of all statin molecules. New drugs with novel mechanisms of action, including biologics, on the horizon may cause drug spend in this category to regain its upward trend in the future.
- **High Blood Pressure** – Express Scripts Canada believes this therapy class entered a phase of declining trend due to a decrease in the cost per script with the availability of generics. Only a handful of "me-too" drugs – Coversyl®, Olmetec®, Tevetan®, Edarbi – remain as single source.
- **Mental Health** – In 2012, use of depression and antipsychotic medications grew 1.9% and 5.7% respectively year over year. Mental-health issues within the workplace gained prominence within the past year with the release of a national mental health strategy by the Mental Health Commission of Canada (MHCC).

SPECIALTY THERAPY CLASSES

- **Cancer** – Use of cancer medications increased in 2012 in part due to new high-cost drugs released in 2012. Seven of the top 30 highest-cost drugs were cancer drugs. These new drugs were predominately oral agents which are administered by patients at home to treat very specific niche forms of the disease.
- **Inflammatory Conditions** – In 2012, Remicade® became the number-one drug by overall spend, the first time a Specialty drug has occupied top spot. This was primarily due to an increase in utilization. In the near future, Express Scripts Canada anticipates that new oral agents will be introduced in this therapy class, beginning with tofacitinib, which possesses a novel mechanism of action, with a high likelihood to enter the market in 2013. Express Scripts Canada believes that potential adaptation of the earlier and more aggressive treatment approach, which involves the use of existing biologics along with novel oral agents, will definitely lead to a higher drug spend for this therapy class.
- **Multiple Sclerosis** – The overall spend for Multiple Sclerosis drugs grew by 5.78% in 2012, primarily due to an increase in cost per script. Gilenya®, the first oral disease-modifying drug available in this therapy class, quickly captured more than 10% of market share in 2012 after being approved in March 2011. With more oral disease-modifying drugs expected to come to market shortly, Express Scripts Canada predicts that drug spend in this therapy class will increase rapidly.

DIABETES

Diabetes is a chronic disease characterized by **high glucose levels** in the blood. Long-term diabetes may lead to complications involving blood vessels and nerve damage, affecting multiple organs and body systems. **With proper management**, it is possible to prevent complications and **improve quality of life**.

YEAR IN REVIEW

- Drug spend continues to grow at a constant pace, with an overall upward trend of 8% in 2012 and 2011. Trend for the most recent year was primarily driven by an increase in cost per prescription of 5.6%, with a smaller increase in utilization of 2.4%.
- The key drivers were Januvia®, Janumet® (combination of Januvia® and metformin) and Victoza®.
- Januvia®, a DPP-4 inhibitor for the treatment of Type 2 diabetes, comprised 14% of the Diabetes market share in 2012; it rose to 23rd place in drug spend in 2012, compared with 36th place in 2011. With respect to claims volume, Januvia® went to 86th place in 2012 from 104th place in the preceding year.
- Similarly, Victoza®, a GLP-1 receptor agonist for the treatment of Type 2 diabetes, accounted for 9% of the Diabetes market share last year; as a result, it rose to 41st place for spend in 2012, compared with 90th place in 2011. With respect to claims volume, Victoza® placed 220th 2012, a significant increase over the preceding year when it ranked 284th.

A CLOSER LOOK

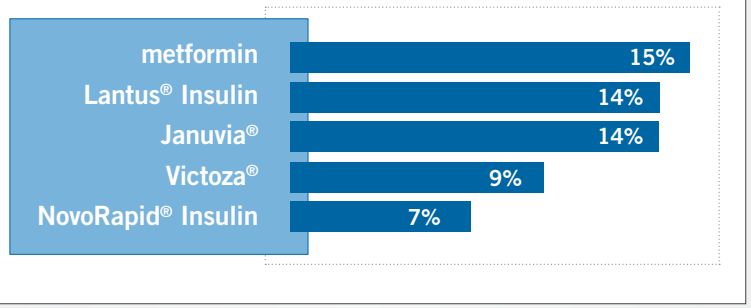
- A new position statement jointly issued in 2012 by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) stressed an individualized approach to designing treatment strategies. These strategies are essentially in alignment with existing Canadian treatment guidelines. New Canadian Diabetes Association (CDA) guidelines were announced for release in early 2013.
- The International Diabetes Federation (IDF) estimates that more than 370 million adults are living with diabetes worldwide. This represents overall prevalence of 8.3% with 50% not yet being diagnosed with the disease.
- In Canada, IDF reports that there are approximately 2.7 million adults with diabetes, which is representative of a disease prevalence of 10.5%. More than 17,000 deaths in 2011 were attributed to diabetes.
- Many of those with diabetes have other comorbidities, such as high cholesterol, high blood pressure and depression.
- Significant long-term complications of diabetes include vision problems, dental problems, cardiovascular complications, kidney failure, gastrointestinal dysfunction, sexual dysfunction, peripheral vascular disease, and foot problems.

WHAT'S AHEAD

Express Scripts Canada believes that diabetic drugs with novel and unique mechanism of actions that are in the drug-development pipelines of pharmaceutical companies will continue to drive utilization and spend.

- A new class of oral medication has been approved in Europe and is expected to be approved in Canada in 2013 – sodium glucose transporter-2 (SGLT2) inhibitors which prevent the reabsorption of glucose in the kidneys. The first in this class, canagliflozin (proposed trade name: Invokana™), is expected to receive approval in the first half of 2013; dapagliflozin (marketed as Forxiga) has been approved by the European Union.
- Other new classes of oral medications are being developed. A GPR40 (G-protein-coupled receptor 40) agonists that potentiate insulin secretion, specifically TAK-875, is currently in late stage (Phase III trials. Another class is the glimins of which imeglimin is currently in mid-stage (Phase II) development. Imeglimin acts on the three key defects of Type 2 diabetes, inhibiting hepatic gluconeogenesis, increasing muscle glucose uptake and restoring normal insulin secretion.
- A new, ultra-long-acting insulin, insulin degludec, is expected to be approved and released in Canada in 2013. It is uncertain whether the refusal by the United States Food and Drug Administration to grant approval for this drug in 2012 will have any impact on the receipt of an approval from the Therapeutic Product Directorate branch of Health Canada.
- Biosimilar products for insulin analogs are currently in development. This, at some point, could offer potential cost savings.
- Teplizumab, a biologic drug, designed to preserve beta-cell function in patients with recent onset Type 1 diabetes, is currently under development.

TOP DRUGS FOR DIABETES
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
+8%	5.54%	6.63%	$70.42	6.1%

HIGH CHOLESTEROL

High Cholesterol increases the risk of heart disease when **fat and cholesterol are deposited** on the walls of the arteries. In time, narrowing or **clogging of the coronary arteries** can produce the signs and symptoms of heart disease, including chest pain, stroke, and even heart attacks.

YEAR IN REVIEW

- Overall trend has been declining since the availability of generic Lipitor® and Crestor®. In 2012, the decrease of 18.4% was more substantial than the decline of 14.1% recorded in 2011.
- Utilization stayed flat, with a slight increase of 0.3%, which reflected that the overall trend decrease was solely driven by the huge decrease of 18.63% in cost per script.
- Generic fluvastatin (Lescol®, a low-potency statin) was approved in 2012. With this approval, generic alternatives are now available for all statins approved for sale in Canada.
- The most potent statins – rosuvastatin (Crestor®) and atorvastatin (Lipitor®) – control almost 75% of the High Cholesterol market; 2012 marked the first full calendar year that generic versions of both these high-potency statins were available.
- While use of rosuvastatin is still increasing, spending for this drug has decreased due to the presence of generics. This drug has become the most cost-effective, cholesterol-lowering therapy available in terms of clinical and therapeutic effectiveness – and cost.

A CLOSER LOOK

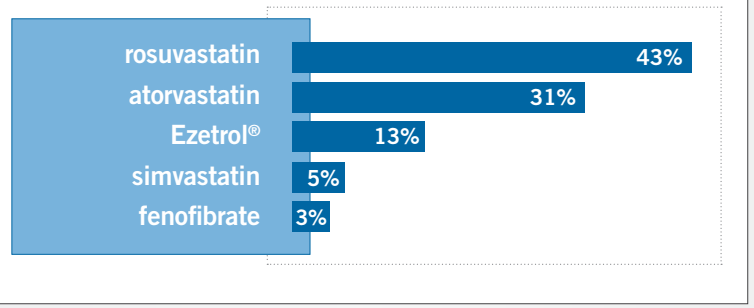
- Cholesterol management – particularly LDL cholesterol – is recognized to be an integral component toward the reduction of risk of cardiovascular events such as heart attack and stroke. As stated in the 2012 Canadian Cardiovascular Society Guidelines, statins are the first-line mainstay of therapy for high cholesterol because they have been proven to reduce an individual's relative cardiovascular disease risk by 25%-35%.
- Statins were once seen to increase the incident risk of diabetes; however, new analyses have shown that the cardiovascular benefits of statin therapy far outweigh the increased risk of developing diabetes.
- Ezetrol®, a non-statin gastrointestinal cholesterol absorption inhibitor, continues to increase in utilization and spend. It is substantially more costly than statins, with an annual price tag of approximately $730, compared with $200 for generic versions of Crestor®, with no direct evidence of efficacy in reducing cardiovascular event risk.
- In late 2012, new Canadian dyslipidemia guidelines were issued. These include a systematic approach through which to deal with purported statin intolerance; it recognizes that statin adherence is suboptimal, which could result in increased morbidity and mortality. The guidelines further acknowledge that the efforts expended to deal with statin intolerance should be proportional to the patient's individual risk profile for cardiovascular disease.

