MARCH 2016

Express Scripts **2015 Drug Trend Report**

THE **EXPRESS SCRIPTS** LAB™

Content

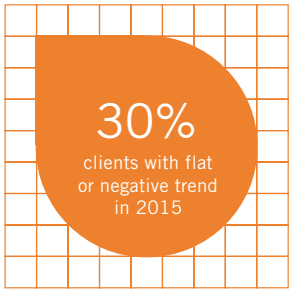
Introduction

Drug trend year in review

2015 drug trend reduction reflects bold actions

Payers faced a seismic shift in the pharmacy landscape in 2014, which led to the highest annual increase in drug spending in more than a decade. As they have for the past 30 years, our clients worked with us in 2015 to implement effective new solutions to address the biggest drivers of that increased spend. Our collective actions helped slow the country's year-over-year increase in drug spending to only 5.2%, roughly half of what it was in 2014. Meanwhile, our members' average out-of-pocket spending on prescription drugs fell 3.2% in 2015, while their overall health outcomes improved.

One thing is clear: taking action works. **Clients who adopted more solutions had an even lower trend.** Our clients who tightly managed their pharmacy benefit held their 2015 increase in drug spending to 3.3% – nearly two percentage points lower than the national average.



Our legacy of client-driven innovation, action and alignment is seen throughout our company's 30 years. Our continued success relies on our commitment to always do what's right for our clients and patients and to always keep patients at the center of everything we do. To all of us at Express Scripts, and to our clients, patients matter most.

In this, the 20th edition of our Drug Trend Report, the impacts of that commitment, and our latest innovations and actions, are clear:

- **Together, we're curing patients with hepatitis C.** In 2015, nearly 50,000 Express Scripts and Accredo patients with hepatitis C received curative treatment. Payers saved more than $1 billion on costly therapies through our Hepatitis Cure Value Program® (HCV). Marketplace competition – ignited by Express Scripts – made these medications more affordable across the U.S., and for many of our plans, accessible to all patients, not just the sickest. Our Accredo specialty pharmacy delivered industry-leading persistency rates for Viekira Pak® (ombitasvir/paritaprevir/ritonavir with dasabuvir) and Harvoni®

To all of us at Express Scripts, and to our clients, **patients matter most**.

(ledipasvir/sofosbuvir) of 93 to 94%, compared to 83 to 92% at retail and specialty pharmacies. New hepatitis C medications coming to market in 2016 will continue to bring down prices.

- **Together, we're eliminating cost and waste.** Payers effectively mitigated the dramatic increases in spending on compounded medications in 2014. They achieved a 97% drop in total plan costs for the class in 2015 through the Express Scripts compound management solution.

- **Together, we're addressing persistent brand price inflation.** Clients who implemented the National Preferred Formulary (NPF) in 2014 will achieve cumulative savings of $3 billion. Fostering competition among existing therapies significantly drives down the cost of care and creates room for payers to cover new, breakthrough therapies.

- **Together, we're innovating.** The Express Scripts Lab is a workshop where we collaborate with clients to create programs that improve patient care and outcomes and tackle unique pharmacy benefit challenges. More than 300 clients participate in pilot programs with Express Scripts, such as our award-winning remote diabetes monitoring program.

- **Together, we're taking on egregious price hikes.** When Turing Pharmacueticals' massive price increase put Daraprim® (pyrimethamine) out of reach for many of those suffering from toxoplasmosis, including many patients with HIV and other conditions that compromise the immune system, Express Scripts partnered with Imprimis Pharmaceuticals to give patients access to a low-cost alternative. Imprimis is offering a compounded oral formulation of pyrimethamine (the active ingredient in Daraprim) and leucovorin (a form of folic acid) for $1 per capsule patients whose pharmacy benefit is managed by Express Scripts.

Still, we have more work to do. A record number of U.S. Food and Drug Administration (FDA) approvals in 2015 and the current pipeline of research and pending approvals will bring promising new therapies to patients, particularly for cancer. This will require new clinical programs and creative approaches to managing spend.

In addition, U.S. drug prices are still on the rise, and the increases are occurring with greater magnitude and frequency than in recent years. In 2015, nearly one-third of branded drugs experienced annual price increases of 20%. Drug maker consolidation and price gouging from a select few pharmaceutical companies are diluting the value of generic medications and lower-cost therapies.

As we've proven over the past three decades, and will continue to prove in the years ahead, our history of alignment and action demonstrates that no test is too great for Express Scripts. We believe there's always a better way to make pharmacy smarter, more accessible and more affordable. We'll continue innovating and taking bold actions, in partnership with our clients, to always keep medicine within reach.

Sincerely,

Glen Stettin, MD
Senior Vice President, Clinical Research & New Solutions and Chief Innovation Officer

Rochelle Henderson, PhD
Senior Director, Research & Clinical Services

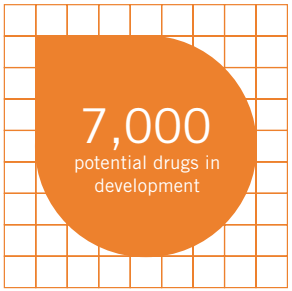
Pharmacy landscape overview

The dynamics underlying anticipated drug cost increases reflect advances in biotechnology, vast improvements in drug development and the superior marketing power of the pharmaceutical industry. Coupled with greater understanding of human genetics, biotechnology promises unique therapies not even imagined when Express Scripts was founded three decades ago. Breakthroughs in the treatment of certain cancers are among the many contributions research brings to the medical marketplace. As a result of pharmaceutical innovation, a record 50 new drugs were approved by the FDA in 2015. Yet, not all increases in spend can be attributed to breakthrough science.

Here's a look at the main factors driving spend in 2015.

High prices for new products

The allocation of pharmacy spend has changed significantly over the last 30 years as more and more dollars are spent on specialty, rather than traditional, medications. In the late '80s and early '90s, most drug development and spend was on traditional, mostly oral, small-molecule solid drugs used to treat conditions such as heartburn/ulcer, depression and diabetes. Today, 37.7% of drug spend is for specialty medications, with the number expected to increase to 50% by 2018 and continue to grow from there. There are 7,000 potential drugs in development, with most aimed at treating the high-use categories of oncology, neurologic disorders and infectious diseases.



High-cost therapies for nonorphan conditions, particularly for cancer, high cholesterol and Alzheimer's disease, will continue to increase the population of patients with high annual drug expenditures.

Oncology therapies

The last decade ushered in an unprecedented number of FDA approvals for oncology medications, with 19 in 2015 alone. These new medications offer oncologists and patients more treatment options and can add months or years of life. Some of these newer medications leverage the body's own immune system to fight cancer. In addition to newer products, medications like Xtandi® (enzalutamide) are used to help patients delay the need to start chemotherapy. These therapies have positive impacts on patient care but come with a hefty price tag – averaging more than $8,000 per prescription.

Increasingly, cancer is becoming a chronic disease that could require more complex, costly and long-term treatment. The average cost for a full-treatment regimen is roughly $150,000 per patient.[1] The cost trend for oncology medications in 2015 was 23.7%, due to growth in both utilization (9.3%) and cost (14.4%). The costs of these medications continue to represent a significant challenge to patients and the overall healthcare system. Some drugs, like Gleevec® (imatinib), are approved to treat multiple types of cancer. However, efficacy may vary for these different indications. The annual cost of Gleevec was $92,000 in 2012, and the economic burden is substantial, due to its multiple indications, wide use and effectiveness.[2]

The future does offer some financial solace for patients who are taking Gleevec, as it lost patent protection in February 2016. Although only one generic manufacturer has 180-day exclusivity, generics from multiple manufacturers are expected to be released in late summer 2016, a competition that should bring lower prices.

High cholesterol therapies

Repatha™ (evolocumab) and Praluent® (alirocumab), new cholesterol-lowering drugs known as PCSK9 inhibitors, entered the market in the second half of 2015. The self-injectable medications block a protein that interferes with the liver's ability to clear "bad" cholesterol from the bloodstream. These new medications are appropriate for only a small number of patients dealing with very specific and

rare forms of high cholesterol that are unresponsive to available statin therapies. The challenge, of course, is that these drugs are priced at more than $14,000 per year, before discounts – far greater than the cost for statin therapies. Although the clinical trials for Praluent and Repatha have been successful in getting these drugs approved for lowering LDL cholesterol, little has been proven about the long-term effects on heart attack and stroke prevention, the main reason people are treated for high cholesterol. For both patient safety and payer affordability, it's important to ensure this class of drugs is appropriately managed.

While we effectively mitigated the expected impact of cholesterol-lowering drugs Repatha and Praluent, we need to prepare for 2017-2018, when the results of outcome trials regarding the effects of these drugs on myocardial infarction and cerebrovascular incidents are anticipated, as those may drive more use.

Price inflation is persistent and costly

Our exclusive Prescription Price Index (page 58) reveals brand price inflation nearly doubled between 2011 and 2015, with the greatest impact seen in more recent years. Compared to 2014, brand prices in 2015 were 16% higher. Brand medications have increased in price by 164% between 2008 and 2015.

Consider the case of Gleevec: In 2015, Novartis, the exclusive manufacturer, engaged in the prevalent practice of increasing the price of a medication in the year prior to patent expiration, and raised the price of Gleevec by 32% to $112.37 per 100mg tablet. Between 2005 and 2015, the price of Gleevec increased three-fold, from $25.50 to $112.37.

On the whole, generic prices continue to decline and deliver significant cost savings to payers and patients. Of greater concern, however, are the increases seen among prices for specific generic drugs, including drugs for diabetes and skin conditions.

Several industry factors are influencing the increase in generic drug pricing. The first is consolidation among pharmaceutical manufacturers that's driving down marketplace competition. For example, Horizon Pharma purchased the product Vimovo® (naproxen/esomeprazole magnesium), then increased the price by 175% in 2015, far exceeding the healthcare value.[3] Other high-profile examples include the greater than 5,000% increase in the price of Daraprim by Turing pharmaceuticals, and the 800% price increase by Valeant Pharmaceuticals on Glumetza®, a branded form of the drug metformin for the treatment of diabetes.

Captive pharmacies circumvent effective cost management

In 2015, we observed the emergence of "captive pharmacies," or pharmacies that enter arrangements to be owned or operated by pharmaceutical manufacturers. Captive pharmacies typically promote the manufacturer's products instead of other lower-cost, equally effective medications. The intent is to circumvent formulary management programs designed to protect the patient and the plan sponsor from unnecessarily filling high-cost medications. The most high-profile captive pharmacy arrangements were between Valeant Pharmaceuticals International and Philidor Rx Services, and Horizon Pharma PLC and Linden Care Pharmacy.

Solutions

How we can deliver better health at a lower cost

Only patient-centric solutions deliver better outcomes and true overall value. Building upon our previous bold actions, we created Express Scripts SafeGuardRx℠, a collection of novel solutions designed to mediate the high cost of new medications through a combination of clinical programs and strategic reimbursement solutions.

SafeGuardRx leverages the clinical specialization at our Therapeutic Resource Centers℠ to target and manage the medication classes that will pose the largest budgetary threats to payers.

In addition to our groundbreaking Hepatitis Cure Value Program (HCV), SafeGuardRx includes our Cholesterol Care Value Program℠ (CCV), Oncology Care Value Program℠ (OCV) and our industry-first Inflation Protection Program.

SafeGuardRx is a **collection of novel solutions** designed to mediate the high cost of new medications through a combination of clinical programs and strategic reimbursement solutions.

Cholesterol Care Value Program

We're already seeing the impact of the Cholesterol Care Value Program, which combines discounts and rigorous utilization management for both Praluent and Repatha, and which offers additional protection by capping plan cost in 2016 for PCSK9 inhibitors. Created to ensure coverage of these medications for patients with rare familial hypercholesterolemia, the program is holding down current spending on this new class of therapy for high cholesterol.

Oncology Care Value Program

Introduced in 2016, this program is designed to ensure cancer patients obtain the treatment they need while helping to protect payers from the high cost of their medications. The approach addresses inefficiencies in the market, whereby some cancer treatments produce a wide range of outcomes across different indications and treatment scenarios, yet prices charged remain the same.

As the country's first program to factor these differences into value-based prescription drug payments, the Express Scripts Oncology Care Value Program takes a multifaceted approach to align cost of treatment with outcomes. The program will focus in 2016 on prostate cancer, lung cancer and renal cell carcinoma.

Inflation Protection program

New for 2016, the Express Scripts Inflation Protection program shields participating plans from the full impact of year-over-year price increases on brand drugs by offering inflation guarantees. All payers fear the unknown costs associated with future brand-drug price inflation. By being creative in our contracting with drug manufacturers, and by taking on our own financial risk, Express Scripts is delivering more value and budget predictability to the payers and patients we serve.

SafeGuardRx programs leverage the specialization of our Therapeutic Resource Centers (TRCs). Our TRC teams are extensively trained in specific medical conditions and provide patients with specialized support from patient-care advocates, specialist pharmacists and nurses.

Championing access and affordability

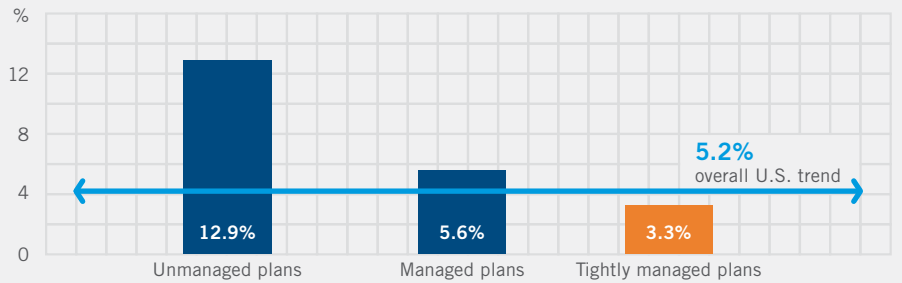
Some drug price increases dominated the industry – and the news – in 2015. Yet those cases are not the only factors driving spend. Guided by an independent panel of clinical experts, our 2016 NPF continues to help payers mitigate rising drug costs. By opening up access to all clinically necessary medications and excluding a handful of "me-too" and other products that have no clinical benefit beyond what's provided by more affordable alternatives, we have leverage to more effectively negotiate with manufacturers and ultimately achieve lower drug prices for the clients and patients we serve.

The 2016 NPF excludes just 80 medications – out of more than 4,000 drugs available on the market – that have clinically equivalent, lower-cost options available. With the NPF, our plan sponsors will save approximately $1.3 billion in 2016, creating more than $3 billion in total savings for those plans that have implemented the NPF since 2014.

Equally important is ensuring that patients receive the most clinically appropriate and cost-effective medications, every time. By using a combination of drug cost management and clinical programs, clients can eliminate waste and maximize the value of every dollar spent.

In our examination of multiple utilization-management and cost-management strategies on traditional drug spend in 2015, we found that "unmanaged" plans experienced an annual average increase in per-member-per-year (PMPY) spend of 12.9% in 2015, compared to 3.3% trend for "tightly managed" plans.

UNMANAGED VS TIGHTLY MANAGED TREND



Therapy class review

A look at drug trend for 2015

Total plan sponsor drug trend for the commercially insured population, including health plans and self-insured plans, increased by 6.4% in 2015. This is roughly half the increase reported in the 2014 Drug Trend Report, noting the change to include rebates in the calculation of trend numbers. Including the impact of member cost share of -1.2%, overall trend was 5.2% in 2015. The largest contributors to rising trend were increased unit cost and utilization for specialty medications. The largest contributors to mitigating trend were the reduction in compounded therapies and cost-saving initiatives for hepatitis C drugs.

