

Express Scripts Specialty Benefit Services

SPECIALTY DRUG TREND REPORT

Complex Challenges · New Solutions



A Market and Behavioral Analysis

Published June 2011

Presented by



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The authors would like to thank the many individuals throughout the Express Scripts and CuraScript organizations who contributed time and insight toward the completion of the *2010 Specialty Drug Trend Report*.

Visit Express-Scripts.com/Research for additional evidence-based research regarding the pharmacy benefit.

Dear Colleagues:

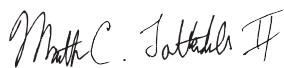
We are pleased to present the *2010 Specialty Drug Trend Report*, which offers fresh insights and unique solutions to help plan sponsors address specialty cost and care challenges. We look forward to working with you to enable better health and lower costs.

The economic climate remains challenging. Thus the need to effectively manage specialty drug benefits is more acute than ever. At the same time, the benefits landscape has grown increasingly complex. Specialty drugs continue to be covered under both the pharmacy and medical benefit, causing patients to experience gaps in care and presenting plan sponsors with unique management challenges. With the implementation of the Patient Protection and Affordable Care Act, there are additional changes on the horizon. One thing remains certain: plan sponsors need proven methods for providing quality care at an affordable cost across the entire pharmacy-medical spectrum.

Some of the most dramatic growth in specialty drug spending over the past several years occurred in the medical benefit, which typically lacks the drug management programs found in the pharmacy benefit. Without actively managing these drugs, plan sponsors waste healthcare dollars. To solve for this problem, we launched Specialty Benefit Services, the industry's most complete specialty benefits organization for managing specialty drugs in both the pharmacy and medical benefit.

In addition to analyzing what causes trend and in which benefit it occurs, we explore who is causing trend and for what reasons. Like last year, the *2010 Specialty Drug Trend Report* explains the behavioral factors that influence trend and contribute to wasteful spending along with market factors. There continues to be waste due to suboptimal pharmacy-related behavior on the part of the patient – the consumer. Regardless of clinicians' best efforts in diagnosis and treatment, what stands between knowledgeable healthcare providers and the attainment of high-quality outcomes is consumer behavior.

Moving forward, plan sponsors will seek programs that effectively manage specialty spend wherever it occurs. Specialty Benefit Services will continue to offer a wide range of solutions that span both the pharmacy and medical benefit and help patients realize healthcare-related behaviors that drive out waste.



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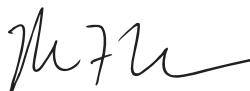
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Introduction

YEAR IN REVIEW

PHARMACY LANDSCAPE OVERVIEW

By nearly every measure, plan sponsors face a specialty pharmacy landscape that is growing increasingly more complex. Specialty drug costs continue to escalate in part because much of the utilization is left largely unmanaged in the medical benefit. New therapies entering the market offer life-saving solutions to patients with complex conditions, but nonadherence and fragmented care across the pharmacy and medical benefit present significant challenges to achieving optimal outcomes for patients. Plan sponsors face considerable uncertainties from the slow economic recovery and the implementation of the Patient Protection and Affordable Care Act (PPACA). Despite this shifting landscape, one thing is clear:

Now more than ever, plan sponsors need proven methods for providing quality care at an affordable cost.



High Cost of Specialty Drugs

The 1990s and first part of the twenty-first century saw rapid increases in pharmacy costs; as recently as 2004¹, plan sponsors faced double-digit trend in overall pharmacy spend. For traditional medications, the days of runaway pharmacy trend seem far behind us. But for specialty medications, many years of unsustainable cost increases appear to lie ahead.