WHAT'S AHEAD

Express Scripts Canada expects that the High Cholesterol therapy class will continue to experience a downward trend in 2013, as generic prices continue to drop due to provincial reforms. That said, for 2014 and beyond, Express Scripts Canada believes that this will turn into a flat trend once the generic prices are stabilized. New drugs in the pipeline – especially those with unique mechanism of actions – will then be expected to drive the trend up when those products receive regulatory approval and are introduced to the market.

- REGN727/SAR236553 (REGN727) is an investigational, fully human, monoclonal antibody that is highly specific for human PCSK9, and blocks its interaction with the LDL receptor. Based on current data available, this biologic therapy may be particularly useful for patients with the rare familial hypercholesterolemia disorder (genetic mutation that causes very high cholesterol), and for patients for whom statins do not appear to sufficiently reduce the risk for a CV event.
- Despite initial negative results, work continues on cholesterlester-transfer protein (CETP) inhibitors. Failures were torcetrapib and dalcetrapib; however anacetrapib is currently in phase III trials
- A new genetic-based therapy for familial hypercholesterolemia, a rare genetic form of high cholesterol that causes very high blood levels of LDL (the "bad" form of cholesterol) which are only partially managed with usual cholesterol medications, called mipomersen (Kynamro™, Isis Pharmaceuticals), received approval in January 2013 from the United States Food and Drug Administration. This drug, which carries an estimated annual cost of US$200,000-US$300,000 per patient, would substantially drive up spend for the High Cholesterol therapy class if it enters the Canadian market.

TOP DRUGS FOR HIGH CHOLESTEROL
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
-18.37%	6.17%	6.40%	$59.37	15.03%

HIGH BLOOD PRESSURE

High Blood Pressure is commonly called **"the silent killer"** because you can't feel it and you can't see it. Over time, hypertension damages the heart and blood vessels. Eventually, untreated hypertension **can lead to life-threatening health problems**, such as heart disease and stroke.

YEAR IN REVIEW

- The High Blood Pressure therapy class, like the High Cholesterol therapy class, posted a trend decrease of 15.4% in 2012, compared with a decline of 10.1% in 2011.
- The overall trend was driven primarily by the 14.2% decrease in cost per script in 2012, as generic alternatives for most medications were introduced to the market.
- Utilization dropped by 1.2% to 13% of total claims in 2012. This decline is best explained by the increasing availability of combination products which help to improve administration convenience, enhance adherence, and combine two prescriptions into one. For example, many angiotensin-converting-enzyme (ACE) inhibitors are combined with a diuretic in a pill, such as Altace® HCT, which contains two active ingredients – ramipril and hydrochlorothiazide.
- High Blood Pressure remains the top-ranked therapy class by utilization. In 2012 it had the highest prevalence among all chronic conditions, with one in every five claimants obtaining at least one drug to treat it.
- High Blood Pressure dropped to second place in the ranking by spend in 2012, as did its share of overall spend (13% in 2012, compared with 13.2% in 2011).

A CLOSER LOOK

- Recent new drugs, although they are new molecular entities, are "me-too" products:
  - ✔ **Edarbi** (azilsartan) – the eighth angiotensin receptor blocker (ARB) to come to market; an accompanying combination product has also been released, **Edarbyclor** (azilsartan + chlorthalidone [diuretic]).
  - ✔ **Bystolic®** (nebivolol) – the 13th beta-blocker to be released in Canada.
  - ✔ All, or most, of the other drugs in the categories, have generics available.
- The angiotensin-converting-enzyme (ACE) inhibitor, Coversyl® and its diuretic combination product, Coversyl® Plus, are the only single-source brand products within the ACE inhibitor drug class. Considering the multiple therapeutic options available, these two products made up 13% of total spend in the High Blood Pressure therapy class. It is also important to note that both of these drugs are listed in the top five therapies indicated for the treatment of the disease.
- The ALTITUDE study, which was terminated at the end of 2011, led to an end of the last possible renin angiotensin system combination therapy of the direct renin inhibitor, aliskiren (Rasilez®) with either an ACE inhibitor or angiotensin reception blocker (ARB). The utilization and spend of Rasilez® dropped by half in 2012 – year over year, the number of scripts decreased from 0.10% of total claims to 0.05%; spend decreased from 0.11% of overall spend to 0.06%.

- The effective management of high blood pressure is essentially focused on cardiovascular risk management and vascular protection. Proactive management of these risk factors are integral to prevent complex medical complications such as heart attack, stroke, and kidney failure.

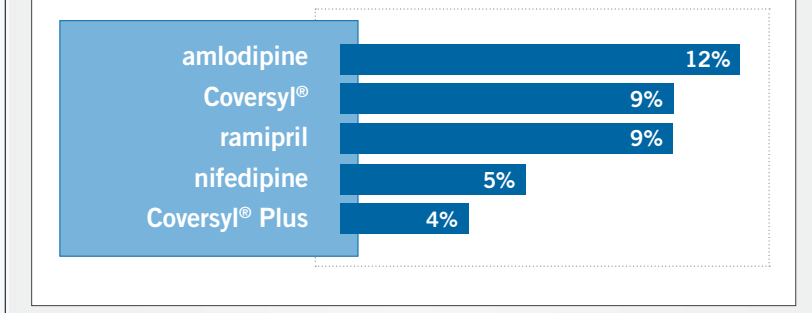
WHAT'S AHEAD

Express Scripts Canada predicts that the trend for the High Blood Pressure therapy class will continue to be similar to High Cholesterol, with trend remaining negative in 2013 due to further reductions of prices for generic alternatives. As there are fewer drugs in development pipelines in this therapy class, Express Scripts Canada believes trend will stay relatively flat in the near-term.

- Continued improvements in understanding issues related to adherence to prescribed medications and targeting therapies appropriately to high-risk individuals is expected lead to improved overall cardiovascular-risk outcomes.

- A drug with a new mechanism of action – a vasopeptidase inhibitor called ilepatril – is currently in phase IIb/phase III clinical trials for hypertension. This drug is also currently being investigated for diabetic nephropathy.
- A dual-mechanism ARB/nepilysin inhibiting compound, LCZ696, is under development for the treatment of hypertension.

TOP DRUGS FOR HIGH BLOOD PRESSURE
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
-15.36%	13.02%	7.63%	$33.29	20.74%

MENTAL HEALTH

The **Mental Health** therapy class is primarily comprised of drugs for the common indications of **depression and antipsychotic**. Both of these Traditional drug classes are among the few that have **shown increases** in proportion of total spend over the past five years.

YEAR IN REVIEW

- Utilization for depression increased 1.94% in 2012. Conversely, the average cost per script decreased 1.05%. These resulted in an overall trend increase of 0.88%, compared with a decline of 1.50% in 2011.
- Utilization and cost for antipsychotic increased 5.69% and 0.30% respectively in 2012. This led to an overall trend increase of 6%.
- A new antipsychotic drug, Latuda™, was released in 2012. While there are some differences in receptor subtype activity from other antipsychotics, Express Scripts Canada does not believe this has the potential to become a breakthrough molecule in this therapy class.

A CLOSER LOOK

- Over the past five years, spend on depression increased to 7% of overall spend in 2012, compared with 6.5% in 2007. Similarly, antipsychotics increased to 1.35% of overall spend, up from 1.2% for the corresponding five-year period. These increases support a growing medical concern in society – not only might mental-health issues worsen a patient's quality of life, but they may also have an adverse impact on overall workplace productivity.
- In early 2012, the Mental Health Commission of Canada (MHCC) issued the first mental strategy for Canada. The strategy included an employer's action guide designed to help protect employees' psychological health and safety. It also articulated the need to maintain a psychologically healthy workplace that keeps workers safe, engaged and productive.
- Many of the newer antipsychotic medications are also used adjunctively for depression, which is driving a major portion of utilization for this therapy class.

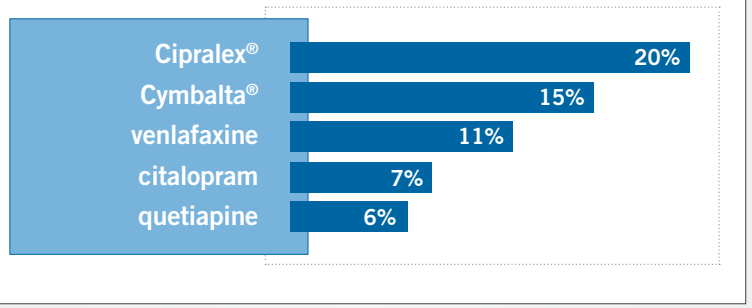
- Statistics published in the January and March 2012 issues and January 2013 issue of *Benefits Canada* magazine indicate that 15%-30% of working-age individuals will experience a mental disorder during their working lives. Additionally, 12% of current employees have diagnosed mental-health issues; however, 17% delay the decision to seek help due to fear of negative stigma from family, friends and colleagues. Many fear that they will lose or compromise their opportunities to advance their careers by revealing their mental-health issues in the workplace. It is not known whether this is causing lower utilization levels and suboptimal pharmacotherapy. Mental-health issues account for approximately 30% of all disability claims and 70% of the associated plan costs.