Overall drug trend reflects two factors: utilization and unit cost. In 2015, overall trend for traditional medications was almost flat, at 0.6%. Utilization of traditional medications increased by just less than 2%, while unit cost declined 2.1%, the result of programs that drive better discounts and shift share to more cost-effective generics and plan-preferred medications. Overall specialty spend increased 17.8% in 2015. Utilization of specialty medications rose almost 7% for 2015, while unit cost increased by 11.0%. At 37.7%, specialty medications contributed to overall spend more than ever – 5.7% more than in 2014.

COMPONENTS OF TREND

2015

		TREND		
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	$708.09	1.9%	-2.1%	**-0.1%**
Specialty	$352.66	6.8%	11.0%	**17.8%**
TOTAL TREND	**$1,060.75**	**2.0%**	**3.2%**	**5.2%**

January-December 2015 compared to same period in 2014, commercially insured.
Reflects total cost for both payers and patients.

Traditional therapy classes and insights: commercially insured

The top 10 traditional therapy classes have shifted compared to last year, yet diabetes remains the most expensive traditional therapy class when ranked by PMPY spend for the fifth consecutive year. Total trend was negative for four of these top classes (high blood cholesterol, high blood pressure/heart disease, asthma and compounded drugs). These decreases in total spend were due to unit cost decreases, with the exception of compounded drugs, which declined in spend due to the sharp decrease in utilization of 55.7%. This decrease reflects commercially insured clients adopting multiple strategies. Utilization increased for all but three of the top 10 therapy classes (high blood cholesterol, heartburn/ulcer disease and compounded drugs).

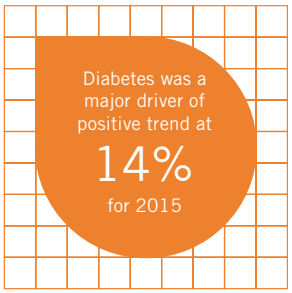
The top three classes by spend (diabetes, pain/inflammation and high blood cholesterol) contributed more than 25% of total traditional drug spend in 2015. High blood cholesterol medications dropped to number three, while pain/inflammation rose to second in spend. Attention disorder medications is number four for 2015, and mental/neurological disorders is number seven. The depression therapy class fell from this top list, replaced by skin conditions at number 10.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2015 PMPY SPEND

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

Highlights



- Diabetes remains a major driver of positive trend within the traditional therapy classes. Trend for this category was 14.0%, reflecting increases in both utilization and unit cost. New cases of diabetes continue to occur, and approximately 27.8% of adults with diabetes are currently undiagnosed.[4] Since diabetes is a chronic condition, utilization will undoubtedly continue to increase, especially as patients increasingly use multidrug regimens. Brand inflation continues to drive the rising unit cost of diabetes medications, which is affected by the lack of generics available in this class. Additionally, new therapies, such as Invokana® (canagliflozin) and Janumet® (sitagliptin/metformin), drove trend through increases in both utilization and unit cost.

- Drugs to treat heartburn and ulcer disease had the largest total trend this year, 35.6%, heavily influenced by a 36.3% increase in unit cost. Although generic medications account for most of the medications filled in this class, the price-per-unit trend was heavily influenced by the increase in branded products such as Nexium® (esomeprazole), Dexilant® (dexlansoprazole) and Prevacid® (lansoprazole). The availability of generic Nexium in February 2015 should result in lower overall unit cost increases for the class in the future.

- At 27.8%, medications used to treat skin conditions, such as psoriasis, had the second largest overall trend of the top 10 therapy classes. This trend was largely due to a 26.4% increase in unit cost of medications in the class, which occurred among both brand and generic therapies. Mergers and acquisitions of manufacturers of drugs in this class have led to a less-competitive market. Of the top 10 drugs in spend for this class, six are generics. Eight of the top 10 drugs in this class by spend increased in unit cost, five of them by more than 40%.

- Medications used to treat high blood cholesterol declined in spend by 9.2% in 2015, moving it down to the third therapy class in spend after over a decade in the top two. Most of the top drugs in this class are generic therapies that continue to decrease in unit cost. Utilization for this class remained almost stable, with a decline of only 0.3%. Despite a decline of conventional generic therapies, such as statins, a 78.2% increase in utilization was noted for omega-3 acid ethyl esters, which are prescription-strength formulations of fish oil. This increase put fish oils as the number four drug in spend for this therapy class. The increase in utilization could reflect patients processing these therapies through the pharmacy benefit.

- Compounded medications had a -53.9% trend in 2015, reflecting the bold actions taken by Express Scripts to ease the staggering increase in spend during 2014. The negative trend reflects the 55.7% decline in utilization of compounded drugs for 2015.

TRADITIONAL SPEND RANK 1

Diabetes

Diabetes medications were the most expensive among traditional therapies, with an overall trend of 14.0%, influenced equally by utilization and unit cost increases. Three of the top five drugs in spend across all traditional therapy classes were diabetes medications: Lantus® (insulin glargine), Januvia® (sitagliptin) and Humalog® (insulin lispro).

Four of the top 10 diabetes drugs by spend were insulins – three dispensed as pre-filled insulin pens. Unit cost for the top insulin, Lantus, decreased 13.7%. However, unit cost trend reflects the increased price for most pre-filled insulin pens and the availability of newer and more expensive treatments – Trulicity® (dulaglutide) and Synjardy® (empagliflozin/metformin) – which launched in 2015. Another pre-filled insulin pen, Levemir® FlexTouch® (insulin detemir), approved in late 2014, rose to seventh place for diabetes drug spend in 2015.

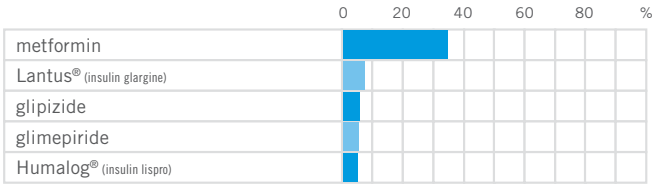
Currently, no generic insulins are available, but Basaglar® (insulin glargine) – the first "follow-on" insulin to Lantus – will launch in December 2016. Four of the most commonly used diabetes treatments – metformin, glipizide, glimepiride and pioglitazone – have been generic for years. Approximately 53% of diabetes prescriptions were generic in 2015.

Spend increased by **14.0%** influenced equally by utilization and unit cost.

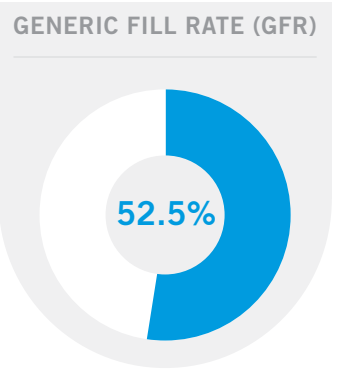
			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	**Diabetes**	**$77.50**	**6.7%**	**7.4%**	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

- 0.82 number of prescriptions PMPY
- 5.1% prevalence of use
- $94.21 average cost per prescription
- 42.8% of patients are nonadherent

TRADITIONAL SPEND RANK 2

Pain/inflammation

Medications used to treat pain and inflammation became the second-highest cost therapy class in 2015, reflecting the consolidation of opioids, nonsteroidal anti-inflammatory drugs (NSAIDS) and gamma-aminobutyric acid (GABA) analogs into a combined pain and inflammation class. Small increases in utilization (0.8%) and unit cost (2.1%) contributed to an overall increase of only 2.9% in PMPY spend.

Trend in this class reflects both the reclassification of some controlled substances and the increasing availability of generics. In October 2014, hydrocodone combination products (HCPs) were reclassified as Schedule II controlled substances, making them harder to obtain since fewer prescribers are allowed to write prescriptions for them. In 2015, hydrocodone/acetaminophen (a generic combination) increased in plan cost by 18.3% but decreased in utilization by 14.7%. This utilization decline could be a response to tighter regulations, with unit cost increasing by manufacturers in an attempt to recoup revenue from decreased sales. Generic introductions for Celebrex® (celecoxib) in December 2014 prompted a switch of almost all prescriptions to the generic form throughout 2015, influencing the lower 2.1% unit cost trend.

Despite the additional generic availability in the class, two branded drugs led spend this year: Lyrica® (pregabalin) and the reformulated tamper-resistant, extended-release form of oxycodone, OxyContin® (oxycodone extended release). Although Lyrica increased in spend by 19.8%, OxyContin decreased by 4.4%, mostly due to a utilization decline.

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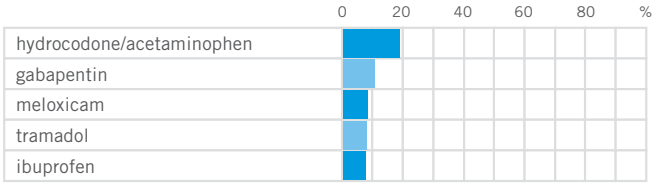
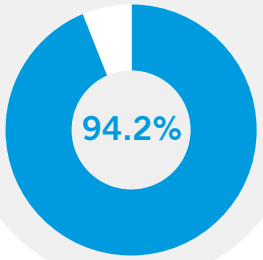


GENERIC FILL RATE (GFR)



By the numbers

1.06 number of prescriptions PMPY

22.1% prevalence of use

$38.36 average cost per prescription

TRADITIONAL SPEND RANK 3

High blood cholesterol

A decrease in both utilization and unit cost resulted in a downward trend of 9.2% in spend for high blood cholesterol treatments in 2015. The class moved down to the third most costly traditional therapy class.

Overall trend is heavily influenced by the availability of generic medications, which represent 83.1% of the market share in this class. Four of the top 10 drugs in this class are statins. Most are available as generics and had negative unit cost increases. Omega-3 acid ethyl esters, prescription-only formulations of fish oil, have increased in plan cost by 57.8%, influenced by a 78.2% utilization trend and a -20.4% unit cost trend. This increase may be the result of patients filling through the pharmacy benefit.

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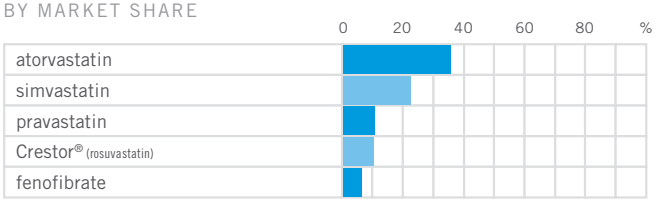
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

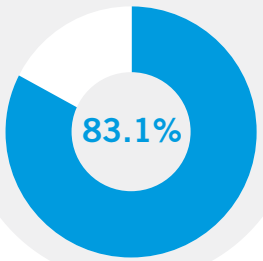
A decrease in both utilization and unit cost **decreased trend by 9.2%**.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

1.1 number of prescriptions PMPY

10.6% prevalence of use

$29.78 average cost per prescription

28.0% of patients are nonadherent

TRADITIONAL SPEND RANK 4

Attention disorders

PMPY spend for medications used to treat attention disorders increased 8.5% in 2015, driven by a 5.9% increase in utilization and a 2.5% increase in unit cost.

Vyvanse® (lisdexamfetamine), one of the leading brands in this class, increased in both utilization and unit cost. Spend for Vyvanse won't decrease soon, as its manufacturer has secured patent protection until at least 2023, and in January 2015 received an additional indication for treating adults with binge eating disorder (BED).

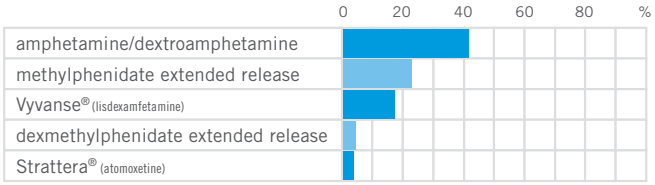
The first generic of Intuniv™ (guanfacine), a nonstimulant attention disorder medication, became available in December 2014, followed by several others in June 2015. Guanfacine became the sixth most utilized attention disorder drug in 2015. Most of the top 10 drugs in spend and utilization are stimulants, and five are branded formulations. Increased utilization for this therapy class reflects increased prevalence of use by adults, including in the elderly population.

The **8.5%** trend was influenced by increased utilization by adults.

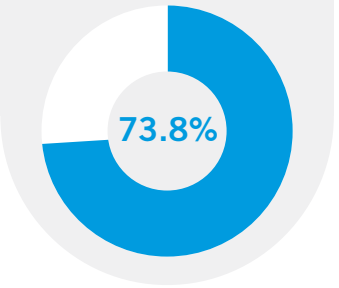
			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	14.0%
2	Pain/inflammation	$40.65	0.8%	2.1%	2.9%
3	High blood cholesterol	$32.66	-0.3%	-8.8%	-9.2%
4	**Attention disorders**	**$29.44**	**5.9%**	**2.5%**	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	-12.5%
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	35.6%
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	0.2%
8	Asthma	$22.72	5.8%	-7.5%	-1.6%
9	Compounded drugs	$20.62	-55.7%	1.8%	-53.9%
10	Skin conditions	$20.18	1.4%	26.4%	27.8%
	TOTAL TRADITIONAL	$565.00	1.9%	-1.4%	0.6%

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.23 number of prescriptions PMPY

2.8% prevalence of use

$125.96 average cost per prescription

TRADITIONAL SPEND RANK 5

High blood pressure/ heart disease

Spend for medications used to treat high blood pressure/heart disease decreased for a second year, this year by 12.5%. The decrease was driven mostly by a 14.9% decline in unit cost. Generic medications made up 95.7% of total 2015 market share. The number of PMPY prescriptions for high blood pressure/heart disease medications was the highest among the traditional therapy classes in the top 10.

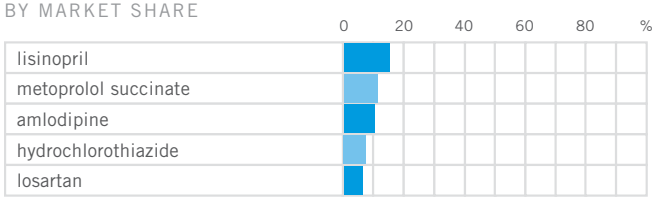
Although overall cost in this class is stable and some branded drugs have increased in unit cost, patent expirations have decreased the unit costs of specific therapies. The first U.S. generic for Diovan® (valsartan) was launched in mid-June 2014 with multiple generic options available by early 2015, thus further decreasing spend for generic valsartan in 2015. Overall, in this therapy class there was a small increase in utilization of 2.4%, possibly due to affordability within the class.

The **12.5%** decrease in trend was driven mostly by the decline in unit cost.

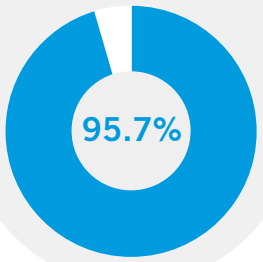
			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	**High blood pressure/heart disease**	**$25.70**	**2.4%**	**-14.9%**	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

2.46 number of prescriptions PMPY

16.7% prevalence of use

$10.45 average cost per prescription

33.3% of patients are nonadherent

TRADITIONAL SPEND RANK 6

Heartburn/ulcer disease

In 2015, PMPY spend for medications used to treat heartburn, ulcer disease and gastroesophageal reflux disease (GERD) increased 35.6%.