Specialty drugs continue to represent the fastest-growing segment of drug spend. By 2014, specialty drug spend is expected to constitute 22% of worldwide drug spend.² We estimate that in the United States specialty medications will

comprise a greater share – 40% of 2014 drug spend³ (including both medical and pharmacy spending). This higher estimate is not surprising given the generally higher prices for prescription drugs typically paid in the United States.⁴

Increasingly, plan sponsors face a significant challenge from high-cost biologics and other specialty medications. Limited generic competition plus a dearth of statistically valid head-to-head comparisons combine to make branded specialty agents expensive. To take advantage of the situation, many pharmaceutical companies have shifted their research and development dollars from traditional medications to specialty medications. Effectively managing the specialty side of pharmacy benefits is increasingly complicated due to many factors, including:

- The traditional component of the pharmacy benefit is increasingly well managed, making the profitability of blockbuster medications less certain.
- Patent protection on specialty medications remains highly favorable for brands. Most biosimilars will not be AB rated, so automatic substitutions will not occur. Trend programs are needed for effective long-term management.
- The number of indications for many products is increasing.
- Difficult-to-manage, complex diseases often require multiple therapeutic agents.

Specialty Spend in the Medical Benefit

We estimate that 55% of total specialty drug spend occurs in the medical benefit.⁵ Typically, medically billed drugs have lacked the comprehensive drug utilization and management programs found in the pharmacy benefit. Although plan sponsors have implemented a wide range of trend management programs on the pharmacy side, many are simply unaware of what their specialty spend is under medical. A number of factors contribute to fragmented care and mounting waste in this area of healthcare, including inappropriate utilization, the use of the most expensive site of care, and lax reimbursement practices. Without actively managing these specialty drugs and their administration with the latest tools, plan sponsors unnecessarily waste healthcare dollars and patients continue to experience suboptimal outcomes.

By 2014, specialty drug spend is estimated to comprise 40% of U.S. drug spend.³

Healthcare Reform

The passage of the PPACA includes sweeping changes to our healthcare system. Although the final outcome of healthcare reform remains unclear, it is certain that implementation of this legislation will be both complicated and fluid.

Over the next decade, the PPACA calls for nearly \$1.2 trillion to pay for the expansion of existing coverage as well as new coverage for more than 30 to 35 million people. It also includes significant changes to the Medicare Part D program, such as closing the coverage gap (commonly referred to as the “doughnut hole”), changing the taxation of the Retiree Drug Subsidy and allowing copayment waivers on some generic drugs.

Although the legislation also provides an approval pathway for biosimilars, such a pathway is likely to be convoluted. The U.S. Food and Drug Administration (FDA) plans to issue guidance in the near future, but the pathway currently includes a 12-year exclusivity period for brands. In the budget recently sent to Congress, the President again pressed for legislation that would reduce the exclusivity period to seven years, which represents significant savings opportunities, if passed.

Pharmacogenomics and Genetic Testing

Pharmacogenomics reflects remarkable scientific and technological breakthroughs, which hold the promise of identifying optimal medications and doses based on individual genetic profiles. Furthermore, direct costs of available tests appear to be trending down. But, as with most medical technologies, each test must be evaluated carefully – test by test, indication by indication – to determine not only whether it offers a net benefit, but also for which patients and at what cost. Although some genetic tests have passed careful, evidence-based evaluations, many have not.

As always, we look to the best available evidence to make informed recommendations for plan sponsors. Four questions must be answered to determine whether a pharmacogenomic test is clinically sound and cost effective:

- How well does the test perform?
- Do the results change subsequent care?
- Does the change in care lead to better health outcomes?
- What is the impact on overall cost?

Answering these questions is critical given the novelty of many pharmacogenomic tests as well as the complexity involved in giving and interpreting their results. Two especially crucial considerations are whether the results of the test change care in the clinical setting and whether changes in care lead to better health outcomes in clinical practice. Although these two requirements seem intuitive and straightforward, evidence for them presently is sparse (or even negative) for many pharmacogenomic tests.⁶

We recommend only those pharmacogenomic tests that are rooted in evidence, improve clinical decision making and are cost-effective. Additionally, we fully integrate our recommendations into our clinical and trend management programs, including Prior Authorization, drug utilization review and other services.