WHAT'S AHEAD

Express Scripts Canada research shows that one in every seven claimants (13.37%) was prescribed at least one depression medication in 2012. Mental health is often under-recognized and its major indirect cost, loss in productivity, is often high. Express Scripts Canada advises plan sponsors – companies and organizations that provide health benefits to their employees – to evaluate workplace environment and potential contributors to depression, particularly stress, to optimize the overall health of their employees.

- Data recently released suggest that genetic variants and mutations may indicate increased susceptibility to adverse effects of medications as well as increased susceptibility to certain types of mental illness such as schizophrenia, anxiety, attention and mood disorders.
- With recognition that pharmacotherapeutic innovation in psychiatry has essentially stalled with no new agents with new mechanisms of action – all new drugs are essentially "me-too" entrants. In the United States, the National Institutes of Health (NIH), through the National Institute of Mental Health (NIMH), has started a new initiative to stimulate diagnostic and drug discoveries for psychiatric conditions.

TOP DRUGS FOR MENTAL HEALTH
By Market Share



KEY FACTS

TREND
+1.81%

PERCENTAGE OF TOTAL CLAIMS
9.25%

PERCENTAGE OF TOTAL SPEND
8.37%

AVERAGE COST PER SCRIPT
$51.50

PREVALENCE
Depression: 13.4%
Antipsychotic: 2%

CANCER

Cancer is a group of diseases characterized by uncontrolled growth or **spread of abnormal cells**. Much time, effort, and money is being directed toward cancer research worldwide.

YEAR IN REVIEW

- Cancer medications had a greater trend increase of 4.66% in 2012, compared to 2% in 2011. Utilization and cost per script had modestly increased by 2% and 2.7%, respectively.
- Seven of the 30 highest cost-per-prescription drugs that received Health Canada approvals, and were released in 2012, were cancer drugs:
  - ✔ **Xalkori™** (crizotinib). Orally administered drug indicated for the treatment of anaplastic lymphoma kinase (ALK)-positive advanced (not amenable to curative therapy), or metastatic non-small-cell lung cancer (NSCLC). Cost – $7,762 per prescription.
  - ✔ **Yervoy™** (ipilimumab). Intravenous injection indicated for the treatment of unresectable or metastatic melanoma. Cost – $8,143 per prescription
  - ✔ **Zelboraf™** (vemurafenib). Taken by mouth for the treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma. Cost – $7,642 per prescription.
  - ✔ **Inlyta™** (axitinib). Orally administered drug indicated for the treatment of metastatic renal cell carcinoma (RCC) of clear cell histology. Cost – $4,444 per prescription.
  - ✔ **Jakavi®** (ruxolitinib). Orally administered drug for the treatment of splenomegaly and/or its associated symptoms in adult patients with primary myelofibrosis. Cost – $5,170 per prescription.
  - ✔ **Treanda®** (bendamustine). Intravenous injection used to treat relapsed indolent B-cell non-Hodgkin lymphoma and symptomatic chronic lymphocytic leukemia. Cost – $5,512 per prescription.
  - ✔ **Caprelsa®** (vandetanib) Taken by mouth for the treatment of symptomatic or progressive medullary thyroid cancer in adult patients with unresectable locally advanced or metastatic disease. Cost – $6,061 per prescription.
- All of the aforementioned drugs – except Treanda® (a chemotherapeutic agent) and Yervoy™ (a monoclonal antibody) – are targeted, personalized medicine, oral agents used by individual patients at home.

A CLOSER LOOK

- The increase in spend for drugs to treat cancer nearly doubled to 2.8% in 2012 from 1.7% of overall spend in 2007.
- Much of the increase in costs for cancer drugs is driven by the development and introduction of new drugs to treat unique genetic or proteomic profiles, a trend that has increased in recent years. All of the high-cost drugs approved in 2012 for cancer – except for Treanda® – are targeting genetic anomalies that are associated with various cancers.
- The development of medications that target specific molecular and genetic changes in human cells that cause cancer requires additional research. Often, this also means that additional research-and-development costs are incurred, which results in higher prescription costs, as more patients begin treatment regimens on these newer, more-expensive therapies, rather than trying older oncology medications as first-line treatments.

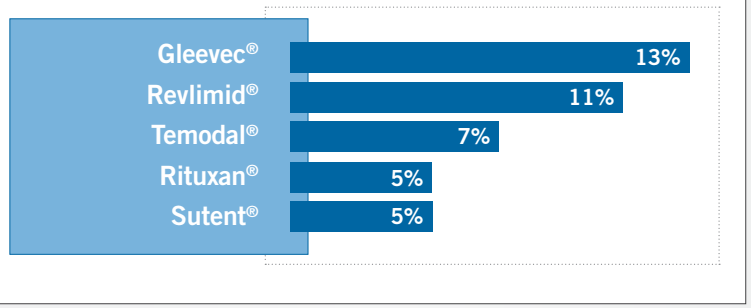
- Oral agents are typically not covered on hospital formularies and coverage on provincial drug formularies is scarce, leaving the patients and private payers to pay for the majority of costs.

WHAT'S AHEAD

Express Scripts Canada expects that the Cancer therapy class will continue to expand with the growing number of drugs in the development pipeline. Express Scripts Canada further expects the shift to in-home administration with novel oral agents to continue to gain traction throughout the country.

- Work continues to try to better understand the genetic basis of cancer. Express Scripts Canada believes this will lead to new targeted therapies, which will provide clinical benefits to a relatively small patient population. However, given such a low anticipated rate of utilization, the anticipated cost per patient for these medications is expected to be substantively high.
- New Cancer drugs are also receiving approvals for a larger number of indications, thus expanding the target population. For example, the mTOR kinase inhibitor, everolimus (Afinitor*), was initially approved for the treatment of advanced kidney cancer; it has since been approved by Health Canada to treat patients with advanced breast cancer.
- Antibody drug combinations being investigated to deliver highly potent chemotherapeutic drugs targeted specifically to the interior of certain types of cancer cells. Some, such as Adcetris® (brentuximab), have recently been approved.
- The private-payer spend on Cancer therapies is expected to be influenced by public coverage decisions, which will likely vary by province. For example, a decision by provincial governments to agree cover the full cost of oral cancer drugs could alleviate the financial burden on patients and plan sponsors.

TOP DRUGS FOR CANCER
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
+4.66%	0.60%	2.81%	$301.71	1.69%

INFLAMMATORY CONDITIONS

The **Inflammatory Conditions** therapy class includes drugs that treat a variety of **complex and severe medical conditions** that involve the modulation of pathologic inflammatory processes – rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, and psoriasis. The **common factor** among these inflammatory conditions is the **shared immunologic etiology**. Biologic immune response modifiers show **excellent clinical response rates** in patients with these disorders – especially those who do not respond to conventional treatments.

YEAR IN REVIEW

- Upward trend of 13.79% was primarily driven by a 10% increase in utilization and 3.8% increase in the cost per script.
- New treatment guidelines released for rheumatoid arthritis in Canada and the United States in late 2011 and mid-2012, and for psoriasis, which now advocate the early initiation of biologic DMARD, continued to drive utilization.
- Remicade® is now ranked first in total spend, followed closely by Humira® (3) and Enbrel® (6).
- Health Canada-approved indications for treatment continued to expand for biologic DMARDs. For example, Humira® received its sixth official indication – more specifically, for the treatment juvenile idiopathic arthritis in November 2012.
- Utilization of Stelara® increased 33% year over year, although it is only indicated for the treatment of moderate to severe plaque psoriasis.

A CLOSER LOOK

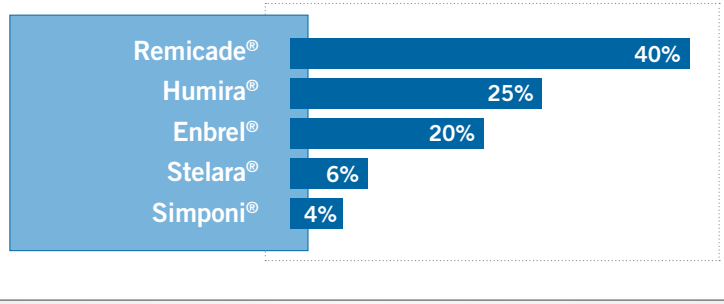
- Increasing product availability and regulatory approval for more indications drove the spend on Inflammatory Conditions to more than double in the past five years – to 9.5% in 2012 from 4.5% of the overall spend in 2007.
- In 2012, patents expired for several Specialty drugs, such as Remicade® and Rituxan®. But unlike small molecule-branded drugs, the approval of subsequent-entry biologics (SEBs) is governed by a different regulatory regime, which creates complexities and uncertainties to product development and potential launch.
- Regulatory hurdles, as well as uncertainty in the final regulatory framework in the United States, have prompted some potential manufacturers of SEBs to abandon their efforts.

WHAT'S AHEAD

Express Scripts Canada predicts that the Inflammatory Conditions therapy class may again experience double-digit growth like it did in 2012 (13.79%) and 2011 (14.3%). And Express Scripts Canada further expects that new oral pipeline drugs – particularly tofacitinib and apremelast – will likely push cost and utilization even higher in the near future.