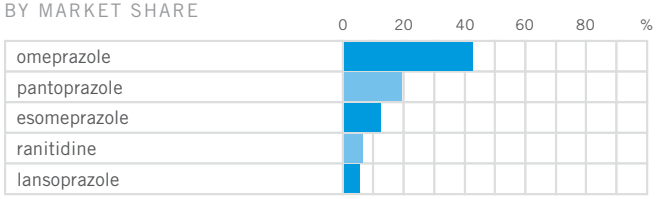
Drugs to treat heartburn and ulcer disease had the largest total trend this year, heavily influenced by a 36.3% increase in unit cost. All of the top five ulcer drugs by market share are generic medications, which now make up 92.3% of total market share in the class. Although dominated by generics, the price per unit trend for heartburn and ulcer medications was heavily influenced by the increase in branded products like Nexium, Dexilant and Prevacid. The availability of generic Nexium in February 2015, and some shift to over-the-counter Nexium, should result in lower overall unit cost increases for the class.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	**Heartburn/ulcer disease**	**$23.95**	**-0.7%**	**36.3%**	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

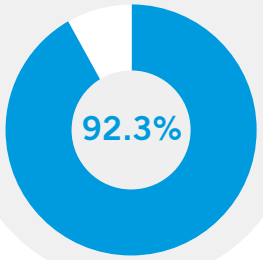
Generic medications represent **92.3%** of medications filled in this class.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.56 number of prescriptions PMPY

7.8% prevalence of use

$43.14 average cost per prescription

TRADITIONAL SPEND RANK 7

Mental and neurological disorders

Overall trend in this class was relatively flat (0.2%), influenced by a small increase in utilization offset by a small decrease in unit cost. The negative cost trend is heavily influenced by the availability of generic medications, including aripiprazole, the generic version of Abilify® (aripiprazole), an antipsychotic that lost patent protection in April 2015. Conversely, the branded products in this class, including Namenda® (memantine), Abilify and Seroquel® (quetiapine), had moderate increases in unit costs of 5.7%, 4.9% and 6.7%, respectively.

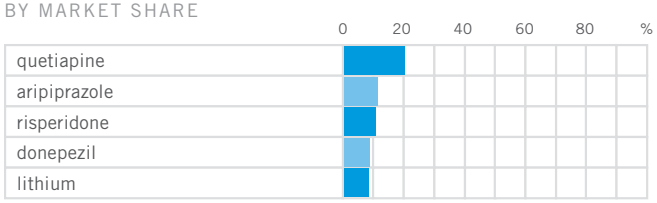
Modest decreases in utilization were observed across the majority of medications in this class. The largest utilization increases influencing the 2.4% increase in trend were observed for mood stabilizers and bipolar disorder therapies.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	**Mental/neurological disorders**	**$23.28**	**2.4%**	**-2.2%**	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

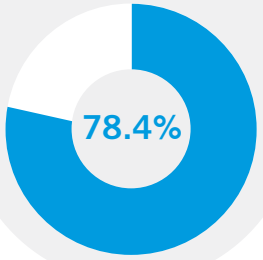
Overall trend in this class was **0.2%**, influenced by a small increase in utilization offset by a small decrease in unit cost.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.12 number of prescriptions PMPY

1.5% prevalence of use

$199.62 average cost per prescription

TRADITIONAL SPEND RANK 8

Asthma

Spend for asthma medications decreased 1.6%. A 5.8% increase in utilization was more than offset by a 7.5% decrease in unit cost, moving asthma down to the eighth most expensive traditional therapy class. Montelukast, the generic of Singulair®, is the most commonly prescribed asthma therapy. However, it has decreased in spend by 37.4% due to a sharp decline of 45.4% in unit cost, despite an 8.0% increase in utilization. This oral tablet holds 33.6% of market share for this therapy class. The next four asthma drugs by utilization are all branded inhalers.

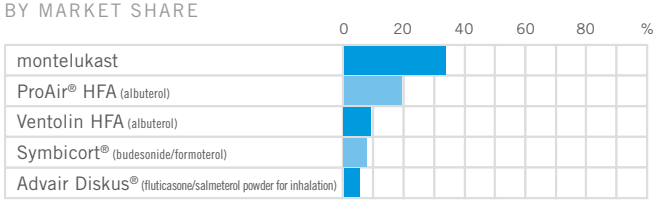
Advair Diskus® (fluticasone/salmeterol powder for inhalation), an inhaler therapy, declined sharply in unit cost – by 29.6%. Utilization increased, possibly due to this decrease in cost. Of the top 10 most utilized asthma drugs, only Flovent® HFA (fluticasone inhalation aerosol) decreased in utilization, by 10.7%, among commercial members. As asthma prevalence continues to rise, spend for branded inhalers will increase.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	**Asthma**	**$22.72**	**5.8%**	**-7.5%**	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	$565.00	1.9%	-1.4%	0.6%

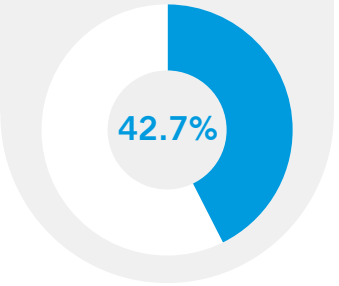
With **-1.6%** trend, asthma moved down to the **eighth** most expensive traditional therapy class.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.44 number of prescriptions PMPY

9.0% prevalence of use

$51.37 average cost per prescription

55.2% of patients are nonadherent

TRADITIONAL SPEND RANK 9

Compounded drugs

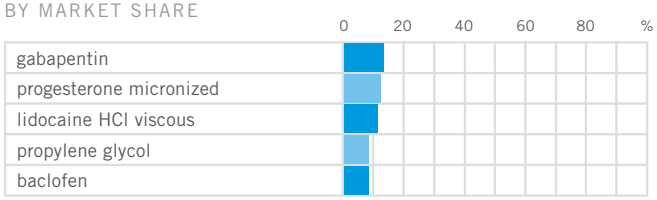
For the first time last year, compounded drugs appeared in the top 10 traditional therapy classes by spend, ranking third in overall spend. Due to various compound management solutions, utilization dropped 55.7% in 2015. Regulations that were implemented in 2012 required that all components of compounded drugs be specified and billed at the ingredient level. Previously, they were billed by the cost of the most expensive ingredient. Consequently, bulk manufacturers and compounding pharmacies raised prices substantially for many components of compounded medications, resulting in much higher drug spend in 2014. Uptake of compound management solutions within the commercial sector yielded a 53.9% decrease in PMPY spend for compounded drugs in 2015. The most common ingredients within compounded drugs were muscle relaxants, hormones and pain medications.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	**Compounded drugs**	**$20.62**	**-55.7%**	**1.8%**	**-53.9%**
10	Skin conditions	$20.18	1.4%	26.4%	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

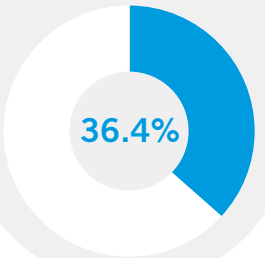
Uptake of compound management solutions within the commercial sector yielded a **53.9% decrease** in PMPY spend.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.02 number of prescriptions PMPY

0.6% prevalence of use

$1,182.83 average cost per prescription

TRADITIONAL SPEND RANK 10

Skin conditions

The skin conditions therapy class had a large increase in overall trend of 27.8%. This trend was largely due to a nearly 26.4% increase in unit cost of medications in the class, which occurred with both brand and generic therapies. Mergers and acquisitions of manufacturers of drugs in this class have led to a less competitive market. Of the top 10 drugs in spend for this class, six are generics. Eight of the top 10 drugs in this class by spend increased in unit cost, five of them by more than 40%.

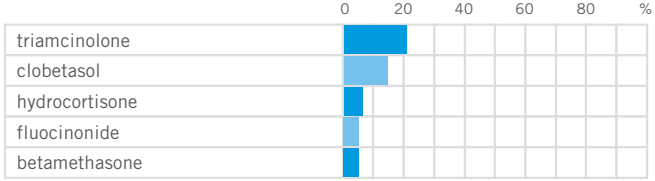
Nine of the 10 most utilized drugs were generics, and many had sharp cost increases. For example, the two most utilized drugs, clobetasol and triamcinolone – both generic corticosteroids – increased in unit cost by 96.2% and 28.0%, respectively.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Diabetes	$77.50	6.7%	7.4%	**14.0%**
2	Pain/inflammation	$40.65	0.8%	2.1%	**2.9%**
3	High blood cholesterol	$32.66	-0.3%	-8.8%	**-9.2%**
4	Attention disorders	$29.44	5.9%	2.5%	**8.5%**
5	High blood pressure/heart disease	$25.70	2.4%	-14.9%	**-12.5%**
6	Heartburn/ulcer disease	$23.95	-0.7%	36.3%	**35.6%**
7	Mental/neurological disorders	$23.28	2.4%	-2.2%	**0.2%**
8	Asthma	$22.72	5.8%	-7.5%	**-1.6%**
9	Compounded drugs	$20.62	-55.7%	1.8%	**-53.9%**
10	**Skin conditions**	**$20.18**	**1.4%**	**26.4%**	**27.8%**
	TOTAL TRADITIONAL	**$565.00**	**1.9%**	**-1.4%**	**0.6%**

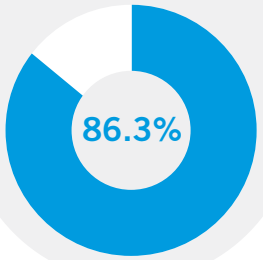
The **27.8%** trend was largely due to a nearly **26.4%** increase in unit cost.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.15 number of prescriptions PMPY

7.2% prevalence of use

$136.61 average cost per prescription

Top 10 traditional drugs

Only six of the top 10 drugs in 2015 were branded medications when ranked by PMPY spend, compared to nine branded medications on the list in 2014. Two of the 2014 top 10 traditional drugs, Nexium and Abilify, became available as generics in 2015. Their equivalents, esomeprazole and aripiprazole, both appear in the top 10. Esomeprazole ranks second and encompasses 2.3% of traditional drug spend. The two other generic therapies on the list are for attention disorders: amphetamine/dextroamphetamine, the generic form of Adderall®, and methylphenidate, the generic for Ritalin®. Lantus, a branded insulin, now takes the top place, with more than 2.5% of total traditional drug spend, despite a double-digit decrease in unit cost. The sharp 46.9% decline in utilization of Abilify is due to brand-to-generic shift, but the branded therapy remained in the top 10 traditional drugs in spend for 2015, since generic formulations weren't available until the end of April.

Two of the 2014 top 10 traditional drugs, Nexium and Abilify, became **available as generics** in 2015.

TOP 10 TRADITIONAL THERAPY DRUGS

RANKED BY 2015 PMPY SPEND

					TREND		
RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL TRADITIONAL SPEND	UTILIZATION	UNIT COST	TOTAL
1	Lantus® (insulin glargine)	Diabetes	$14.24	2.5%	2.3%	-13.7%	**-11.4%**
2	esomeprazole	Heartburn/ulcer disease	$13.28	2.3%	–	–	–
3	Crestor® (rosuvastatin)	High blood cholesterol	$10.20	1.8%	-7.1%	12.4%	**5.3%**
4	Lialda® (mesalamine)	Inflammatory conditions	$8.29	1.5%	0.8%	10.3%	**11.1%**
5	Humalog® (insulin lispro injection)	Diabetes	$8.18	1.4%	8.2%	9.0%	**17.2%**
6	amphetamine/dextroamphetamine	Attention disorders	$7.71	1.4%	9.7%	-12.2%	**-2.5%**
7	Januvia® (sitagliptin)	Diabetes	$7.54	1.3%	5.5%	14.3%	**19.8%**
8	aripiprazole	Mental/neurological disorders	$7.23	1.3%	–	–	–
9	methylphenidate extended release	Attention disorders	$7.01	1.2%	0.0%	16.2%	**16.3%**
10	Vyvanse® (lisdexamfetamine)	Attention disorders	$6.70	1.2%	7.4%	11.5%	**18.9%**

Specialty therapy classes and insights: commercially insured

Specialty medications contributed 37.7% of total drug spend in 2015, with an overall trend of 17.8%. All of the top 10 therapy classes increased in spend, and all had increases in unit cost of medications. Together, spend for the top three specialty therapy classes when ranked by PMPY spend – inflammatory conditions, multiple sclerosis and oncology – contributed 56.3% of the spend for all specialty medications billed through the pharmacy benefit in 2015. Therapies for inflammatory conditions (such as rheumatoid disease and psoriasis) remained at the top, while transplant disappeared from the top 10. This year, we further sub-categorized the miscellaneous specialty conditions, resulting in cystic fibrosis and sleep disorders making the top 10 list, ranked at 7 and 10, respectively.

The **top three** specialty therapy classes accounted for **56.3%** of all specialty spend.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

RANKED BY 2015 PMPY SPEND

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
3	Oncology	$49.62	9.3%	14.4%	**23.7%**
4	Hepatitis C	$38.44	-2.2%	9.2%	**7.0%**
5	HIV	$31.53	4.6%	12.0%	**16.6%**
6	Growth deficiency	$7.12	2.8%	2.8%	**5.6%**
7	Cystic fibrosis	$6.64	12.5%	40.9%	**53.4%**
8	Pulmonary hypertension	$5.85	13.4%	4.8%	**18.1%**
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

Highlights

- Trend for cystic fibrosis (CF) medications reached 53.4% in 2015. The entire therapy class contains only 10 drugs, with an average cost per prescription of $6,441.27. Many of the therapies in this class are different dose forms of tobramycin, several of which are now either inhaled solutions or powder form. Orkambi® (lumacaftor/ivacaftor), one of the two most costly drugs in this class, was approved in mid-2015, driving trend.

- Inflammatory conditions, trending at 25.0%, remained at the top of the specialty therapy classes when ranked by PMPY spend, as the top two drugs, Humira® Pen (adalimumab) and Enbrel® (etanercept), had double-digit unit cost increases. Brand innovation is driving some of this increased spend, with newer drugs like Otezla® (apremilast) and Entyvio® (vedolizumab), both approved in 2014, showing triple-digit utilization increases.

- There were 19 new FDA approvals in 2015 for oncology therapies, contributing greatly to the 23.7% increase in spend for this class. Both increased utilization and unit cost of the drugs in this class drove trend. Gleevec, the oncology treatment with the largest market share, increased in unit cost by 19.3%, a common practice by pharmaceutical manufacturers before an expected patent expiration.

- Hemophilia drugs continued to rise in spend for 2015, driven by a 15.4% increase in unit cost of medications. Brand inflation occurred for clotting and antihemophilic factor drugs such as Eloctate® (antihemophilic factor [recombinant], Fc fusion protein), which had triple-digit utilization and unit cost increases. Trends for expensive medications to treat rare conditions such as hemophilia are susceptible to small changes in a plan sponsor's patient populations.

- Trend for HIV medications was driven by brand inflation and utilization, as all of the top 10 HIV therapies are brand medications. Six of these top drugs increased in spend in 2015 by double and triple digits. The top two drugs in utilization, Atripla® (efavirenz/emtricitabine/tenofovir disoproxil fumarate) and Truvada® (emtricitabine/tenofovir disoproxil fumarate), were also the top two drugs in spend; both had unit cost increases in 2015, and utilization of Truvada increased by 29.3%.

There were **19 new FDA approvals** in 2015 for oncology therapies, contributing to the **23.7%** increase in spend for this class.

SPECIALTY SPEND RANK 1

Inflammatory conditions

Inflammatory conditions topped spend in specialty drugs for the seventh year in a row, trending upward by a total of 25.0%, driven by 14.7% trend in unit cost and 10.3% increase in utilization. Most of the top drugs in this category are disease modifying anti-rheumatic drugs (DMARDs), which treat rheumatoid arthritis, inflammatory bowel diseases, psoriasis and several other conditions.

Spend for all of the leading inflammatory condition drugs increased in 2015, with an average cost per prescription of $3035.95. Together, the top two, Humira Pen and Enbrel, captured more than 66% of market share for the class and almost 15% of overall specialty market share. Unit costs for each increased more than 17% in 2015, proving these are major trend drivers.

Overall utilization trend was influenced by positive utilization trend of Humira Pen, Xeljanz® (tofacitinib) and Stelara® (ustekinumab). Two medications approved in 2014 – Otezla, for plaque psoriasis and psoriatic arthritis, and Entyvio, for ulcerative colitis and Crohn's disease – affected utilization.

Inflammatory conditions topped spend in specialty drugs for the **seventh year in a row**.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	**Inflammatory conditions**	**$89.10**	**10.3%**	**14.7%**	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
3	Oncology	$49.62	9.3%	14.4%	**23.7%**
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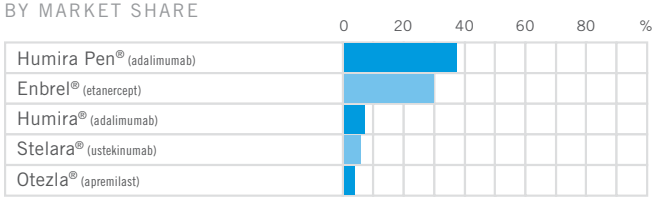
7	Cystic fibrosis	$6.64	12.5%	40.9%	**53.4%**
8	Pulmonary hypertension	$5.85	13.4%	4.8%	**18.1%**
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

TOP DRUGS

BY MARKET SHARE



By the numbers

0.03 number of prescriptions PMPY

0.3% prevalence of use

$3,035.95 average cost per prescription

43.7% of patients are nonadherent

SPECIALTY SPEND RANK 2

Multiple sclerosis

Total trend for multiple sclerosis (MS) medications was 9.7%, due to increases in unit cost (6.2%) and utilization (3.5%). Overall trend was influenced by the unit price increase of the top five most-prescribed medications in the class, which accounted for 84% of the spend. Unit cost increases for these medications ranged from 3.8% to 9.4%. Copaxone® (glatiramer) is the most widely used and had the highest spend in this class. Glatopa™ (glatiramer), a generic alternative for Copaxone's 20mg/mL dosage form, was launched in June 2015.

Several injected interferon beta-1 drugs had decreases in utilization: Avonex® (-16.8%), Betaseron® (-21.0%) and Rebif® (-13.9%). Tecfidera® (dimethyl fumarate) and Gilenya® (fingolimod), oral medications introduced in the last few years, have similar outcomes but fewer side effects than the interferons, making them preferable to patients.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	**Multiple sclerosis**	**$53.31**	**3.5%**	**6.2%**	**9.7%**
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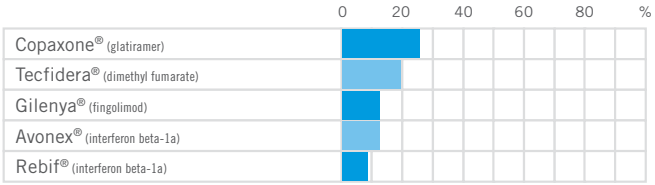
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	$341.21	6.8%	11.0%	17.8%

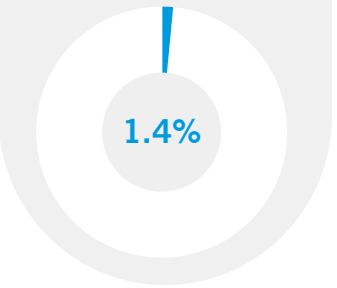
The **9.7%** trend was due to increases in unit cost and utilization.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.01 number of prescriptions PMPY

0.1% prevalence of use

$4,549.22 average cost per prescription

25.1% of patients are nonadherent

SPECIALTY SPEND RANK 3

Oncology

For 2015, trend for the oncology therapy class increased by 23.7%, due to growth in both utilization (9.3%) and unit cost (14.4%). Together, the two drugs that captured the most spend, Gleevec and Revlimid® (lenalidomide), accounted for more than 22% of market share for oncology drugs.

Gleevec, the oncology treatment with the largest market share, increased in unit cost by 19.3%, a common practice by pharmaceutical manufacturers before an expected patent expiration. Utilization trend for Gleevec was relatively flat at 1.1%.

Several oncology drugs had substantial increases in utilization. Imbruvica® (ibrutinib), now approved for multiple types of cancer, is the only FDA-approved Bruton's tyrosine kinase (BTK) inhibitor; its effectiveness for hard-to-treat cancers, oral dosing and relatively mild side effects resulted in a 2015 utilization surge of 78.1%. Utilization for capecitabine, a generic to Genentech's chemotherapy drug Xeloda®, rose 39.3%, following its launch in April 2014. Xtandi, an oral hormone modifier for prostate cancer, increased in utilization by 39.0%.

The two drugs that captured the most spend accounted for more than **22%** of market share for oncology drugs.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
3	**Oncology**	**$49.62**	**9.3%**	**14.4%**	**23.7%**
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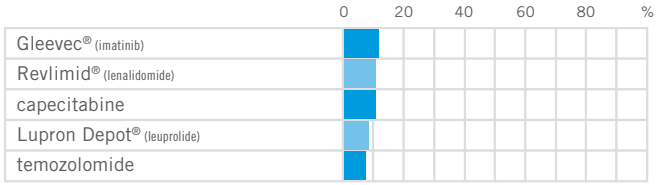
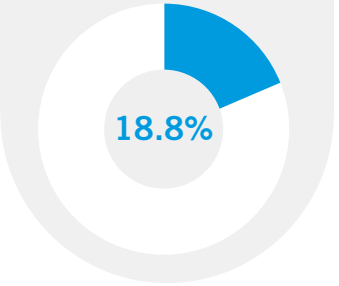
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	$341.21	6.8%	11.0%	17.8%

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.01 number of prescriptions PMPY

0.1% prevalence of use

$7,158.53 average cost per prescription

38.4% of patients are nonadherent

SPECIALTY SPEND RANK 4

Hepatitis C

Hepatitis C drug spend increased 7.0% in 2015. After the 2014 record increase in spend due to a few new and effective, but expensive, oral antiviral therapies, 2015 trend was lower. While utilization decreased 2.2%, a 9.2% increase in unit cost drove most of the change in spend. Viekira Pak and Harvoni, two of the therapies approved in 2014, together captured more than 57% of market share for this therapy class. Many of the other therapies concurrently fell in utilization, with several dropping in use by more than 75%.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	25.0%
2	Multiple sclerosis	$53.31	3.5%	6.2%	9.7%
3	Oncology	$49.62	9.3%	14.4%	23.7%
4	**Hepatitis C**	**$38.44**	**-2.2%**	**9.2%**	**7.0%**
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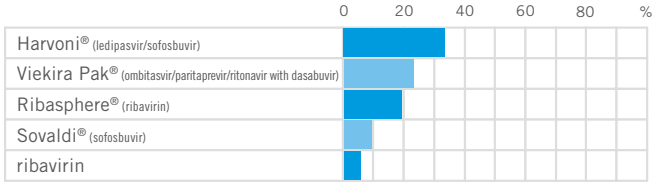
9	Hemophilia	$5.79	4.9%	15.4%	20.4%
10	Sleep disorders	$4.57	5.5%	18.5%	24.1%
	TOTAL SPECIALTY	$341.21	6.8%	11.0%	17.8%

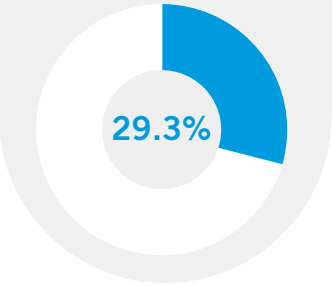
Increase in unit cost drove most of the **7.0%** change in spend.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

- 0.002 number of prescriptions PMPY
- 0.05% prevalence of use
- $17,090.18 average cost per prescription
- 8.9% of patients are nonadherent

SPECIALTY SPEND RANK 5

HIV

A 4.6% increase in utilization and a 12.0% unit cost increase resulted in an overall 2015 trend increase of 16.6% in PMPY spend for HIV treatments, moving them up to the fifth most costly specialty therapy class.

The average unit cost increase for the top 10 most commonly prescribed medications was 4.8%. In addition, for the most prescribed medications, unit cost was influenced by large price increases in medications with smaller market share. At 48.7% and 997.8%, respectively, two of the largest spend increases were for Stribild® (cobicistat/elvitegravir/emtricitabine/tenofovir disoproxil fumarate), and Triumeq® (abacavir/dolutegravir/lamivudine). These are attributable to large upticks in utilization trend, as more patients move to combination therapies. All but one of the drugs in the top 10 for HIV had only small unit cost increases. Three new combination treatments for HIV hit the U.S. market in 2015: Evotaz™ (atazanavir/cobicistat), Prezcobix® (darunavir/cobicistat), and Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide).

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
3	Oncology	$49.62	9.3%	14.4%	**23.7%**
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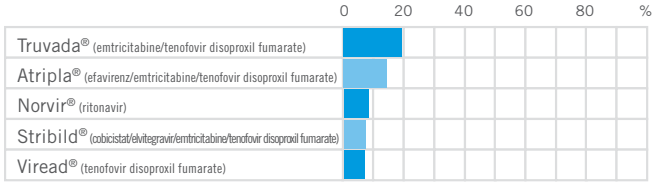
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

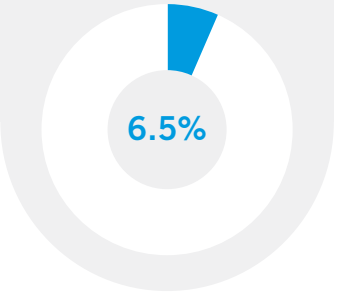
The **16.6%** increase in PMPY spend moved HIV up to the **fifth** most costly specialty therapy class.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.02 number of prescriptions PMPY

0.20% prevalence of use

$1,272.01 average cost per prescription

24.9% of patients are nonadherent

SPECIALTY SPEND RANK 6

Growth deficiency

In 2015, growth deficiency medications trended 5.6%, from equal trends in utilization (2.8%) and unit cost (2.8%). Norditropin® FlexPro® (somatropin) continued to dominate this class for the fourth year in a row, capturing 49.1% of market share. It's also the drug with the highest spend in this therapy class, increasing in both utilization and unit cost by approximately 11%. For Genotropin® (somatropin), the second drug in spend for 2015, trend decreased 12.0%, due mostly to a 11.2% decrease in unit cost. Increlex® (mecasermin) had the highest trend this year, with an overall increase in spend of 140.6%, mostly due to a 126.8% increase in utilization. Increlex treats a rare condition, primary insulin-like growth factor deficiency (IGFD), which affects approximately 6,000 children in the United States. Trends for expensive medications to treat rare conditions, such as growth deficiency, are susceptible to small changes in a plan sponsor's patient population.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
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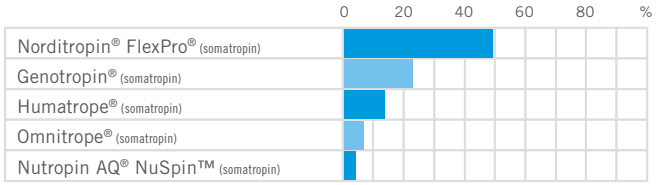
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

Growth deficiency medications trended **5.6%** from equal trends in utilization and unit cost.

TOP DRUGS

BY MARKET SHARE



By the numbers

0.003 number of prescriptions PMPY

0.03% prevalence of use

$2,735.29 average cost per prescription

39.9% of patients are nonadherent

SPECIALTY SPEND RANK 7

Cystic fibrosis

In 2015, drugs that treat cystic fibrosis broke into the top 10 therapy classes in spend for the first time. Currently, the therapy class contains only 10 drugs. Of those 10, only one is available as a generic and many therapies have been recently approved. CF drugs trended 53.4% in 2015, largely from a 40.9% increase in unit cost that was mostly due to use of Orkambi, one of the new branded therapies that hit the market in mid-2015. Orkambi is an oral combination therapy, which is clinically effective for CF, but costs more than $20,000 per month. Utilization in the class increased by 12.5%. Together, all the therapies derived from tobramycin, an antibiotic that has been available in generic inhaled form since late 2013, captured 26.4% of market share for this class. Some of the newer, brand-name forms of tobramycin include the TOBI® Podhaler™ (tobramycin inhalation powder), Bethkis® (tobramycin inhalation solution) and the Kitabis™ Pak (tobramycin), averaging approximately $3,500 to $4,700 for a 30-day supply.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	25.0%
2	Multiple sclerosis	$53.31	3.5%	6.2%	9.7%
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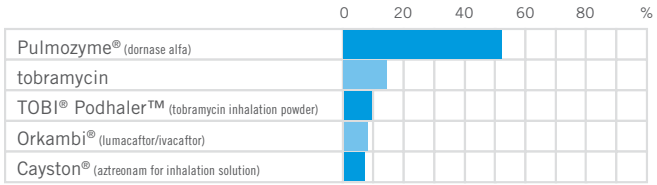
9	Hemophilia	$5.79	4.9%	15.4%	20.4%
10	Sleep disorders	$4.57	5.5%	18.5%	24.1%
	TOTAL SPECIALTY	$341.21	6.8%	11.0%	17.8%

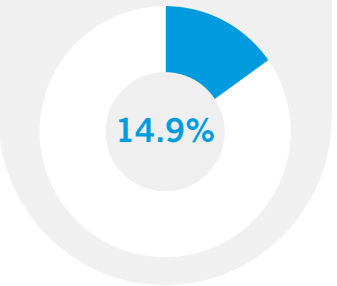
Currently, the therapy class contains only 10 drugs; **only one is available as a generic**.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.001 number of prescriptions PMPY

0.01% prevalence of use

$6,441.27 average cost per prescription

SPECIALTY SPEND RANK 8

Pulmonary hypertension

Spend for pulmonary hypertension increased by 18.1% in 2015. A 13.4% utilization increase and a 4.8% unit cost increase were responsible for the trend. For the top 10 drugs in spend for this class, utilization increased for all but three older drugs. Sildenafil, a generic oral tablet therapy for World Health Organization (WHO) Group 1 pulmonary arterial hypertension, remains the most prescribed drug in this class, with 36.4% of the market share. However, Orenitram® (treprostinil), Opsumit® (macitentan) and Adempas® (rociguat) increased greatly in utilization – by 315.8%, 111.2% and 72.3%, respectively. All three are relatively new drugs, approved in the fourth quarter of 2013 and launched in late 2013 or early 2014, explaining some of their 2015 utilization increases. As oral therapies, they're more convenient than some other PH therapies requiring inhalation or infusion.

In 2015, Orenitram decreased in unit cost by 53.2%, which likely contributed to its utilization increase. Sildenafil's unit cost decreased by 25.1% in 2015. Uptravi® (selexipag), expected to hit the U.S. market early in 2016, is predicted to compete with Orenitram.