- Tofacitinib (marketed in the United States as Xeljanz™), a new oral drug with a new mechanism of action expected to be released in 2013, has disease-modifying effects on rheumatoid arthritis, and is currently being investigated for indication as a treatment for other inflammatory conditions.
- While most of the development in the Inflammatory Conditions therapy class has focused on RA, with expansion of indications to other inflammatory conditions after approval, newer agents are being developed for initial use in other inflammatory conditions.
- Apremelast, a phosphodiesterase-4 inhibitor similar to Daxas™ that is indicated for the treatment of chronic obstructive pulmonary disease (COPD), is a new oral drug being developed for moderate to severe plaque psoriasis. Anti-Interleukin-17 antibodies – brodalumab and ixekizumab – are also under regulatory review as a treatment for psoriasis.
- Two new immunologic agents are under development for systemic lupus erythematosus (SLE) with different mechanisms of action – atacicept (a recombinant fusion protein B cell inhibitor) and tabalumab (an anti-BAFF antibody, similar to Benlysta™).
- GSK-1605786, a selective antagonist of the CC chemokine receptor (CCR9), is being developed as a potential treatment for inflammatory bowel disease, including Crohn's disease.

TOP DRUGS FOR INFLAMMATORY CONDITIONS
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
+13.79%	0.25%	9.48%	$2,342.23	0.41%

MULTIPLE SCLEROSIS

Multiple Sclerosis (MS) is a complex disease, characterized by **damage to the myelin sheath**, or covering, surrounding nerves in multiple areas of the **central nervous system**. MS is often diagnosed in young adults, affecting the daily activities of diagnosed patients.

YEAR IN REVIEW

- Overall trend doubled to 5.78% in 2012, compared with 2.8% in 2011. Cost-trend growth (4.1%) was the primary driver of the overall trend, potentiated by a modest increase in use (1.7%).
- Trend was affected significantly by the oral MS drug, Gilenya®, which was released in 2011. Utilization increased 3.5-fold to 2,575 scripts in 2012, from 845 scripts in 2011. Gilenya® is the first oral disease-modifying MS drug to be marketed. Of all MS drugs, it also has the second-highest average cost per claim (after Tysabri®).

A CLOSER LOOK

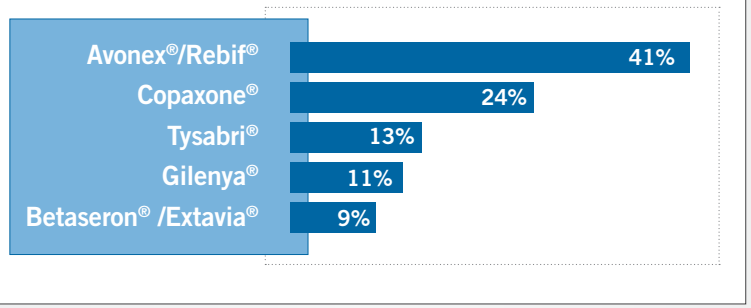
- MS is an unpredictable, often disabling disease of the central nervous system. It attacks the myelin protective covering that lines the nerves of the central nervous system, and causes a variety of neurological symptoms.
- As a proportion of the overall private-payer drug spend Canada, the spend on MS drugs has grown 15% in the past five years to 2.5%, compared with 2.2% in 2007.
- MS is the most common neurological disease affecting young adults in Canada, and Canadians have one of the highest rates of multiple sclerosis in the world. Every day, three people are diagnosed with MS. As such, Express Scripts Canada expects overall utilization to increase.
- Interferons (e.g., Avonex®, Betaseron®) continue to be the standard of care; as such, they comprise 50.5% of the MS spend.
- The oral disease-modifying drug, Gilenya®, has grown to capture over 10% of the market in just one year. Utilization of this drug has driven the bulk of the increase in spend in the category.
- The newest oral drug, Fampyra™, which was approved and released in 2012, is limited to provide improvements in walking and does not have disease-modifying properties. As a result, Express Scripts Canada believes it will have a lesser impact than Gilenya®.

WHAT'S AHEAD

Express Scripts Canada anticipates that the MS therapy class will continue to grow throughout 2013 and beyond. Clinical improvements provided by current oral drugs and those in pipelines are expected to continue to result in increased utilization and spend.

- Several more oral, disease-modifying medications indicated to treat relapsing-remitting cases of MS – triflunomide (approved in U.S. in 2012), dimethyl fumarate (BG-12), and laquinimod – are expected to be approved in the near term.
- BG-12 is expected to be the market leader with high efficacy rates, with moderate safety concerns, such as gastrointestinal intolerance and flushing, which have been shown to subside with use.
- With additional oral MS products in the pipeline, Express Scripts Canada believes that plan sponsors will be challenged to manage the therapy offered by these more convenient but much more costly drugs.
- Biologic drugs that require intravenous injection and currently are approved for other conditions may receive additional indications, allowing them to expand into the MS market. They include alemtuzumab, which is currently approved to treat chronic lymphocytic leukemia, and daclizumab, a transplant medication.

TOP DRUGS FOR MULTIPLE SCLEROSIS
By Market Share



KEY FACTS

TREND	PERCENTAGE OF TOTAL CLAIMS	PERCENTAGE OF TOTAL SPEND	AVERAGE COST PER SCRIPT	PREVALENCE
+5.78%	0.08%	2.53%	$1,783.61	0.11%

TREND OVERVIEW 2

THERAPY CLASS REVIEW 32

DRIVING BETTER DECISIONS

DRIVING BETTER DECISIONS

REDUCING WASTE AND CLOSING GAPS IN CARE

Although great clinical care starts with clinicians – physicians, pharmacists, nurses and other health-care providers – provider expertise alone is insufficient. If a physician correctly diagnoses a condition and prescribes the most efficacious treatment but the patient fails to take medication as prescribed, optimal health outcomes are not achieved. When a patient uses a delivery channel that is more expensive, or a medication that costs more but offers no clinical advantage, waste ripples through the system.

Express Scripts Canada's proprietary research has determined that poor decisions contribute up to $5.1 billion in annual drug-spend waste. This is equivalent to 33% of the $15.4 billion in prescription drug spend in Canada.

FIGURE 24 | Waste Running Wild
Billions of Dollars Wasted Each Year on Prescription Drugs in Canada

Express Scripts Canada research has determined that aproximately $5.1 billion – or up to 33% of the $15.4-billion total private health-plan spend on prescription drugs in Canada – is wasted by paying more for maintenance medications that generate no additional health benefits.

DRUG-MIX WASTE
$3.9 BILLION
Using higher-cost medications that generate no additional benefits

CHANNEL WASTE
$1.2 BILLION
Using less-than-optimal dispensing intervals

With respect to waste within the prescription drug benefit, Express Scripts Canada defines waste as "spending more without improving health outcomes." There are two key sources of drug-spend waste: where people get their medications (Channel Waste), and which medications they receive (Drug-Mix Waste).

- **Channel Waste.** Waste in drug spend that is created by using suboptimal dispensing intervals for maintenance drugs and by not using the more cost-effective distribution channels.
- **Drug-Mix Waste.** Waste in drug spend that is created by using higher cost medication that generates no additional health benefits.

Drug-spend waste notwithstanding, gaps in care due to patient non-adherence are cause for additional concern as this can lead to a worsening of a condition that creates additional costs for plan sponsors, including the cost of additional drug therapy, increased absenteeism, decreased productivity, and most importantly, increased disability costs.

Waste and gaps in care can be avoided if patients engaged in three simple pharmacy-related behaviours:

- Use safer, more cost-effective delivery channels
- Use lower-cost, clinically effective medications
- Take medications as prescribed

Given that many patients fail to engage in these three behaviors, health-care plans do not achieve optimal clinical outcomes at financially sustainable costs. These behavioural mishaps aren't just limited to patients. In the absence of complete information about drug prices and benefits-plan design, physicians often fail to provide patients with more cost-effective options that are equally as effective. The costs of these often unintentional missteps take an enormous financial toll on plan sponsors in Canada and do not improve the health of the workforce.

FIGURE 25 | Waste Made Worse

Non-Adherence Costs Billions More per Year

When patients fail to take medications as prescribed, the impact of prescription drug waste is magnified by the additional health-care spending required to treat worsening medical conditions.

Short-Term Disability Insurance	Additional Drug Therapy	Absenteeism	Presenteeism
Emergency Room Visits	Additional Physician Visits	Extra Lab Tests	Hospital Admissions

Better Decisions...
...Lower Costs,
Healthier Results

Over the past few years, Express Scripts research has repeadedly demonstrated that better care and zero waste often go hand-in-hand – the most effective care often costs the least.