For the top 10 drugs in spend for this class, utilization increased for all but **three** older drugs.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
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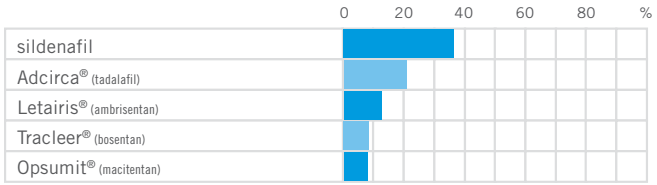
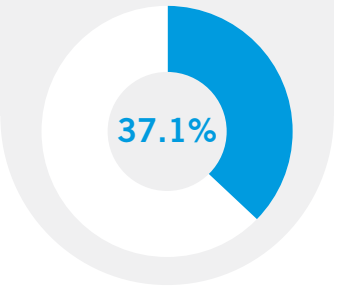
TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.002 number of prescriptions PMPY

0.02% prevalence of use

$3,892.31 average cost per prescription

31.3% of patients are nonadherent

SPECIALTY SPEND RANK 9

Hemophilia

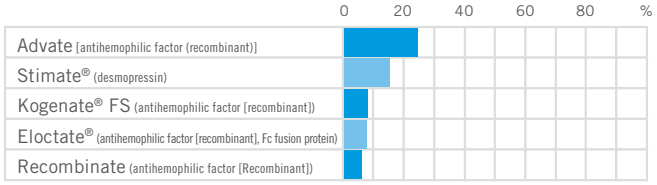
Of the top 10 classes, hemophilia drugs have the lowest market share. In 2015, trend of 20.4% was driven by a 15.4% increase in unit cost and a 4.9% increase in utilization. Eloctate and Alprolix® (coagulation factor IX [recombinant], Fc fusion protein), two long-acting therapies that were approved in 2014, are now in the top 10 in spend for this class. In 2015, each had large increases in utilization of more than 400%, in 2015. Eloctate also had a unit cost trend of 141.0%. Because this class has such small market share and high average cost of therapy, even a small increase in utilization can have a large impact on overall spend. The average 2015 cost per 30-day adjusted prescription for the top 10 utilized hemophilia drugs was $22,857.79.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
2	Multiple sclerosis	$53.31	3.5%	6.2%	**9.7%**
3	Oncology	$49.62	9.3%	14.4%	**23.7%**
4	Hepatitis C	$38.44	-2.2%	9.2%	**7.0%**
5	HIV	$31.53	4.6%	12.0%	**16.6%**
6	Growth deficiency	$7.12	2.8%	2.8%	**5.6%**
7	Cystic fibrosis	$6.64	12.5%	40.9%	**53.4%**
8	Pulmonary hypertension	$5.85	13.4%	4.8%	**18.1%**
9	**Hemophilia**	**$5.79**	**4.9%**	**15.4%**	**20.4%**
10	Sleep disorders	$4.57	5.5%	18.5%	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

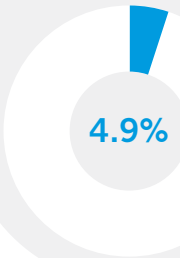
Because this class has such **small market share** and **high average cost of therapy**, even a small increase in utilization can have a **large impact** on overall spend.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



By the numbers

0.0002 number of prescriptions PMPY

0.005% prevalence of use

$25,668.55 average cost per prescription

SPECIALTY SPEND RANK 10

Sleep disorders

In the 2014 Express Scripts Drug Trend Report, sleep disorders were included in the miscellaneous specialty conditions therapy class. With an average cost of approximately $9,000 per prescription, sleep disorders medications easily made the top 10 specialty medications ranked by PMPY spend, despite low market share. In 2015, the PMPY spend for medications to treat sleep disorders increased by 24.1%, influenced by an 18.5% increase in cost and a 5.5% increase in utilization. Xyrem® (sodium oxybate) and Hetlioz® (tasimelteon) account for 100% of the market share in the sleep disorder therapy class.

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory conditions	$89.10	10.3%	14.7%	**25.0%**
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3	Oncology	$49.62	9.3%	14.4%	**23.7%**
4	Hepatitis C	$38.44	-2.2%	9.2%	**7.0%**
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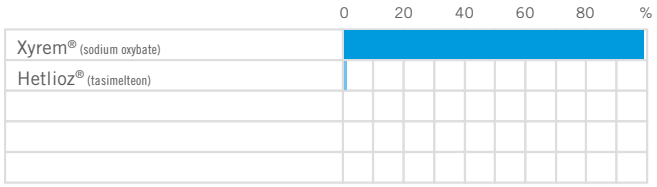
6	Growth deficiency	$7.12	2.8%	2.8%	**5.6%**
7	Cystic fibrosis	$6.64	12.5%	40.9%	**53.4%**
8	Pulmonary hypertension	$5.85	13.4%	4.8%	**18.1%**
9	Hemophilia	$5.79	4.9%	15.4%	**20.4%**
10	**Sleep disorders**	**$4.57**	**5.5%**	**18.5%**	**24.1%**
	TOTAL SPECIALTY	**$341.21**	**6.8%**	**11.0%**	**17.8%**

Xyrem and Hetlioz account for **100%** of the specialty market share in the sleep disorder class.

TOP DRUGS

BY MARKET SHARE



By the numbers

0.0005 number of prescriptions PMPY

0.01% prevalence of use

$8,928.96 average cost per prescription

Top 10 specialty drugs

In 2015, all but two of the top 10 specialty drugs increased in PMPY spend, and all but one with increased in unit cost. Seven of the top 10 therapies had increases in utilization. Humira Pen remained the drug with the highest spend, with 9.8% of total specialty drug spend. Harvoni and Viekira Pak moved into the top 10 specialty drugs, leading in the highest trends for utilization and unit cost. Enbrel moved down to the second most expensive drug, capturing 7% of total specialty drug spend. Two oncology drugs, Gleevec and Revlimid, remained among the most expensive specialty drugs, with increases in both utilization and unit cost. Three drugs for multiple sclerosis and one HIV drug, Atripla, comprise the remainder of this list. Atripla and Copaxone were the only top specialty drugs with a decrease in overall spend in 2015. Atripla decreased in spend despite a 6.3% increase in unit cost. The decline was due to downward utilization trend by 8.9%, which was the result of new, competing HIV therapies rising in popularity. Decrease in Copaxone spend was due to a decline in utilization, a result of the availability of a generic alternative.

TOP 10 SPECIALTY THERAPY DRUGS

RANKED BY 2015 PMPY SPEND

					TREND		
RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL SPECIALTY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Humira® Pen (adalimumab)	Inflammatory conditions	$33.54	9.8%	10.5%	18.1%	**28.6%**
2	Enbrel® (etanercept)	Inflammatory conditions	$23.85	7.0%	-5.2%	17.7%	**12.5%**
3	Harvoni® (ledipasvir/sofosbuvir)	Hepatitis C	$21.35	6.3%	293.6%	-16.7%	**276.9%**
4	Copaxone® (glatiramer)	Multiple sclerosis	$13.76	4.0%	-5.4%	3.8%	**-1.6%**
5	Tecfidera® (dimethyl fumarate)	Multiple sclerosis	$11.81	3.5%	9.8%	9.2%	**19.0%**
6	Viekira Pak® (dasabuvir/ombitasvir/ paritaprevir/ritonavir)	Hepatitis C	$9.85	2.9%	–	–	–
7	Gleevec® (imatinib)	Oncology	$7.85	2.3%	1.1%	19.3%	**20.4%**
8	Revlimid® (lenalidomide)	Oncology	$7.74	2.3%	6.4%	8.3%	**14.7%**
9	Gilenya® (fingolimod)	Multiple sclerosis	$7.30	2.1%	20.3%	7.5%	**27.8%**
10	Atripla® (efavirenz/emtricitabine/tenofovir)	HIV	$7.23	2.1%	-8.9%	6.3%	**-2.6%**

2016 – 2018 trend forecast

Traditional trend forecast

Traditional trend will continue with modest increases over the next few years. Diabetes will continue to be a significant contributor to trend, driven by increases in both utilization and unit cost. The trend forecast is negative for several of the top 10 classes over the next three years, primarily due to decreases in unit cost. It's important to note that unit cost reflects the price change across the class, including both the brand and generics within that class. These forecasted numbers include the anticipated effects of SafeGuardRx inflation protection to ensure that drug price increases will be mitigated. The significant increase in trend in 2015 for heartburn/ulcer disease medications is not likely to be sustained. High 2015 trend for the skin conditions class should moderate as well. Although compounded drugs remained in the top 10 therapy classes in 2015, they're expected to continue to decrease in trend over the next three years, as more clients adopt the Express Scripts trend management solutions. The compounded medication class may drop out of the top 10 in the near future.

Diabetes

PMPY drug spend for diabetes medications is projected to increase slightly, then stabilize in the upper teens for 2016 through 2018. Positive utilization trend is a result of increasing disease prevalence. As type 2 diabetes progresses, patients may require more than one therapy to adequately control the disease. Many of these therapies have been merged into new combination products that entered the market in 2014 and 2015. As patients switch from older regimens that require multiple pills per day to the new combination products, increased spend is anticipated, since these combination therapies are branded. Additional continuing unit cost increases are likely due to steady price increases for branded drugs, especially insulin. The first follow-on insulin product, Basaglar, which will compete with Lantus and other basal insulins, will be launched in the U.S. in December 2016. A number of Lantus biosimilars are in development, which will lead to additional competition.

2016 – 2018 TREND FORECAST

	2016	2017	2018
TOTAL OVERALL	**6.8%**	**7.3%**	**8.4%**

TREND FORECAST FOR KEY TRADITIONAL THERAPY CLASSES

2016 – 2018

	TREND FORECAST		
THERAPY CLASS	**2016**	**2017**	**2018**
Diabetes	18.0%	17.7%	16.6%
Pain/inflammation	2.9%	10.2%	12.1%
High blood cholesterol	-11.5%	-14.1%	-13.3%
Attention disorders	9.2%	6.5%	5.5%
High blood pressure/heart disease	-4.6%	-9.1%	-7.6%
Heartburn/ulcer disease	-11.8%	-9.8%	-10.7%
Mental/neurological disorders	-4.0%	-7.0%	-3.0%
Asthma	4.0%	6.1%	0.0%
Compounded drugs	-7.7%	-6.4%	-5.1%
Skin conditions	21.2%	16.2%	11.1%
Other traditional classes	-3.6%	-4.5%	-4.5%
TOTAL TRADITIONAL	**0.4%**	**0.7%**	**1.3%**

Pain/inflammation

The pain/inflammation therapy class is the second highest cost therapy class for 2015. PMPY spend for pain and inflammation drugs is forecast to go up modestly in 2016 and then by double digits in 2017 and 2018, driven almost entirely by increases in unit cost. The October 2014 reclassification of hydrocodone combination products as schedule II controlled substances limits ease of refill on the most utilized drugs in the class. Although the class is dominated by generics, three brand-name drugs are in the top five pain/inflammation drugs according to 2015 PMPY spend and are expected to continue to dominate the class. Generics for the leading brand, Lyrica, are not due until 2019. Additionally, reformulated tamper-resistant or abuse-deterrent opioids, such as the number two drug, OxyContin, are only available as branded therapies. Abuse-deterrent formulations (ADF) of opioids are typically much more expensive than non-ADF alternatives. Additionally, the new formulations give years of extra patent protection to the brand manufacturer.

High blood cholesterol

Although expensive injectable treatments known as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were approved in 2015, statins remain the standard of therapy for most patients with high blood cholesterol. PCSK9s are currently indicated for a small and specific subset of patients. Thus they're examined within a separate specialty therapy class. Negative trends for traditional high blood cholesterol therapies are forecast for the next several years, mostly as a result of decreases in drug costs. In May 2016, Generic competition for the last popular brand statin, Crestor® (rosuvastatin) will be followed by generics for Zetia® (ezetimibe) in December 2016 and Vytorin® (ezetimibe/simvastatin) in April 2017. New guidelines for treating high blood cholesterol and the introduction of PCSK9s have not yet caused significant changes in utilization, but statins are prescribed widely for preventative use and for patients who have had a cardiovascular event. Any potential increases in utilization will be more than offset by overall generic cost savings and savings from the uptake of the Express Scripts Cholesterol Care Value Program as a part of SafeGuardRx.

Attention disorders

We expect trend for drugs used to treat attention disorders to increase at progressively smaller rates from 2016 through 2018. There's a shift in the population that utilizes attention disorder medications, as pediatric patients who utilized medications in this therapy class grow into adulthood and continue therapy. Positive utilization trend is likely as this patient population continues to age. Unit cost for medications used to treat attention disorders also is forecast to increase in each of the next three years. Generics for the nonstimulant Intuniv, which launched in December 2014, and scheduled patent expiration for Strattera® (atomoxetine) in May 2017 should slightly alleviate cost increases. However, brand loyalty is high in the class, with patients, physicians and caregivers reluctant to switch therapies. The top brand in the class, Vyvanse, was recently approved for binge eating disorder, which may increase its utilization in coming years. Most products in the pipeline are new formulations of currently available amphetamines.

High blood pressure/heart disease

With current market saturation levels and the dominance of generic therapies, the predicted trend decreases for the high blood pressure/heart disease class stem from flat utilization and falling unit costs. Valsartan, the generic for Diovan, was first released in July of 2014, with several manufacturers following with their own generics in January of 2015. All the main subclasses used to treat high blood pressure and heart disease are predominantly generic, resulting in falling unit cost as reflected in the forecasted trend for this class.

Increases in utilization for PCSK9s will be more than offset by overall generic cost savings and savings from the uptake of the Express Scripts Cholesterol Care Value Program as a part of SafeGuardRx.

Heartburn/ulcer disease

No new drugs are in development for heartburn/ulcer disease. The two remaining principal brands aren't among the most commonly used drugs in the class, indicating Nexium had high cost increases leading up to the introduction of a generic in February 2015. Negative trends are forecast for 2016 through 2018, since patients will continue using less expensive generic and over-the-counter (OTC) versions of the most common medications in the class. Over the next three years, the anticipated generic competition for Nexium should drive unit cost down, resulting in decreased overall trend.

Mental/neurological disorders

Trend for medications used to treat mental/neurological disorders is forecast to decrease for each of the next three years. Utilization may increase marginally, as atypical antipsychotics are used more for treatment-resistant depression and other difficult-to-manage psychiatric conditions. Generics for Abilify, which launched in May 2015, brought both utilization and cost down by more than 40% for what had been the top drug in the class. Several other brands are in the top 10 drugs by spend, contributing to expected brand inflation for the class. Unit cost trend for multiple popular generics was down significantly in 2015, helping to mitigate some brand cost increases. This effect is expected to continue over the next three years and is reflected in the forecast.

Asthma

PMPY spend for asthma medications will increase slightly in 2016 and 2017 from anticipated brand inflation. For 2018, however, trend is forecasted to drop to zero after the first generic for Advair Diskus is approved by the FDA, which is expected in late 2017. Another popular inhaler, ProAir® HFA (albuterol), could face generic competition in December 2016. However, a settlement agreement will only allow limited supplies of the generic to become available, which will decrease competition in the market and result in reduced cost savings.

Compounded medications

Continued decreases in utilization for compounded medications will be seen, as more clients adopt the Express Scripts compound utilization management program. However, the drops in trend will not be as significant over the next three years, as some of the utilization in this class has been already been affected. The lower, more moderate trend is likely to be driven exclusively by this decrease in utilization, as there is no expectation that the prices for these medications will decrease over the next few years, given their continued rise in 2015. The forecast in this category is dependent upon client adoption of utilization management strategies, rather than events within the compounded medications market itself.

Skin conditions

This year's skin condition therapy class incurred a 34.9% increase in unit cost, with both brand and generic therapies showing substantially higher costs. Consolidations among drug manufacturers have led to a less competitive market, allowing some companies to increase prices drastically. For the next three years we foresee trends decreasing from 21.0% in 2016 to 11.0% in 2018 as plans continue to reap benefits of the' trend management strategies implemented by Express Scripts in 2015.

Specialty trend forecast

Specialty trend is forecast to increase around 17% annually between 2016 and 2018. Existing specialty drugs will gain approval for other indications and will be prescribed more often, and new therapies will receive approval from the FDA. All of these factors will increase utilization trend. However, the major contributors to rising PMPY spend for specialty medications will continue to be both brand inflation and high starting costs for new, highly targeted therapies.

Inflammatory conditions

Trend for the class is forecast to remain above 25.0% due to increases in utilization and unit cost. Cosentyx® (secukinumab), approved in January 2015 for psoriasis, received expanded approvals for ankylosing spondylitis and psoriatic arthritis in January 2016. It's anticipated to be a major driver of increased utilization trend for this class. However, two competitors for Cosentyx are expected to enter the market in 2016: ixekizumab in March and brodalumab in November, which may drive unit cost down as they compete for marketshare.

Beginning in 2017, potential launches of biosimilars to the top two therapies in the class – Remicade® and Humira – may lower the unit cost of therapy. Several biosimilar-related regulatory issues remain unanswered. Once these are resolved, biosimilars may either be expedited or delayed to the market. Several competitors to Xeljanz, the first FDA-approved Janus kinase (JAK) inhibitor, should reach the market in 2017.