Low-Cost Medications	Low-Cost Channel	High Adherence
Using the lower-cost, clinically effective medications	Using more cost-effective delivery channels	Taking medication as prescribed

DRUG-SPEND WASTE BY REGION

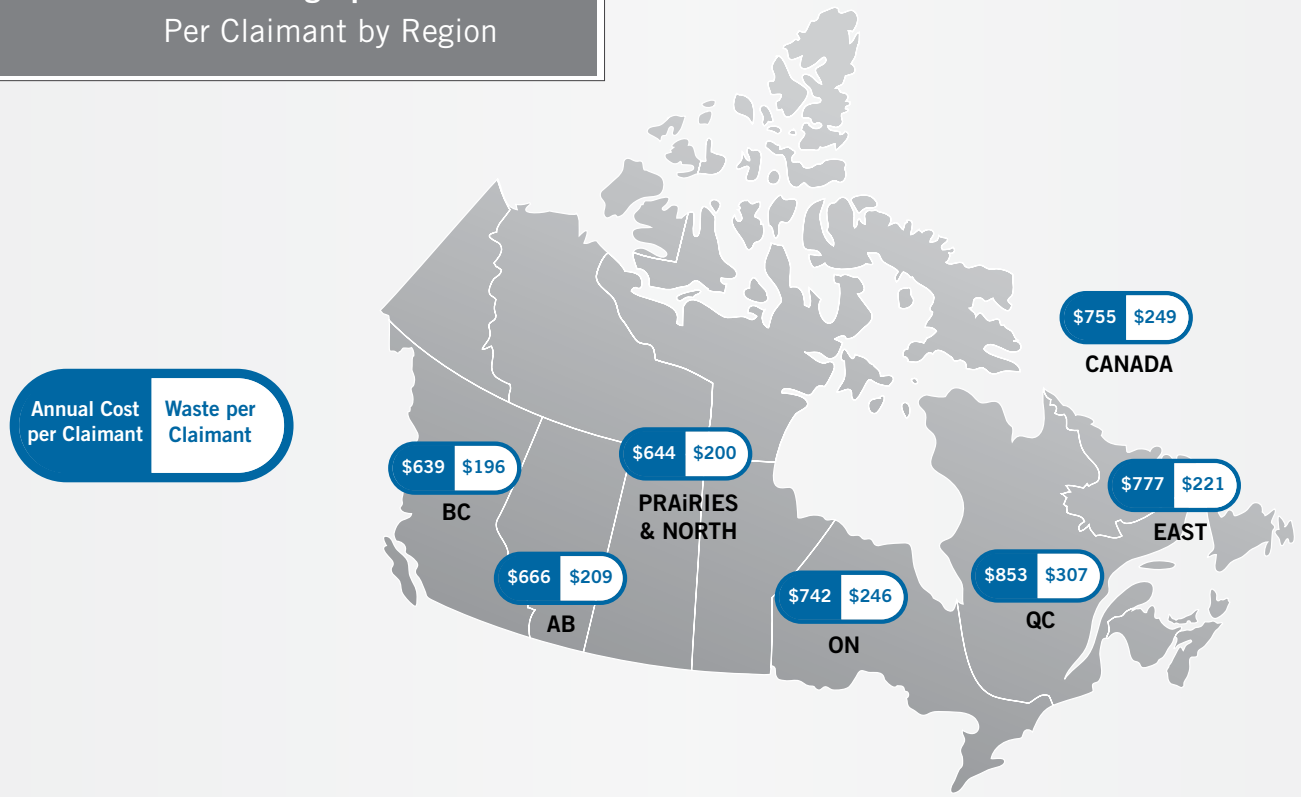
Regardless of provincial pharmacy legislation, and reimbursement variations across Canada, drug-spend waste occurs in each region of the country. On average, 33% of total drug spend in 2012 – or $249 per claimant – was considered waste; that is, spending without improving health outcomes.

The East – Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland & Labrador – collectively had the lowest rate of waste in 2012: 28.5% of total drug spend per claimant ($221 out of $777). This can be attributed primarily to the lower average dispensing fee of $9.20 submitted by retail pharmacies, compared with the national average fee of $10.91.

Conversely, Québec generated the greatest amount of waste with 36% of its total drug spend qualifying as waste. This is best explained by its high channel waste and high drug-mix waste. Québec has a common practice of dispensing a 30-day supply for maintenance medications prescribed to treat ongoing medical conditions; this often results in more dispensing fees than clinically necessary. In addition, private plans are exposed to higher mark-up and dispensing fees due to "usual and customary" pricing in Québec than in other provinces. Québec also had the greatest level of drug-mix waste due to the lowest generic fill rate in Canada at 51.6%. Combining both factors, it is not surprising that much drug spend waste is generated in Québec.

On average, **33%** of total drug spend in 2012 – or **$249 per claimant** – was considered waste; that is spending without improving **health outcomes**

FIGURE 26 | 2012 Drug Spend Waste
Per Claimant by Region



CHANNEL WASTE

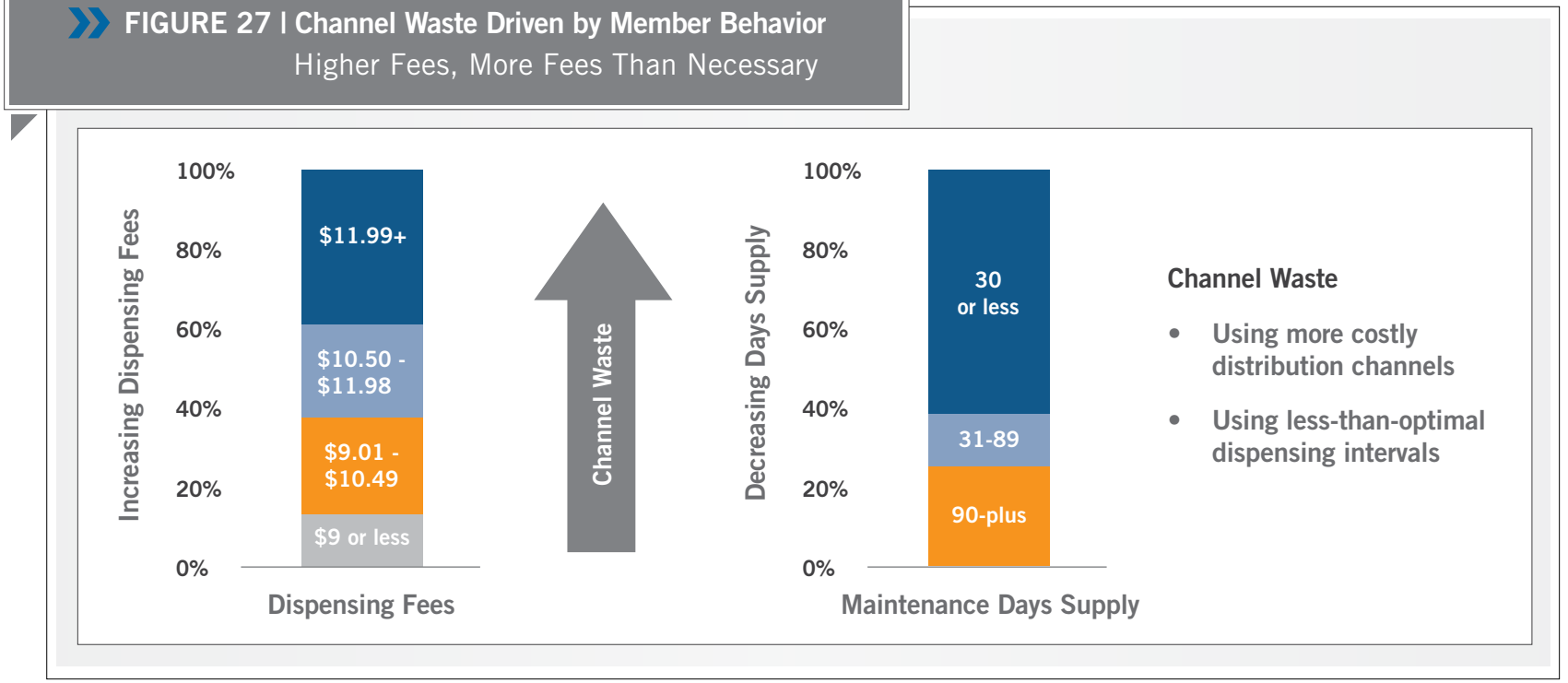
Suboptimal Use of the More Cost-Effective Distribution Channels

A major component of channel waste is created when patients choose to fill their prescriptions at pharmacies that charge high dispensing fees. Express Scripts Canada research shows that the national average for dispensing fees in 2012 was $10.91. It further shows that 58% of all claims were submitted with a fee of $10.50 or greater, and a little more than one-third (37%) of all claims were submitted with a fee of $11.99 or greater. This occurs as utilization is skewed toward high-cost channels due to patient behaviour, which may be unintentional rather than deliberate, and that behaviour resulted in spending more with no improvement in health outcomes.

Suboptimal Dispensing Intervals for Maintenance Medications

The aging Canadian population – and the increasing prevalence of chronic conditions, such as diabetes and high cholesterol – have driven the utilization of maintenance drugs. Research conducted by Express Scripts Canada has determined that maintenance medications represent 55% of drug-benefit costs and 65% of drug- benefit claims, with an average supply of 46 days per script vs. the optimal of 90 days. Express Scripts Canada's database, which houses drug claims for more than 6.5 million Canadians, showed that 63% of all maintenance drugs used on an ongoing basis were filled with 30-day supply. The greatest waste occurred in Québec, where 99.5% of all maintenance drug claims were for a supply of 30 days or less. Lengthening the number of days of supply to 90 from 30 would eliminate unnecessary dispensing fees paid, thus allowing plan sponsors to eliminate waste and otherwise allocate their resources.

FIGURE 27 | Channel Waste Driven by Member Behavior
Higher Fees, More Fees Than Necessary

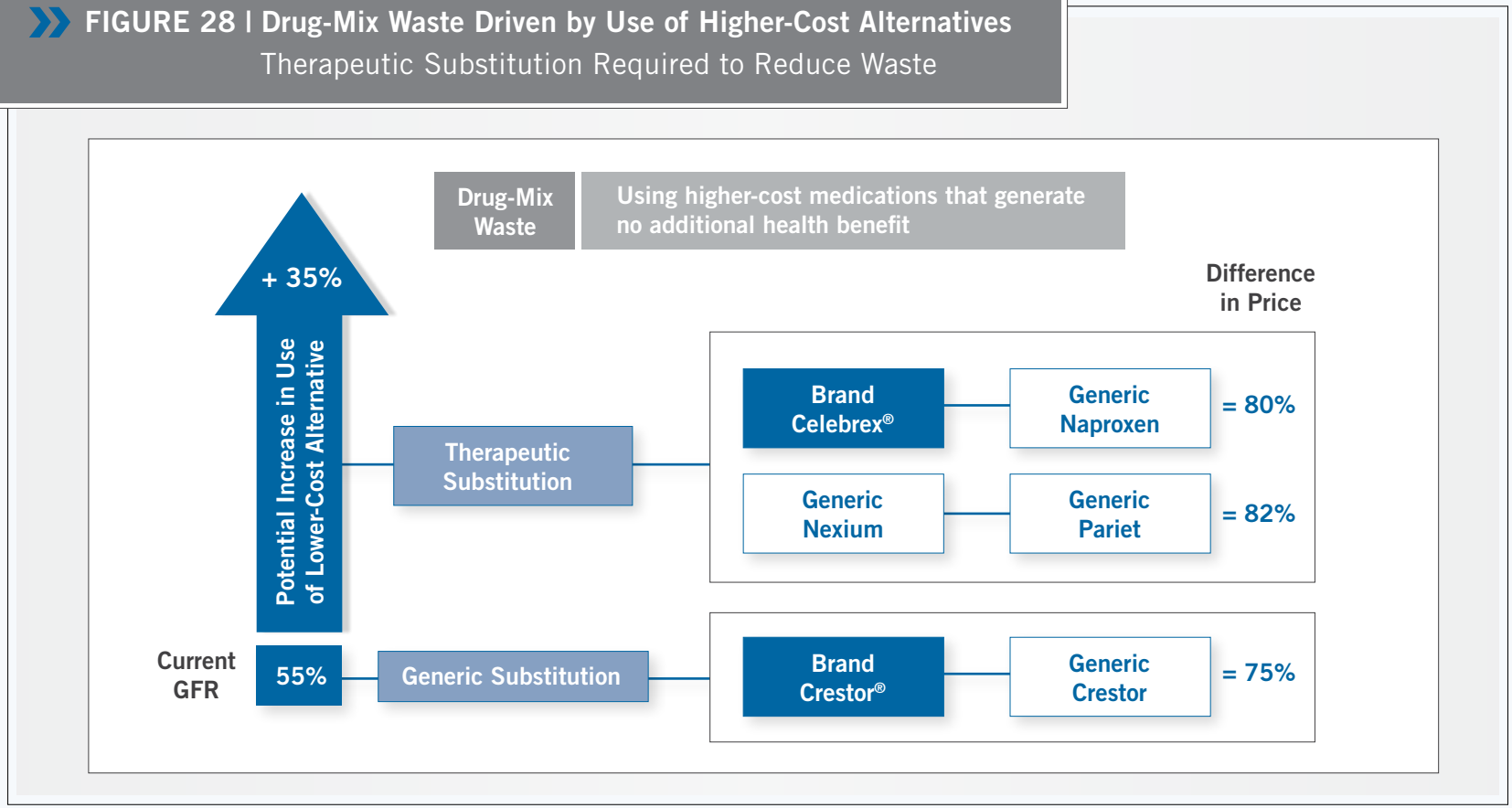


DRUG-MIX WASTE

Drug-mix waste is associated with the use of higher-cost medications that generate no additional health benefit. Express Scripts Canada research for 2012 calculated the cost of drug-mix waste in the private-sector drug spend to be $3.9 billion.

Elimination of drug-mix waste can be achieved by taking full advantage of lower-cost therapeutic alternatives. While patent expiries helped increase the national generic fill rate to 55% in the fourth quarter of 2012, compared with 42% in 2010, Express Scripts Canada has determined that there is the potential to increase the use of lower-cost alternatives by an additional 35%, through both generic and therapeutic substitution.

FIGURE 28 | Drug-Mix Waste Driven by Use of Higher-Cost Alternatives
Therapeutic Substitution Required to Reduce Waste



Generic Substitution

Generic substitution occurs when brand-name medications that have come off patent are switched to lower-cost generic equivalents that have been deemed "interchangeable". This type of substitution happens routinely at the time of dispensing – it helps control drug costs as generics, which are both chemically and therapeutically equivalent, are typically available at 18% to 35% of the brand price. Take for example, when a prescription for brand Crestor® (annual drug cost = $655) is substituted for generic Crestor® (annual drug cost = $155); such a substitution results in savings of $500 per year.

To ensure plan sponsors get the full benefit of financial savings through generic substitution, one must implement a Generic Substitution plan, as this encourages a switch to a generic drug. There are two types of plans available to plan sponsors – a regular Generic Substitution plan and a Mandatory Generic Substitution plan. A regular Generic Substitution plan will cover only the cost of the interchangeable generic, equivalent unless the prescriber indicates "no substitution" or "dispense as written'. A Mandatory Generic Substitution plan will cover only the cost of the interchangeable generic equivalent – regardless of physician indication. Clearly, Mandatory Generic Substitution plans deliver the highest level of savings. As such, provincial drug programs typically incorporate a Mandatory Generic Substitution component to their health-benefits program to optimize the use of lower-cost equivalents and to reduce drug-mix waste.

Therapeutic Substitution

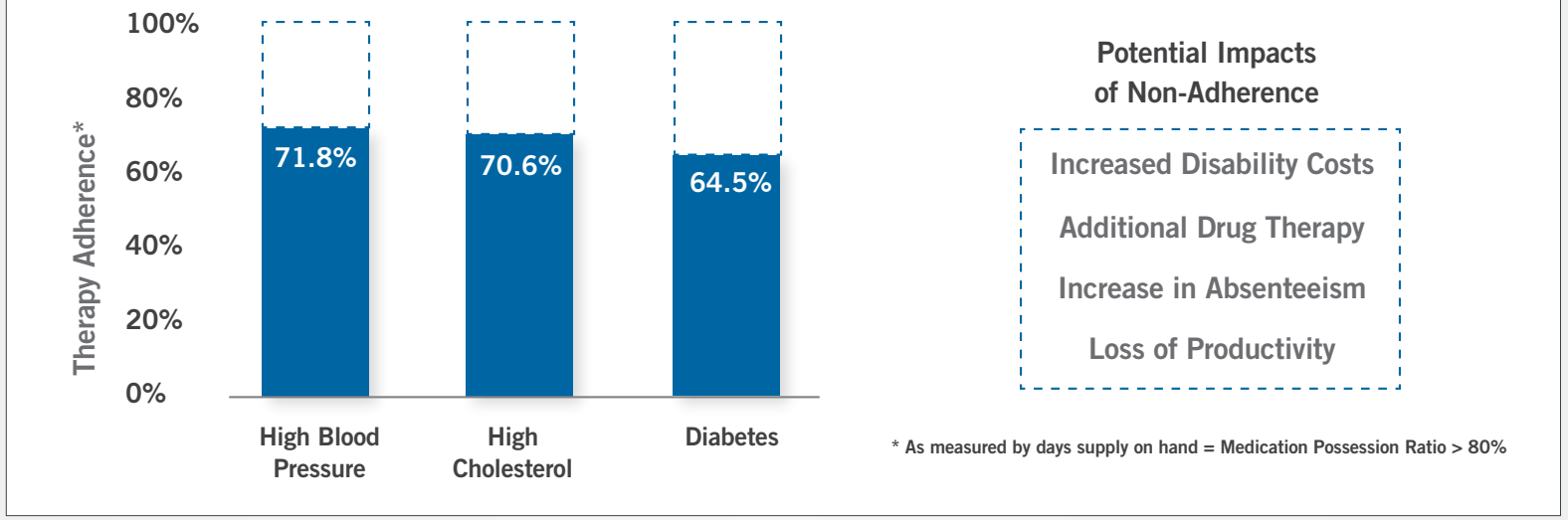
Therapeutic substitution is integral to the elimination of drug-mix waste. Therapeutic substitution refers to switching a prescribed higher-cost drug product to a lower-priced alternative that contains a different chemical entity, but provides a similar therapeutic effect. Since the two products contain different chemical entities, they are not deemed interchangeable, and approval from both the physician and patient is required prior to the switch.

Therapeutic switching – for example, changing a proton-pump-inhibitor-prescription from generic Nexium® (annual drug cost = $682) to generic Pariet® (annual drug cost = $44) – would continue to provide a similar therapeutic effect of preventing gastric ulcers for the majority of patients, but at a much lower cost. Opportunities for therapeutic switching also occur in many other therapy classes. Express Scripts Canada has determined that from a clinical perspective, therapeutic substitution may increase the use of lower-cost alternatives by up to 35%.

Therapeutic substitution requires innovative solutions along with active engagement of both patients and health-care professionals. Express Scripts Canada believes that payers must be proactive with respect to clamping down on drug-mix waste to avoid spending more without improving health outcomes.

FIGURE 29 | Poor Adherence Pressing Issue for Private Payers

Failure to Take Medications as Prescribed Generates Additional Costs



GAPS IN CARE

Gaps in care due to non-adherence is a national issue: patients who fail to take medications, as prescribed, often suffer unnecessary complications and generate additional costs for plan sponsors. Depending on the therapy, these complications can include heart attacks, strokes, heart failure, peripheral vascular disease, amputations, retinopathy, end-stage renal disease and vision loss. Non-adherence to medication therapy is a hidden problem, and one of the most costly and difficult challenges facing plan sponsors.

Express Scripts Canada measures adherence via the Medication Possession Ratio (MPR) – the formula for which is the number of days supply on hand over time. Any patient with a MPR of 80% or above is generally considered as being adherent; while MPR of less than 80% is considered non-adherent.