Multiple sclerosis

Brand inflation continues to be the primary driver of the trend predicted for medications used to treat MS over the next three years. Launched in June 2015, Glatopa – an A-rated generic to Copaxone 20mg/mL – was expected to lessen the previous predicted cost increases for the class. However, many patients were switched to Copaxone's newer 40mg/mL strength before Glatopa was marketed, which may limit uptake. Generics for Copaxone's higher strength are not expected until February 2017. Older, injectable medications with adverse side effects continue to lose ground to newer, more convenient oral MS drugs.

TREND FORECAST FOR KEY SPECIALTY THERAPY CLASSES

2016 – 2018

	TREND FORECAST*		
THERAPY CLASS	2016	2017	2018
Inflammatory conditions	25.5%	25.5%	26.7%
Multiple sclerosis	11.2%	10.2%	7.2%
Oncology	21.1%	20.0%	20.0%
Hepatitis C	10.2%	8.1%	8.0%
HIV	17.7%	17.8%	18.9%
Growth deficiency	9.1%	9.1%	9.0%
Cystic fibrosis	58.2%	36.2%	28.8%
Pulmonary hypertension	16.6%	5.8%	5.9%
Hemophilia	17.3%	18.3%	22.4%
Sleep disorders	22.6%	21.5%	20.5%
Other specialty classes	6.7%	6.4%	6.4%
TOTAL SPECIALTY	**17.4%**	**16.8%**	**17.2%**

*Trend is forecast only for specialty medications billed through the pharmacy benefit.

Oncology

Over the next three years, trend for the oncology class will continue to increase at approximately 20% annually. As more patients survive initial cancer treatment, utilization will increase as these patients may need maintenance therapy or treatment for recurring disease. Additionally, with more oral and self-administered drugs available, coverage shifts from medical benefits to pharmacy benefits continue, causing increases in utilization and cost on the pharmacy side. Cost also will continue to escalate as more expensive, targeted drugs are introduced. The first generic to Gleevec launched in February 2016, and is expected to result in cost savings. A generic for the prostate cancer drug Zytiga® (abiraterone) is expected in October 2018. However, the lower cost of available generics won't offset high prices for branded oncology drugs.

Hepatitis C

In the next three years, moderate increases in trend are likely for drugs to treat hepatitis C. Two new drugs were approved in July 2015. Daklinza™ (daclatasvir) was approved for use with Sovaldi® (sofosbuvir) to treat genotype 3 hepatitis C, and Technivie® (ombitasvir/paritaprevir/ritonavir) was approved to treat genotype 4 for patients without cirrhosis. In January 2016, the approval of Zepatier™ (elbasvir/grazoprevir) introduced another option for genotypes 1 and 4. Multiple regimens that treat more than one genotype are expected to be approved through 2018. As a result, more competition and more affordable pricing may increase utilization and help to alleviate costs. The implementation of the Hepatitis Cure Value Program as a part of SafeGuardRx is reflected in these trend forecasts.

The first generic to Gleevec launched on Feb. 1, 2016, and is expected to result in cost savings.

HIV

Medications used to treat HIV are expected to trend upward with continued use of branded products. Utilization continues to increase modestly, partially because screening for HIV is more accessible and a greater number of patients are surviving longer after diagnosis. Double-digit increases in unit cost are the major driver of trend in 2016. The convenience and improvement of newer drugs that combine several different drugs in a once-daily dose will increase utilization in this class. Additionally, Genvoya, which contains a new version of tenofovir, abbreviated as TAF, is less likely to cause bone and kidney side effects than tenofovir disoproxil fumarate (TDF) and was approved in November 2015. The manufacturer plans to replace several other combinations that contain TDF with new TAF-containing brands, effectively making drugs containing TDF obsolete. As these new, more expensive, branded TAF formulations replace existing TDF brand formulations, unit cost is expected to increase. Patent protection for brands in the market will also lengthen.

Growth deficiency

In 2015, trend for growth hormone products was influenced equally by utilization and unit cost increases. In each of the next few years, positive trend is expected to be roughly 9%. Brand inflation will drive trend in all three years. Utilization is expected to remain flat as utilization management programs ensure that patients requiring the therapy receive appropriate and affordable care. In 2017, some market share may go to new, expensive and long-acting products that are currently in development.

Cystic fibrosis

At 53.4%, 2015 trend for CF was the greatest increase among the top 10 specialty classes. It was driven primarily by drug costs associated with the July 2015 FDA approval of the very expensive combination drug Orkambi, which treats the underlying disease in some patients. Originally, Orkambi was approved only for patients 12 years of age and older. However, approval for use in children ages 6 to 11 could come in 2017. Additional new medications to treat CF are in development for possible approval in 2018. In the meantime, trend for CF should remain high for 2016, and then begin to moderate as these new products reach a saturation point among this population.

Pulmonary hypertension

Steady utilization and a slight increase in drug cost are projected for pulmonary hypertension drugs in 2016. However, with generic formulations of Tracleer® (bosentan) tablets expected to be marketed in 2016, cost trend could be lower in 2017 and 2018. Several generic medications are expected in 2018 that should increase competition and reduce total trend considerably in 2017 and 2018. Generics are expected for Adcirca® (tadalafil) tablets in May, Remodulin® (treprostinil) injection in June, Letairis® (ambrisentan) tablets in July and Tyvaso® (treprostinil) inhalation solution in November.

Hemophilia

Through 2018, double-digit increases are anticipated in PMPY spend for medications used to treat hemophilia and other bleeding disorders. Utilization should be fairly steady as patients use maintenance drugs regularly to prevent bleeds, rather than occasionally to control bleeding episodes. Although utilization is expected to remain steady, unit cost – and therefore overall trend – will rise, due to increasing use of longer-acting products that were launched in 2014 and 2015.

Sleep disorders

PMPY spend for medications used to treat sleep disorders is expected to increase by double digits for the next three years resulting from unit cost increases. Utilization is expected to remain relatively flat over the next three years.

Through 2018, **double-digit increases** are anticipated in PMPY spend for medications used to treat hemophilia and other bleeding disorders.

Looking to the future

Express Scripts is constantly monitoring and anticipating indications with potential for high-cost and high-use drugs, and preemptively developing strategies to counter widespread drug spend problems before they occur. Nonalcoholic steatohepatitis and Alzheimer's disease (AD) are two such disease states.

Nonalcoholic steatohepatitis

According to the National Institutes of Health (NIH), 2% to 5% (approximately 6 million to 16 million) of Americans are affected by nonalcoholic steatohepatitis (NASH). NASH is inflammation and damage of the liver due to fatty buildup in people who drink little or no alcohol. Most prevalent in middle-age individuals who are overweight or obese, NASH affects more than 25% of obese Americans. Although NASH may be asymptomatic, it can lead to cirrhosis or permanent liver damage. Currently, the best treatment options are weight reduction or a balanced diet and physical activity, as well as avoidance of alcohol and substances that cause liver damage. While no true pharmacologic treatments are currently specific for NASH, several products are in various stages of development, with the first approvals expected in 2016. The prevalence of NASH, coupled with a PCSK9-like price tag, could dramatically affect drug spend.

Alzheimer's disease

As the baby boomer generation reaches the age of 65, the potential financial and clinical impact of pharmacotherapy to prevent, delay or treat AD looms large. It's estimated that each of the 5.4 million Americans who suffers from AD incurs an annual cost of $35,000 in treatment. Currently, fewer than 10 pharmacologic treatments are available. With no cure and no drugs to prevent AD progression, treatments provide only symptomatic relief, temporarily improving brain function in patients with mild to moderate disease. Despite the large potential population, these patients accounted for only $1.92 PMPY in 2015. Many of these medications are generic, with Namenda being the latest to go generic in July 2015. However, newer agents with potential disease-modifying characteristics are entering into clinical Phase III trials. If the pricing for new hepatitis C therapies was any indication of how manufacturers set prices for drugs that demonstrate substantial improvement in clinical outcomes, it's likely that AD medications will come to market with hefty price tags.

It's estimated that each of the 5.4 million Americans who suffers from AD incurs an **annual cost of $35,000** in treatment.

Trend drivers

2015 patent expirations

PATENT EXPIRATION DATE	BRAND (GENERIC) NAME	PRIMARY INDICATION	ESTIMATED ANNUAL SALES (MILLIONS)
Dec. 7, 2015	Patanol® (olopatadine) ophthalmic solution	Eye allergy	$223
Nov. 30, 2015	Viramune XR® (nevirapine extended release)	HIV	$60
Nov. 19, 2015	Jalyn® (dutasteride/tamsulosin)	Benign prostatic hyperplasia	$91
Nov. 5, 2015	Naprelan® (naproxen sodium)	Pain	$58
Oct. 9, 2015	Avodart® (dutasteride)	Benign prostatic hyperplasia	$499
Sep. 28, 2015	Invega® (paliperidone extended release)	Schizophrenia	$612
Sep. 21, 2015	Testred® (methyltestosterone)	Hypogonadism	$15
Sep. 18, 2015	Lescol® XL (fluvastatin extended release)	High cholesterol	$38
Sep. 9, 2015	Exelon® Patch (rivastigmine transdermal system)	Alzheimer's disease	$611
Aug. 24, 2015	hydroxyprogesterone	Female hormone-related conditions	N/A
Aug. 17, 2015	Xenazine® (tetrabenazine)	Huntington's disease	$242
Aug. 12, 2015	Mirapex ER® (pramipexole extended release)	Parkinson's disease	$45
Jul. 28, 2015	Megace® ES (megestrol oral suspension)	Cachexia of AIDS	$44
Jul. 13, 2015	Namenda® (memantine)	Alzheimer's disease	$1,588
Jul. 9, 2015	Targretin® (bexarotene) capsules	Lymphoma	$156
Jul. 9, 2015	Angiomax® (bivalirudin)	Blood clot prevention	$485
Jul. 7, 2015	Axert® (almotriptan)	Migraine	$32
Jul. 1, 2015	Aggrenox® (aspirin/dipyridamole extended release)	Blood modifying	$460
Jun. 29, 2015	Pristiq® (desvenlafaxine)	Depression	$719
Jun. 23, 2015	Zyvox® (linezolid) tablets	Bacterial infections	$470
Jun. 19, 2015	Copaxone® (glatiramer) 20mg	Multiple sclerosis	$2,493
Jun. 1, 2015	Actonel® (risedronate) 5mg, 30mg, 35mg tablets	Osteoporosis	$158
May 28, 2015	Lotronex® (alosetron)	Irritable bowel syndrome with diarrhea	$80
May 18, 2015	Atelvia® (risedronate)	Osteoporosis	$74
Apr. 28, 2015	Abilify® (aripiprazole)	Schizophrenia/bipolar disorder	$7,838
Apr. 24, 2015	Fusilev® (levoleucovorin injection)	Colorectal cancer/methotrexate toxicity	$185
Apr. 15, 2015	Suprax® (cefixime) oral suspension	Bacterial infections	$120
Mar. 10, 2015	Temovate® (clobetasol 0.05%) cream	Skin conditions	$185
Feb. 26, 2015	Tarka® (trandolapril/verapamil)	High blood pressure/heart disease	$24
Jan. 26, 2015	Nexium® (esomeprazole magnesium)	Gastroesophageal reflux	$5,931

Jan. 26, 2015	Lamictal® ODT™ (lamotrigine) orally disintegrating tablets	Seizures	$51
Jan. 12, 2015	AndroGel® (testosterone gel) 1%	Hypogonadism	$1,267
Jan. 12, 2015	Clobex® (clobetasol) Spray	Psoriasis	$100
Jan. 9, 2015	Zyvox® (linezolid) injection	Bacterial infections	$260

Highlights

- At the end of April, the FDA approved the first AB-rated generics for Abilify tablets. An atypical antipsychotic, aripiprazole is indicated to treat mental and neurological disorders, including autism, bipolar disorder, depression, mania, schizophrenia and Tourette's syndrome. Generics from four manufacturers were approved and at least one launched immediately, despite continuing litigation concerning three patents that might have covered Abilify for several more years. According to the IMS Institute for Healthcare Informatics, nondiscounted spend for Abilify in the United States amounted to $7.8 billion in 2014, making it second only to the hepatitis C drug Sovaldi among the country's top-selling drugs. Other atypical antipsychotics are available – many in generic versions – and two new brands, Rexulti® (brexpiprazole) and Vraylar™ (cariprazine), were approved in 2015.

- In December 2015, the FDA announced the approval of Basaglar, a long-acting human insulin analog to improve glycemic control in patients with diabetes. Although it's a new branded insulin, it has the same amino acid sequence as Sanofi's Lantus. The FDA designated it as a "follow-on," not a biosimilar, because insulins are FDA approved under provisions of the Food, Drug, and Cosmetic Act while biologic products are granted approval under a different law, the Public Health Service Act. Following terms of a settlement agreement, Basaglar will launch in December 2016. It will be dispensed in 3mL cartridges, 100 units/mL for KwikPen® delivery devices. Dosing is once daily.

- The first FDA-approved generic to Targretin® (bexarotene) capsules was introduced to the U.S. market on July 9, 2015. Originally approved by the FDA in December 1999, it's used for the treatment of cutaneous (skin) manifestations of cutaneous t-cell lymphoma for patients who are refractory to at least one prior systemic therapy. Generics to topical Targretin gel 1% aren't expected until October 2016 at the earliest.

- Glatopa, an A-rated generic to Copaxone, launched in mid-June 2015. Glatiramer is a disease-modifying drug administered by subcutaneous (SC) injection to treat relapsing forms of MS. It's not a biological drug, but it's more complex and difficult to replicate than most traditional drugs. Copaxone has been available for nearly 20 years as a 20mg/mL formulation that's injected once daily. Several patents on the original formulation expired in 2014, but litigation over a later patent delayed the release of a generic. In addition, Copaxone 40mg/mL – a strength that's needed only three times a week – was FDA approved in January 2014. It will have protection from direct generic competition until at least May 2017, but likely longer following the issuance of additional patents. Up to 70% of patients shifted to the higher strength before Glatopa launched.

- In August 2015, the FDA approved a generic for Delalutin® (hydroxyprogesterone) injection, 250 mg/mL, even though the brand was discontinued in 1999. Hydroxyprogesterone treats a wide variety of female hormone-related conditions, including advanced uterine cancer and abnormal uterine bleeding. Since the original brand product was withdrawn from the market for business, not safety or effectiveness reasons, the FDA approved the generic. Launch isn't expected until mid-2016. Hydroxyprogesterone in the same strength is in the branded drug Makena®, which is indicated only to prevent premature births.

- Generics for the $1 billion seller Namenda tablets were released in July 2015. Namenda is indicated twice a day for treating moderate to severe dementia of Alzheimer's type. A settlement agreement allowed several other generics after a secondary Namenda patent expired in October. A once-daily follow-on product, Namenda XR® (memantine extended release), was marketed in June 2013, and the brand manufacturer intended to discontinue Namenda before the patent expired. However, in December 2014, a district court ruled that Namenda tablets were required to remain on the market. In this instance, the "hard switch" strategy, in which a manufacturer discontinues one formulation of a product in favor of another, was prevented. Still, a majority of Namenda patients have transitioned to the longer-acting form.

- The FDA approved the first AB-rated generics to Janssen's Invega® (paliperidone) extended-release tablets. Invega is indicated to treat schizophrenia in adults and adolescents 12 years of age and older. It's also approved for the treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizing and/or antidepressant therapy in adults. Since Invega was first approved, longer-lasting injectable versions have also received FDA approval. Invega Sustenna® is injected once a month for treating bipolar disorder and schizophrenia. More recently, Invega Trinza™ won FDA approval in May 2015, for treating adult patients with schizophrenia. Each intramuscular (IM) Invega Trinza injection, which must be given by a healthcare provider, lasts for three months. Before starting on Invega Trinza, patients have to be treated with monthly Invega Sustenna injections for at least four months.