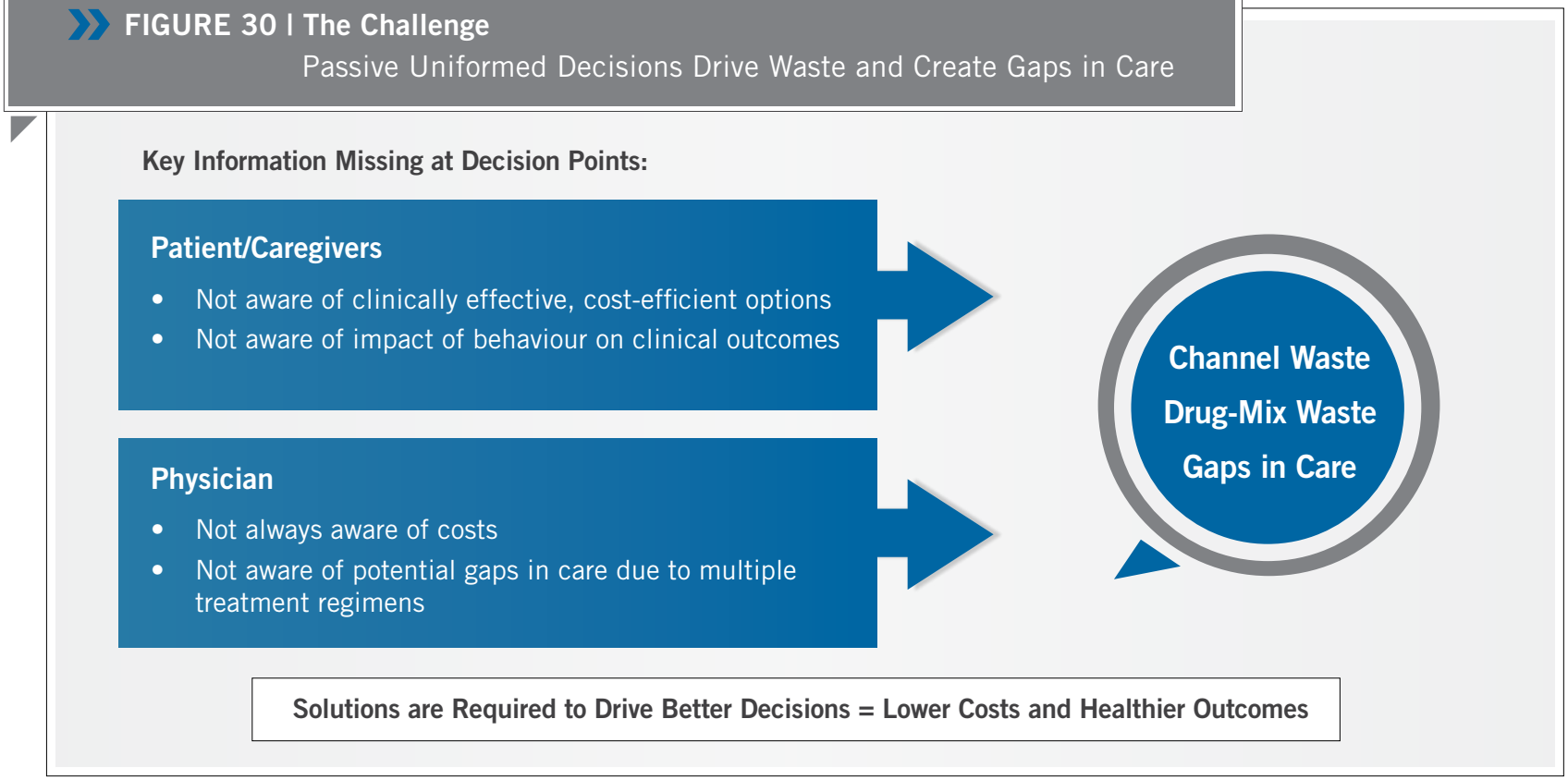
Express Scripts Canada has found poor adherence across many therapy classes; more specifically, the percentage of claimants who are adherent for High Blood Pressure is 71.8%, 70.6% for High Cholesterol, and 64.5% for Diabetes. Given these three chronic conditions can lead to debilitating complications if left undertreated, the potential costs of non-adherence for the private sector includes the cost of additional drug therapy, increased absenteeism, decreased productivity and, most importantly, increased disability costs. As such, plan sponsors should attempt to close gaps in care in order to avoid these unnecessary expenditures.

SOLUTIONS TO REDUCE WASTE AND CLOSE GAPS IN CARE

To better understand the root cause of poor decisions that create waste within the prescription drug benefit and gaps in care, one needs to consider the process through which patients secure their drug treatment.

A typical patient has some knowledge of their health condition, but generally has a poor understanding of their benefit plan. The 2012 Sanofi Canada Healthcare Survey reports that only 13% of employees say they understand their benefits extremely well, down from 19% in 2005. As such, it is also safe to assume that a typical patient has little knowledge of drug-treatment alternatives, and their corresponding savings opportunities. Consequently, patients may unknowingly make several uniformed decisions in the process of securing their drug therapies. Furthermore, physicians do not typically provide patients with choices regarding more cost-effective options that are equally as effective as they may not be aware of drug costs.

FIGURE 30 | The Challenge
Passive Uniformed Decisions Drive Waste and Create Gaps in Care



Health-benefits solutions that provide patients and physicians with key pieces of missing information are needed to drive better decisions which, in turn, can lead to lower costs and healthier outcomes. Express Scripts Canada has found that this can be achieved through the use of Active Pharmacy Benefit Management (PBM) best practices that engage, inform, influence and drive better plan member decisions (see **Appendix 1- Express Scripts Active PBM**). These solutions have been effectively deployed by Canadian plan sponsors which have enjoyed significant savings with minimal employee disruption (see **Appendix 2 – Canadian Case Study**).

In summary, the reduction of waste within the prescription drug benefit and closing gaps in care is absolutely critical to increase the likelihood that plan members achieve healthier outcomes at lower costs. Research by our parent, Express Scripts, shows better care and zero waste often go together: the most effective care doesn't always have to be the most expensive alternative. Therefore, the objective is to make these goals compatible in a manner that is tenable for both plan members and plan sponsors. Research has further revealed the biggest gap is not between what plan sponsors want and what patients want, but rather between what patients want and what patients do. So the real gap is between good intentions and observed behaviour.

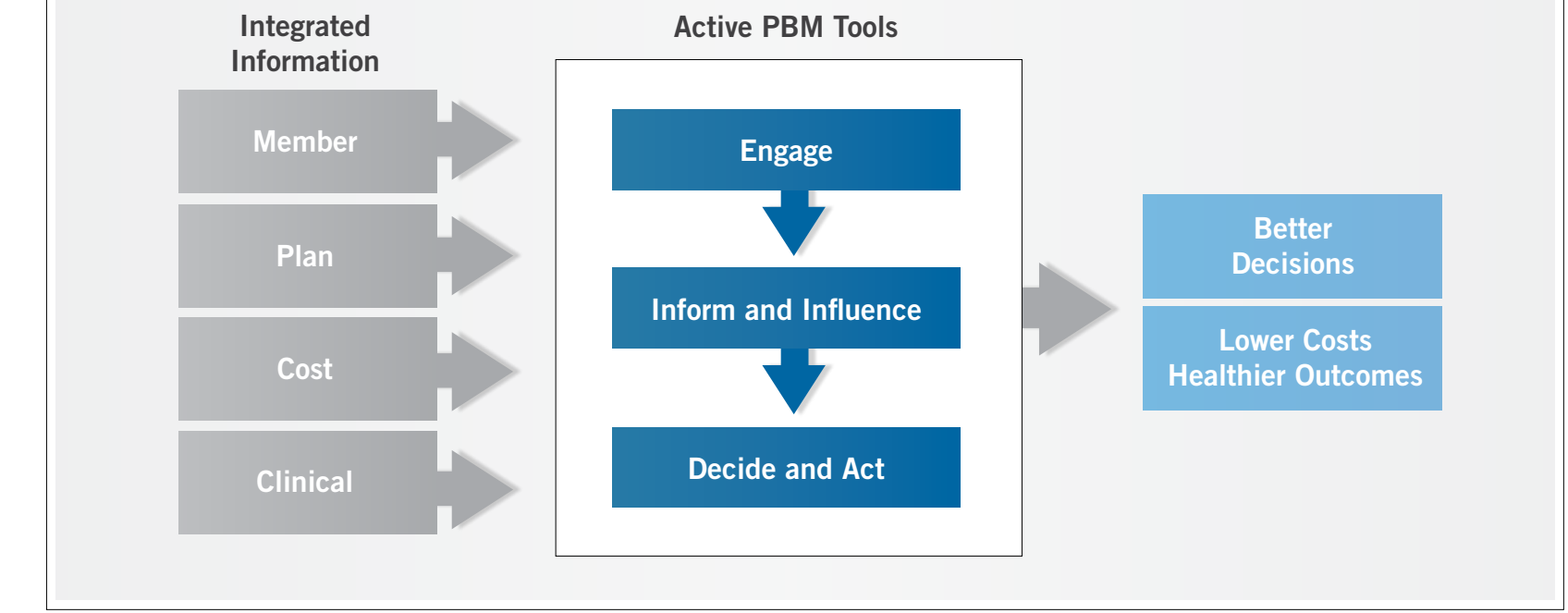
Express Scripts Canada continues to leads the way in bringing unique approaches to the Canadian marketplace that provide plan sponsors with practical solutions that achieve optimal health outcomes at financially sustainable costs.