- In August 2015, the first A-rated generic to Xenazine® (tetrabenazine) tablets was launched in the U.S. Tetrabenazine is the only FDA-approved drug that treats chorea (involuntary, unpredictable movements) associated with Huntington's disease. Its individualized dosing requires careful weekly titration. The first week's starting dose is 12.5mg daily with a maximum recommended dose of no more than 100mg per day for most adults. Although Xenazine is only available through a limited network of specialty pharmacies, tetrabenazine is marketed through open distribution.

In the instance of Namenda, the **"hard switch" strategy**, in which a manufacturer discontinues one formulation of a product in favor of another, **was prevented**.

2015 brand approvals

APPROVAL DATE	BRAND (GENERIC) NAME	PRIMARY INDICATION	PRODUCT UNIQUENESS
Dec. 22 2015	Zurampic® (lesinurad)	Gout	New mechanism of action
Dec. 21, 2015	Uptravi® (selexipag)	Pulmonary arterial hypertension	Similar to existing products
Dec. 15, 2015	Bridion® (sugammadex)	Neuromuscular blockade reversal	New mechanism of action
Dec. 11, 2015	Alecensa® (alectinib)	ALK-positive lung cancer	Similar to existing products
Dec. 11, 2015	Vistogard® (uridine triacetate)	Fluorouracil toxicity	New mechanism of action
Dec. 10, 2015	Otiprio™ (ciprofloxacin) otic suspension	Otitis media	Refinement of an existing product
Dec. 8, 2015	Kanuma™ (sebelipase alfa)	Lysosomal acid lipase deficiency	New mechanism of action
Dec. 7, 2015	Bendeka™ (bendamustine)	Chronic lymphocytic leukemia/non-Hodgkin lymphoma	Refinement of an existing product
Dec. 4, 2015	QuilliChew ER™ (methylphenidate) extended release	Attention deficit hyperactivity disorder	Existing product with new dosing form
Nov. 30, 2015	Empliciti™ (elotuzumab)	Multiple myeloma	New mechanism of action
Nov. 24, 2015	Portrazza™ (necitumumab)	Non-small cell lung cancer	Similar to existing products
Nov. 20, 2015	Ninlaro® (ixazomib)	Multiple myeloma	New mechanism of action
Nov. 18, 2015	Narcan® (naloxone) Nasal Spray	Opioid overdose	Existing product with new dosing form
Nov. 16, 2015	Darzalex™ (daratumumab)	Multiple myeloma	New mechanism of action
Nov. 13, 2015	Targrisso™ (osimertinib)	Non-small cell lung cancer	New mechanism of action
Nov. 13, 2015	Adynovate [antihemophilic factor (recombinant)],	Hemophilia A	Refinement of an existing product
Nov. 10, 2015	Cotellic™ (cobimetinib)	Melanoma	New mechanism of action
Nov. 5, 2015	Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide)	HIV	Refinement of an existing product
Nov. 4, 2015	Nucala® (mepolizumab)	Asthma	New mechanism of action
Oct. 29, 2015	Seebri™ Neohaler® (glycopyrrolate/indacaterol)	Chronic obstructive pulmonary disease	New combination of existing products
Oct. 29, 2015	Ultibron™ Neohaler® (glycopyrrolate)	Chronic obstructive pulmonary disease	New mechanism of action
Oct. 27, 2015	Imlygic™ (talimogene laherparepvec)	Melanoma	New mechanism of action
Oct. 23, 2015	Belbuca™ (buprenorphine) buccal film	Pain	Existing product with new dosing form
Oct. 23, 2015	Strensiq™ (asfotase alfa)	Hypophosphatasia	New mechanism of action
Oct. 23, 2015	Yondelis® (trabectedin)	Soft tissue sarcomas	Similar to existing products
Oct. 22, 2015	Vivlodex™ (meloxicam) capsules	Osteoarthritis	Existing product with new dosing form
Oct. 22, 2015	Onivyde™ (irinotecan) liposomal injection	Pancreatic cancer	Existing product with new dosing form
Oct. 21, 2015	Veltassa™ (patiromer)	Hyperkalemia	Similar to existing products
Oct. 20, 2015	Coagadex® (coagulation factor X, human)	Hereditary Factor X Deficiency	New mechanism of action

Oct. 19, 2015	Dynavel™ XR (amphetamine) oral suspension, extended release	Attention deficit hyperactivity disorder	Existing product with new dosing form
Oct. 16, 2015	Praxbind® (idarucizumab)	Pradaxa® (dabigatran) anticoagulant reversal	New mechanism of action
Oct. 16, 2015	Enstilar® (calcipotriene/betamethasone dipropionate) Foam	Psoriasis	Existing product with new dosing form
Oct. 6, 2015	Aristada™ (aripiprazole lauroxil)	Schizophrenia	Refinement of an existing product
Oct. 2, 2015	MorphaBond™ (morphine) extended-release tablets	Pain	Existing product with new dosing form
Sep. 25, 2015	Tresiba® (insulin degludec)	Diabetes	Similar to existing products
Sep. 25, 2015	Ryzodeg®70/30 (insulin aspart/insulin degludec)	Diabetes	New combination of existing products
Sep. 22, 2015	Lonsurf® (trifluridine/tipiracil)	Colorectal cancer	New mechanism of action
Sep. 17, 2015	Vraylar™ (cariprazine)	Schizophrenia/Bipolar disorder	Similar to existing products
Sep. 15, 2015	Nuwiq® (human coagulation factor VIII (rDNA), simoctocog alfa)	Hemophilia A	Similar to existing products
Sep. 4, 2015	Xuriden™ (uridine triacetate)	Hereditary orotic aciduria	New mechanism of action
Sep. 4, 2015	Durlaza™ (aspirin) extended-release capsules	Heart attack/stroke prevention	Existing product with new dosing form
Sep. 2, 2015	Varubi™ (rolapitant)	Chemotherapy-induced nausea and vomiting	Similar to existing products
Aug. 27, 2015	Repatha™ (evolocumab)	Familial hypercholesterolemia	Similar to existing products
Aug. 26, 2015	Synjardy® (empagliflozin/metformin),	Diabetes	New combination of existing products
Aug. 18, 2015	Addyi™ (flibanserin)	Female hypoactive sexual desire disorder	New mechanism of action
Aug. 13, 2015	Ximino® (minocycline) extended-release capsules	Acne	Existing product with new dosing form
Jul. 31, 2015	Spritam® (levetiracetam)	Seizures	Existing product with new dosing form
Jul. 29, 2015	Finacea® (azelaic acid) Foam 15%	Rosacea	Existing product with new dosing form
Jul. 24, 2015	Technivie® (ombitasvir/paritaprevir/ritonavir)	Hepatitis C	New combination of existing products
Jul. 24, 2015	Daklinza™ (daclatasvir)	Hepatitis C	New mechanism of action
Jul. 24, 2015	Odomzo® (sonidegib)	Basal cell carcinoma	Similar to existing products
Jul. 24, 2015	Praluent® (alirocumab)	Familial hypercholesterolemia	New mechanism of action
Jul. 15, 2015	Epiduo® Forte (adapalene/benzoyl peroxide) Gel	Acne	Refinement of an existing product
Jul. 10, 2015	Envarsus® XR (tacrolimus extended-release)	Transplant rejection	Existing product with new dosing form
Jul. 10, 2015	Rexulti® (brexpiprazole)	Schizophrenia/Depression	Similar to existing products
Jul. 7, 2015	Entresto™ (sacubitril/valsartan)	Heart failure	New mechanism of action
Jul. 2, 2015	Orkambi® (lumacaftor/ivacaftor)	Cystic fibrosis	New mechanism of action
Jun. 22, 2015	Kengreal™ (cangrelor)	Blood clot prevention	New mechanism of action
Jun. 22, 2015	Tuxarin ER® (codeine/chlorpheniramine)	Cough and cold	New combination of existing products
May 27, 2015	Viberzi® (eluxadoline)	Irritable bowel syndrome with diarrhea	New mechanism of action
May 21, 2015	Stiolto™ Respimat® (tiotropium/olodaterol)	Chronic obstructive pulmonary disease	New combination of existing products

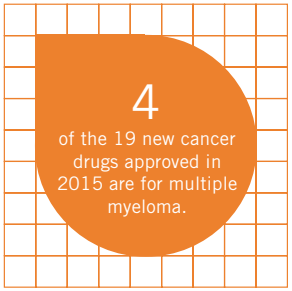
May 19, 2015	Invega Trinza™ (paliperidone) extended-release injectable suspension	Schizophrenia	Refinement of an existing product
Apr. 30, 2015	Tuzistra™ XR (codeine polistirex/chlorpheniramine polistirex)	Cough and cold	New combination of existing products
Apr. 29, 2015	Ixinity® (coagulation factor IX [recombinant])	Hemophilia B	Similar to existing products
Apr. 29, 2015	Kybella® (deoxycholic acid)	Submental fat	New mechanism of action
Apr. 17, 2015	Aptensio XR™ (methylphenidate)	Attention deficit hyperactivity disorder	Refinement of an existing product
Apr. 15, 2015	Corlanor® (ivabradine)	Heart failure	New mechanism of action
Mar. 31, 2015	ProAir® RespiClick (albuterol) dry-powder inhaler	Reversible obstructive airway disease	Refinement of an existing product
Mar. 30, 2015	Jadenu™ (deferasirox)	Chronic iron overload	Refinement of an existing product
Mar. 17, 2015	Cholbam® (cholic acid)	Bile acid synthesis disorders	New mechanism of action
Mar. 10, 2015	Unituxin™ (dinutuximab)	Neuroblastoma	Similar to existing products
Mar. 6, 2015	Cresemba™ (isavuconazonium)	Invasive aspergillosis/Invasive mucormycosis	New mechanism of action
Feb. 26, 2015	Liletta® (levonorgestrel-releasing intrauterine system)	Contraception	Refinement of an existing product
Feb. 25, 2015	Toujeo® (insulin glargine)	Diabetes	Similar to existing products
Feb. 25, 2015	Avycaz™ (ceftazidime/avibactam)	Complicated intra-abdominal infections/Complicated urinary tract infections	New mechanism of action
Feb. 23, 2015	Farydak (panobinostat)	Multiple myeloma	New mechanism of action
Feb. 13, 2015	Lenvima™ (lenvatinib)	Thyroid cancer	Similar to existing products
Feb. 6, 2015	Dutrebis™ (lamivudine/raltegravir)	HIV	New combination of existing products
Feb. 3, 2015	Ibrance® (palbociclib)	Breast cancer	New mechanism of action
Jan. 30, 2015	Pazeo® (olopatadine ophthalmic solution) 0.7%	Eye allergy	Refinement of an existing product
Jan. 30, 2015	Glyxambi® (empagliflozin/linagliptin)	Diabetes	New combination of existing products
Jan. 30, 2015	Zohydro® ER (hydrocodone) with abuse deterrents	Pain	Refinement of an existing product
Jan. 29, 2015	Evotaz™ (atazanavir/cobicistat)	HIV	New combination of existing products
Jan. 29, 2015	Prezcobix® (darunavir/cobicistat)	HIV	New combination of existing products
Jan. 23, 2015	Natpara® (parathyroid hormone)	Hypocalcemia of hypoparathyroidism	New mechanism of action
Jan. 23, 2015	Triferic® (ferric pyrophosphate citrate)	Chronic kidney disease	New mechanism of action
Jan. 21, 2015	Cosentyx™ (secukinumab)	Psoriasis	New mechanism of action
Jan. 21, 2015	Prestalia® (amlodipine/perindopril)	High blood pressure	New combination of existing products
Jan. 9, 2015	Duopa™ (carbidopa/levodopa) enteral suspension	Parkinson's disease	Existing product with new dosing form
Jan. 8, 2015	Savaysa® (edoxaban)	Blood clot prevention	Similar to existing products
Jan. 7, 2015	Rytary™ (carbidopa/levodopa)	Parkinson's disease	Refinement of an existing product

Highlights

Approvals

- Addyi™ (flibanserin) was approved by the FDA in August 2015 as the first drug to treat female sexual dysfunction. Specifically, it's indicated for acquired, generalized hypoactive sexual desire disorder (HSDD) among premenopausal women. Unlike drugs for male erectile dysfunction, which influence muscle tone, blood supply or testosterone levels, Addyi affects neurotransmitter levels in the brain, increasing the desire for sex. It must be taken daily. Prescribers of Addyi are trained and certified, each potential patient is assessed using a Patient-Provider Agreement Form and the drug is dispensed only through certified pharmacies.

- Four of the 19 new cancer drugs that were FDA approved in 2015 are for treating multiple myeloma. A relatively uncommon, but frequently aggressive cancer of the blood-forming cells in bone marrow, multiple myeloma has an overall five-year survival rate under 50%. Currently, it can't be cured and the incidence of recurrence is high. Additionally, most drug treatments for multiple myeloma lose effectiveness after they've been used repeatedly, so other drugs are needed – usually in combinations.



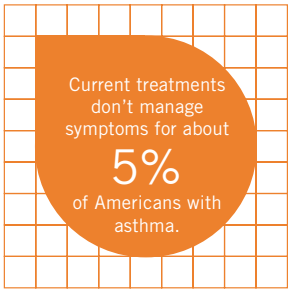
- A new cardiovascular drug, Entresto™ (sacubitril/valsartan), was approved in July 2015. Containing a well-established angiotensin receptor blocker, it also includes the first drug in a new class called neprilysin inhibitors. Entresto is indicated to reduce the risk of cardiovascular death and hospitalization for patients with chronic heart failure and reduced ejection fraction – around 2.2 million Americans. In clinical trials, Entresto outperformed the previous standard of care, angiotensin converting enzyme (ACE) inhibitors. However, it's significantly more expensive than most other cardiovascular drugs.

- In November 2015, the FDA approved the combination drug Genvoya for the once-daily treatment of specific patients who have HIV-1. In addition to three drugs already approved for treating HIV, Genvoya includes a new nucleotide reverse transcriptase inhibitor (NRTI), tenofovir alafenamide (TAF). Although it's similar to Viread® (tenofovir disoproxil fumarate or TDF), TAF is effective in much smaller doses, so it has less risk of causing kidney damage and bone mineral density problems than TDF. Two other combination products that contain TAF are being reviewed by the FDA with action dates in the first half of 2016. They're expected to replace the older TDF-containing combinations.

- Five specialty products were approved in 2015 to treat hemophilia and related conditions. Among them is Coagadex® (Coagulation Factor X [human]), the first drug FDA approved to treat hereditary Factor X deficiency. A rare blood-clotting disorder, Factor X deficiency is estimated to affect between 300 and 600 patients in the United States. Coagadex is used to manage bleeding before, during and after surgical procedures, as well as to treat and control acute bleeding episodes.

- Narcan® Nasal Spray, the first noninjected form of naloxone, was approved by the FDA in November 2015. To treat opioid overdoses in emergency situations, the first spray (4mg) should be administered immediately. One spray is given every two to three minutes until the patient recovers consciousness or emergency medical help arrives. Narcan nasal spray can be used for both adults and children. It will be available by prescription at retail pharmacies across the United States, but in some states a prescription won't be required.

- The FDA approved Nucala® (mepolizumab) injection for use as an add-on maintenance treatment for severe eosinophilic asthma. The first humanized interleukin-5 (IL-5) antagonist monoclonal antibody to be approved, it's injected subcutaneously by a healthcare professional once every four weeks. Current treatments don't manage symptoms for about 5% of the estimated 25.7 million people in the U.S. who have asthma. For many of these resistant cases, Nucala could be added to inhaled corticosteroids and other current asthma treatments. Nucala reduces severe asthma attacks by sticking to IL-5 receptors. Blocking the action of IL-5 decreases eosinophils, white blood cells that contribute to increased sensitivity of the airways among asthma patients.