APPENDIX 1 – EXPRESS SCRIPTS CANADA'S ACTIVE PHARMACY BENEFIT MANAGEMENT SERVICE

Express Scripts Canada's Actively Managed Pharmacy Benefit Management (PBM) service integrates member, plan, cost and clinical information to trigger needs-based, proactive notifications that are specific, timely and relevant to each member. The programs are clinically based, and rely on tools proven to change member behavior in ways that will result in healthier outcomes and lower costs. Further, these programs have been designed to enable companies and organizations to work collaboratively with their employees to make the delivery of the prescription drug benefit sustainable and more affordable.

By offering home delivery of maintenance prescription medications from the Express Scripts Canada Pharmacy™, Express Scripts Canada provides plan sponsors with the ability to significantly reduce the cost of providing prescription drug benefits for maintenance medications to employees.

FIGURE 31 | The Express Scripts Canada Strategy
Active Pharmacy Benefit Management (PBM) Key to Reduce Waste, Close Gaps in Care



Actively Managed Home Delivery Pharmacy

Express Scripts Canada introduced the concept of the Actively Managed Home Delivery Pharmacy to Canada in November 2011. Since then, Express Scripts Canada has helped companies and organizations that provide health benefits to their employees to achieve significant savings while continuing to allow members to choose where to have their maintenance medications filled.

All members of health-benefits plans who implement an Actively Managed Home Delivery program receive a comprehensive suite of tools to assist with program enrollment, prescription transfer and ongoing prescription management. More specifically, these tools include:

- Provision of integrated information to patients (patient, drug plan, clinical, and pricing) that will help them to make more informed decisions with respect to the use of their prescription drug benefit. In Canada, this information is currently dispersed among members, patients, physicians, pharmacies, and insurers
- Proactive intervention services to engage members as they use their drug benefit
- Behavioural economics-based tools (choice architecture, message framing) to influence patient decisions
- Therapy-optimization tools to identify and take action toward the reduction of waste, control prescriptions, dispense medications, counsel and support patients
- Physician-outreach programs to inform doctors about waste within the prescription drug benefit, and seek approval for therapy alternatives
- Campaigns that integrate PBM messaging protocols and outreach tactics to engage, enlighten, inform, and influence patients
- Web-based patient portal that offers tools to manage prescriptions, improve adherence, inform patients of alternative therapies and price medications
- 24/7 access to a pharmacist to answer urgent patient questions
- Member call centre for general inquiries
- Plan-sponsor materials including plans and sample communications, to support easy implementation
- Enhanced reporting to improve plan sponsor insight and control over the costs related to the administration of the prescription drug benefit

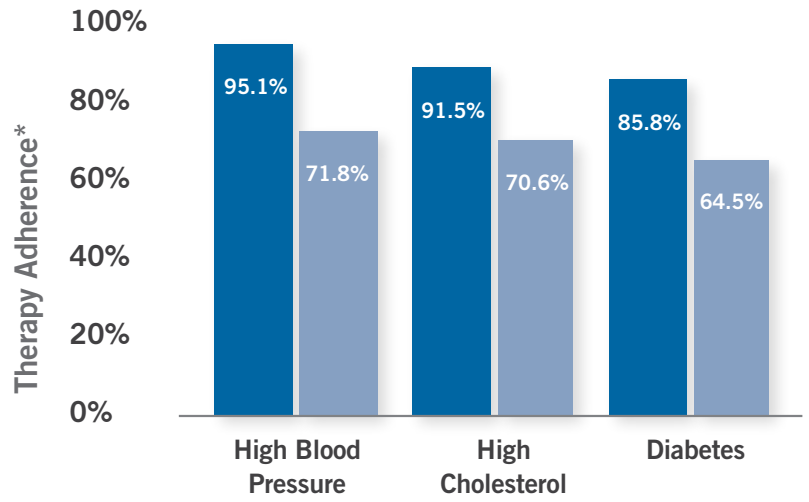
APPENDIX 2 – CASE STUDY

In January 2012, a large, national, publicly traded, Canadian transportation company with more than 13,000 employees across the country identified the need to take proactive steps to reduce waste in the deployment and management of its prescription drug benefit and close gaps in care.

The company's Human Resources Department, which is responsible for the administration, management and delivery of an industry-leading, competitive, health-benefits program to its employees (plan members) – many of which are union members – had become increasingly concerned with some of the costs related to that program. In 2011, the company received $7.8 million in total pharmacy claims, of which $5.2 million was for maintenance prescription medications – a trend it believed significantly threatened the sustainability of its health-benefits program.

To this end, the company decided to work with Express Scripts Canada to implement an Active PBM program that would educate their employees to make better decisions about their use of the prescription drug benefit and, in turn, reduce costs. Critical to the company was the need to actively engage employees in all aspects of the program – among the key points for employees were to embrace the value of the negotiated health benefit; embrace the need to generate savings; and the safety, reliability and convenience of home delivery from the Express Scripts Canada Pharmacy™.

FIGURE 32 | Case Study – Active PBM Service Improves Key Adherence Metrics
Home Delivery Drives Significant Increases Across Multiple Therapy Classes



The Express Scripts Canada Pharmacy™ Difference

- Supply monitoring service
- Proactive outbound notifications
- Auto Refill program
- Higher days supply per script vs. retail pharmacies
- Convenience
- Concierge service

* As measured by days supply on hand = Medication Possession Ratio > 80%

The delivery of the program to employees was scheduled to coincide with the openings of Express Scripts Canada's regional pharmacies throughout Canada – Ontario (November 2011), British Columbia (April 2012); New Brunswick (June 2012) and Manitoba (July 2012). As such, not all employees in all parts of the country had access to the program for a full calendar year.

Express Scripts Canada worked with the company to create comprehensive information kits through which to introduce the program to employees. In addition, representatives from the Express Scripts Canada Pharmacy™, including licensed pharmacists, met with employees groups throughout the country to reiterate the benefits of the program, and to personally answer questions.

In 2012 – as a result of the implementation of Express Scripts Canada's Active PBM service – the company was able to generate the following results:

- **Channel Waste Reduced 90%.** The reduction can, in large part, be attributed to lower total dispensing fees from the Express Scripts Canada Pharmacy. Express Scripts pharmacists work with patients to establish dispensing intervals for maintenance medications that are clinically appropriate while considering dispensing costs. This approach resulted in an increase in average days-supply from 49 to 82, which resulted in fewer dispensing fees. Fewer fees, when combined with Express Scripts Pharmacy's lower-than-average dispensing fee, reduced channel waste by 90%.
- **Drug-Mix Waste Reduced 20%**. Results showed a 7% increase in the use of lowest-cost alternatives which were achieved through preliminary generic- substitution and therapeutic-substitution efforts, within select therapy classes, by the Express Scripts Canada Pharmacy. By the end of the year, the Generic Fill Rate increased from 57% to 64%; this was driven by proactive interventions by Express Scripts Canada pharmacists, which led to a 57% approval rate, by both physicians and patients, for switches to lower-cost, clinically effective therapies.
- **Proportion of Patients Deemed to be Adherent Increased 20%**. Express Scripts Canada measures adherence via the Medication Possession Ratio (MPR) – the formula for which is the number of days for which a patient has medication on hand divided by the total number of days a patient was observed. Any patient with a MPR of 80% or above is generally considered to be adherent. The Express Scripts Canada Pharmacy increased the proportion of patients that were deemed adherent, based on the MPR threshold, thanks in part to proactive outbound notifications. For example, 95.1% of high blood pressure patients who used the service in 2012 were deemed adherent, compared with 71.8% in 2011. Similarly, 91.5% of patients who took medications to manage high cholesterol were deemed adherent, up from 70.6% in the previous year; and the proportion of diabetes patients deemed adherent increased to 85.8%, compared with 64.5% in 2011.
- **Plan Savings of 7%**. Overall, the company experienced plan savings of 7% for the maintenance-medication component of the prescription drug plan. This saving is directly attributable to the reduction of waste – specifically channel waste and drug-mix waste – within the prescription drug benefit.

The successes realized from implementing Active PBM by this large, national, publicly traded Canadian transportation company with operations throughout the country met and, in some areas, exceeded its expectations. Going forward, the company expects to work with the Express Scripts Canada Pharmacy™ to expand its generic-substitution and therapeutic-substitution efforts to additional therapy classes to further optimize therapy and reduce drug-mix waste.

ABOUT EXPRESS SCRIPTS CANADA

Express Scripts Canada, a registered business name of both ESI Canada and Express Scripts Canada Services, each an Ontario partnership, is indirectly owned by Express Scripts Holding Company, a U.S. public entity (formerly Express Scripts, Inc.), and is one of Canada's leading providers of health benefits management services. From its corporate headquarters in Mississauga, Ontario, just outside Toronto, Express Scripts Canada provides a full range of integrated pharmacy benefit management (PBM) services to insurers, third-party administrators, plan sponsors and the public sector, including health-claims adjudication and processing services, home delivery pharmacy services, benefit-design consultation, drug-utilization review, formulary management, and medical and drug-data analysis services, to better facilitate better health decisions and lower costs. For more information about Express Scripts Canada, visit Express-Scripts.ca.

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Visit Express-Scripts.ca/research for additional evidence-based research regarding health benefits in Canada.


EXPRESS SCRIPTS®

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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