- Several orphan drugs, intended to treat patient populations of 200,000 or less, were approved during 2015. Considered specialty drugs, many are the first approved treatments for rare but severe conditions. These drugs include:
    - Cholbam® (cholic acid) – indicated for treating rare disorders of bile acid synthesis caused by an enzyme defect. It's also approved for a group of very serious inherited conditions that result from missing or malfunctioning peroxisomes – parts of cells that produce enzymes to break down fatty acids. Around one person in 50,000 has a condition that Cholbam might treat.
    - Kanuma™ (sebelipase alfa) – for the treatment of patients with lysosomal acid lipase (LAL) deficiency. Individuals with LAL deficiency have defective genes that prevent the proper metabolism and storage of fats, causing damage to the blood vessels, heart, liver and other organs. In the general population, fewer than 20 patients in one million have LAL deficiency.
    - Keveyis™ (dichlorphenamide) – an oral carbonic anhydrase inhibitor. It's indicated for the treatment of primary hyperkalemic and hypokalemic periodic paralysis, inherited disorders that cause episodes of muscle weakness or paralysis for approximately 5,000 patients in the U.S.
    - Xuriden™ (uridine) – oral granules that treat hereditary orotic aciduria (HOA). It's the first approved treatment for this rare metabolic disorder that's been reported in only about 20 patients in the world.
- In the summer of 2015, two specialty drugs were approved for specific types of hard-to-treat high cholesterol. Praluent and Repatha are the first in a new class, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Praluent was approved to be used once every two weeks for treating patients with heterozygous familial hypercholesterolemia (HeFH) and patients with clinical atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of low-density lipoprotein cholesterol (LDL-C). Repatha is indicated once or twice a month for the same two conditions and also for homozygous familial hypercholesterolemia (HoFH). Both drugs are available in self-injectors and each is used in tandem with dietary and statin therapies. About 11 million Americans have one of the three indicated conditions, but the use of PCSK9 inhibitors may expand if results from ongoing clinical trials show they reduce heart disease risks. PCSK9 inhibitors are included on our specialty formulary.
- Pradaxa® (dabigatran) is an oral direct thrombin inhibitor anticoagulant that was approved in 2010 to reduce the risk of stroke and blood clots for patients with nonvalvular atrial fibrillation. It's also approved to treat and prevent deep venous thrombosis (DVT) and pulmonary embolism (PE). Although it's less complicated to use than earlier anticoagulants, its effects couldn't be counteracted when needed. In 2015, the first reversal agent for it, Praxbind® (idarucizumab), was approved for emergency surgery/urgent procedures and in life-threatening or uncontrolled bleeding episodes. Praxbind is a humanized monoclonal antibody fragment that's administered as a single intravenous (IV) infusion.
- In 2015, the FDA approved a number of older drugs redesigned as new dosage forms, developed in new strengths, combined in new ways or repurposed for different indications. They include a new form and dose of aspirin; a topical acne cream remade into a foam for rosacea; a new combination of blood pressure medications; a former glaucoma treatment now approved as the first treatment for a rare condition. Even though many of the drugs have been generic for years, the newly approved versions are all branded. As new technologies become available, more older drugs will probably be repurposed in similar ways.
- In August 2015, the FDA approved Spritam®, a new version of the anti-seizure drug levetiracetam. Spritam is the first FDA-approved drug to be manufactured by a 3-D printing process. Using proprietary technology, the unique process allows layers of powdered medication to be formed into spongy, mint-flavored tablets that disintegrate very quickly when taken.

Among FDA approvals in 2015 are a number of older drugs that have been redesigned as new dosage forms, developed in new strengths, combined in new ways or repurposed for different indications.

New indications

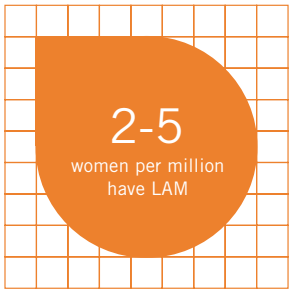
- In April 2015, the FDA granted Breo® Ellipta® a new indication for treating adults with asthma. Initially approved in May 2013 for the treatment of chronic obstructive pulmonary disease (COPD), it includes a corticosteroid (fluticasone furoate) to reduce inflammation and a bronchodilating long-acting beta blocker (LABA), vilanterol. Breo Ellipta isn't indicated for treating asthma patients under the age of 18 and it's not a rescue medicine for acute bronchospasms. For asthma, adult patients use one inhalation daily.

- Clozapine, an oral drug for treating schizophrenia, is used when other antipsychotic medications don't adequately manage symptoms. However, severe and possibly fatal neutropenia – very low numbers of a white blood cell type known as neutrophils – can be caused by taking clozapine. Its prescribing information has been changed to better describe monitoring for and treating neutropenia if needed. Additionally, beginning in October 2015, the registries previously kept separately by manufacturers of clozapine were replaced by a single risk evaluation and mitigation strategy (REMS) program for all patients. Prescribers and dispensing pharmacies now have to be certified, and clozapine is available only through the REMS. Clozapine is available as generic tablets and orally disintegrating tablets, as well as under the brand names Clozaril® tablets, FazaClo® Orally Disintegrating Tablets and Versacloz™ Oral Suspension.

- In March 2015, Kalydeco® (ivacaftor) was FDA approved for use in children age two to five who have CF and who have one of 10 mutations in the CF transmembrane conductance regulator (CFTR) gene. Approximately 300 children in the U.S. age two to five have these mutations. Previously, Kalydeco was indicated only for appropriate patients six years of age and older. The FDA also approved a new oral granule formulation of Kalydeco, which can be mixed in soft foods and liquids.

- Opdivo® (nivolumab) injection is a human programmed death receptor-1 (PD-1) immune checkpoint inhibitor first approved by the FDA in December 2014. It enhances immune response by blocking specific receptors that deactivate immune cells. Originally, it was indicated for treating progressed and malignant melanoma, as well as for second-line, single-agent therapy for advanced squamous and nonsquamous-cell nonsmall cell lung cancer (NSCLC). In 2015, Opdivo also was approved for metastatic renal cell carcinoma (RCC) and as first-line monotherapy for treating patients with inoperable or metastatic BRAF V600 wild-type melanoma.

- After priority review and with orphan and breakthrough designations, the FDA approved Rapamune® (sirolimus) in May 2015 to treat lymphangioleiomyomatosis (LAM). A very rare disease of the lungs, LAM almost exclusively affects women; about two to five women per million have it. In LAM, smooth muscle tissue that grows in the lungs clogs airways, blood vessels and lymph channels, restricting breathing and eventually destroying lung function. Current treatment includes symptom relief with bronchodilators, fluid removal from the lungs and lung transplants. Initially approved more than 15 years ago to help prevent rejection of transplanted kidneys, Rapamune is the first treatment to slow the progression of LAM.



- The FDA approved the over-the-counter (OTC) use of Rhinocort® (budesonide) nasal spray for the temporary relief of symptoms of hay fever or other upper respiratory allergies (nasal congestion, runny nose, itchy nose and sneezing) in adults and children age six and older. An estimated 50 million Americans have nasal allergies. Most treat their symptoms with OTC products. Rhinocort Allergy Spray will compete in the nonprescription market with Flonase® Allergy Relief (fluticasone propionate) and Nasacort® Allergy 24HR (triamcinolone acetonide).

- A new indication for Saphris® (asenapine) was approved in March 2015, under an FDA priority review. An atypical antipsychotic medication that's been on the U.S. market for nearly six years, Saphris is already indicated for both acute and maintenance treatment of adults with schizophrenia and/or bipolar disorder. Now, it's also approved for treating bipolar I disorder for children as young as 10 years. For pediatric patients, it will be used alone to manage acute episodes of mania or mixed manic-depressive behaviors resulting from bipolar I disorder. Saphris is manufactured as sublingual, black-cherry-flavored tablets that may be easier for children to take than other oral dose forms.

- The FDA released a Drug Safety Communication in December 2015 about possible adverse effects from sodium-glucose cotransporter-2 (SGLT2) inhibitors. Following up on a warning issued in May, the FDA found more than 70 reports of ketoacidosis, which is a dangerous accumulation of ketones (a type of fatty acid) in the blood, due to lack of insulin among patients taking an SGLT2 inhibitor. Additionally, the FDA identified cases of urosepsis

(blood infections caused by infections in the urinary tract) and pyelonephritis (kidney infections) associated with SGLT2 inhibitor use. Labeling for all SGLT2 inhibitors will now have warnings about the potential side effects and how to monitor for them. Manufacturers of SGLT2 inhibitors are required to investigate reported incidences of ketoacidosis for the next five years. SGLT2 inhibitors that have been approved in the U.S. include Farxiga™ (dapagliflozin), Glyxambi® (linagliptin/empagliflozin), Invokamet® (canagliflozin/metformin), Invokana, Jardiance® (empagliflozin), Synjardy and Xigduo® XR (dapagliflozin/metformin extended release).

- In January 2015, an expanded indication for the treatment of moderate to severe binge eating disorder (BED) in adults was granted for Vyvanse capsules. Vyvanse is the first drug approved for BED, which results in patients overeating when not feeling hungry. BED patients often eat to the point of being uncomfortably full. Vyvanse, a central nervous system (CNS) stimulant, was already approved as a maintenance treatment for adults and children six years of age and older with attention deficit hyperactivity disorder (ADHD).

Vyvanse is the **first drug** approved for BED, which results in patients overeating when not feeling hungry.

Express Scripts Prescription Price Index

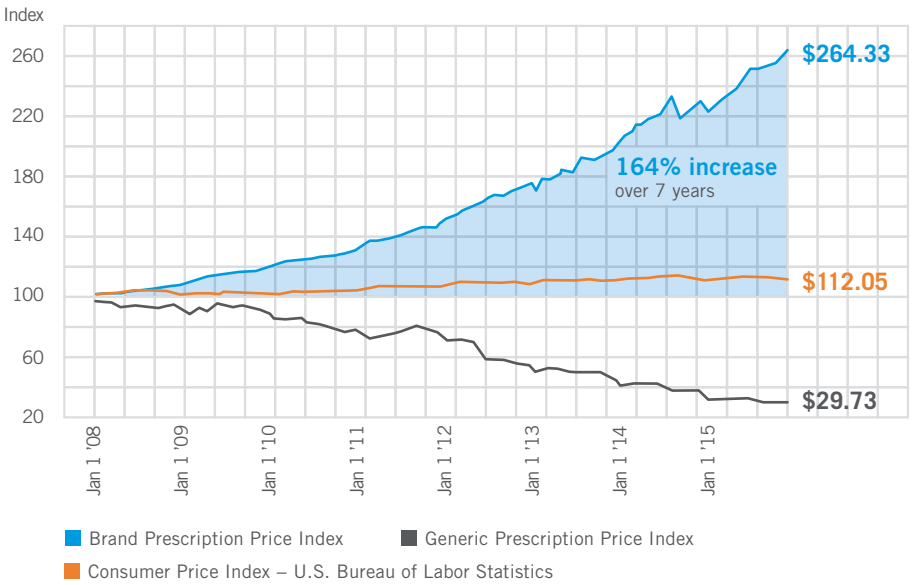
Roughly half of Americans take prescription medications. Generic products comprise 84% of filled prescriptions. By achieving higher generic fill rates, there's still opportunity for employers, state governments, unions and members to ensure cost savings. According to the Express Scripts Prescription Price Index, the average price for the most commonly used brand-name drugs has increased 164% since 2008, whereas generic drug prices have continued to decline. Between 2014 and 2015, the price of generic products, on average, decreased 19.9%, while the price of brand name products increased, on average, 16.2%.

Express Scripts mitigates the risk of drug price inflation for our clients and members by utilizing our task force of clinical experts who assess and recommend additional potential savings measures as they arise.

While news reports focus on a few outliers, payers should remain confident that, on the whole, generic medications continue to deliver significant cost savings. Encouraging use of generics over more expensive brand alternatives, when clinically appropriate, keeps costs down and helps patients adhere to their prescribed therapy.

The gap between brand inflation and generic deflation increased slightly, from 35.5 percentage points in December 2014 to 36.1 percentage points in December 2015. From the base price of $100.00 set in January 2008, in December 2015 prices for the most commonly used generic medications decreased to $29.73 (in 2008 dollars), and prices for the most commonly used brand medications increased to $264.33 (in 2008 dollars). In contrast, a market basket of commonly used household goods costing $100.00 in 2008, as measured by the Bureau of Labor Statistics consumer price index, grew to only $112.05 (in 2008 dollars) by December 2015.

THE EXPRESS SCRIPTS PRESCRIPTION PRICE INDEX



Appendix

The Drug Trend Report methodology

Our research team analyzes prescription drug use data for members with drug coverage provided by Express Scripts plan sponsors[5] for this report. The plan sponsors providing the pharmacy benefit paid at least some portion of the cost for the prescriptions dispensed to their members, providing what is known as a funded benefit.

Both traditional and specialty drugs are included in the data. Specialty medications include injectable and noninjectable drugs that are typically used to treat chronic, complex conditions and may have one or more of the following qualities: frequent dosing adjustments or intensive clinical monitoring; intensive patient training and compliance assistance; limited distribution; and specialized handling or administration. Nonprescription medications (with the exception of diabetic supplies billed under the pharmacy benefit) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings or billed under the medical benefit aren't included.

Trend and other measures are calculated separately for those members with commercial insurance coverage, for Medicaid recipients and for Medicare beneficiaries receiving prescription benefits through Employer Group Waiver Plans (EGWPs), managed Medicare Prescription Drug Plans (PDPs) or Medicare Advantage Prescription Drug Plans (MAPDs). Members used Express Scripts for retail and home delivery pharmacy services; they used Accredo, the Express Scripts specialty pharmacy, for specialty drug prescriptions.

Gross drug trend measures the rate of change in plan costs, which include ingredient costs, taxes, dispensing fees, administrative fees, rebates and member cost share.

Total trend measures the rate of change in plan costs, which include ingredient costs, taxes, dispensing fees and administrative fees. Rebates are included as a component of cost, reflecting more managed trends as noted in this report. Total trend comprises utilization trend and unit cost trend. Utilization trend is defined as the rate of change in total days' supply of medication per member, across prescriptions. Unit cost trend is defined as the rate of change in costs due to inflation, discounts, drug mix, rebates and member cost share. Utilization and cost are determined on a PMPY basis. Metrics are calculated by dividing totals by the total number of member-months, which is determined by adding the number of months of eligibility for all members in the sample.

The Express Scripts Prescription Price Index measures inflation in prescription drug prices by monitoring changes in consumer prices for a fixed market basket of commonly used prescription drugs. Separate market baskets are defined for brand drugs and for generic drugs and are based on the top 80% of utilized drugs.

Please note: Although up to nine decimal places were allowed in making all calculations, in most cases the results were rounded down to one or two decimals for easier reading. Therefore, dollar and percentage calculations may vary slightly.

Citations

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2 Experts in Chronic Myeloid Leukemia. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. Blood. 2013;121(22):4439-4442.

3 Rockoff, J., E. Silverman. Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices. The Wall Street Journal. http://www.wsj.com/articles/pharmaceutical-companies-buy-rivals-drugs-then-jack-up-the-prices-1430096431. April 26, 2015. Accessed Feb. 26, 2016.

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5 Plan sponsors were excluded if they weren't Express Scripts clients in both periods, if they had less than 12 months of claims data in either period, if they had retail-only benefits, if they had 100% or 0% copayment benefits, if they had eligibility shifts exceeding 20% for commercial plans (eligibility shifts exceeding 50% for Medicare and Medicaid plans), or if they were contractually prohibited from inclusion. Individual members might be covered, and thus included, for only a portion of the time periods of interest.

Download the complete 2015 Drug Trend Report
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