Consumer Behavior: Critical for Optimal Clinical Care

Great clinical care starts with clinicians – physicians, pharmacists, nurses and other healthcare providers who carefully diagnose health problems and prudently develop treatment plans designed to deliver excellent clinical outcomes. But provider expertise is hardly enough: frequently, what stands between healthcare providers and the attainment of high-quality outcomes is consumer behavior. Although not the only factor, consumer behavior represents a significant actionable rate limiter of excellent patient outcomes – outcomes that consumers, physicians and plan sponsors profess to want and that are becoming increasingly more important as we move to healthcare reform in 2014.

For example, suppose a physician correctly diagnoses an underlying condition and prescribes the most efficacious treatment. Obviously, if the patient fails to take medication as prescribed, optimal health outcomes are not achieved. When a patient uses a delivery channel that is more expensive and less accurate, or a medication that costs more but offers no clinical advantage, optimal care is threatened. Waste ripples through the system.

Put simply, delivering optimal health outcomes demands an advanced, effective and applied understanding of consumer behavior. And the importance of consumer behavior only will increase as the changes envisioned for 2014 and beyond begin to materialize.

Specialty Waste from Suboptimal Behaviors and a Lack of Effective Management

Wasteful specialty drug spending occurs in both the pharmacy and medical benefit as a result of ineffective drug management and suboptimal patient behavior. Facing a future of seemingly endless rising specialty costs and an increasingly fragmented healthcare system, plan sponsors can no longer afford to ignore the sources of waste or put off effective measures designed to control it.

In the medical benefit, waste is generated not only from member behavior but also from a lack of effective management of the drugs and their administration. Sources of waste may include inappropriate drug utilization, use of the most costly sites of care and ineffective claims and payment management systems.

Consumer behavior stands between the doctor and optimal outcomes.

Regardless of healthcare providers' best efforts in diagnosis and treatment, optimal outcomes are possible only through consumer behavior. The key is structuring interventions and solutions that encourage optimal behavior on the part of the healthcare consumer.



Three Ways to Eliminate Specialty Medical Drug Waste

Ensure Appropriate Drug Utilization

Maximize Use of Optimal Sites of Care

Optimize Reimbursement Systems

Specialty waste in the pharmacy benefit is created not only from poor utilization management practices, but also by suboptimal consumer behavior. By any rational measure, members should engage in three simple pharmacy-related behaviors: take medications as prescribed; use the lowest-cost, clinically effective medication; and use the safest, most cost-effective delivery channel. Yet, many patients fail to engage in these behaviors, and in doing so, swamp the system with waste – avoidable costs that provide no additional health benefits.

Three Ways to Eliminate Specialty Pharmacy-Related Drug Waste

Maximize Adherence

Optimize Drug Mix

Optimize Channel

NEW INSIGHTS, INNOVATIVE SOLUTIONS

Specialty Benefit Services: Offering Next-Generation Solutions Across Pharmacy and Medical

In 2010, we launched Specialty Benefit Services, healthcare's most comprehensive specialty benefits organization to manage specialty drugs in both the pharmacy and medical benefit. By managing drugs in both pharmacy and medical, we offer the most complete approach to enhancing patient care and reducing wasteful specialty spend.

Historically, pharmacy benefit managers (PBMs) offered services in only two areas: specialty pharmacy distribution and benefit management. However, Specialty Benefit Services expands beyond this traditional range of services by adding a vital third component: management of specialty medications billed under the medical benefit – through Care Continuum™, a 16-year old subsidiary of Express Scripts. Only by providing services in all three areas – specialty pharmacy benefit management, specialty pharmacy and distribution, and medical benefit management – can the use and cost of specialty drugs be managed effectively.

Specialty Benefit Services – The only specialty benefits organization in our field to integrate three core services:

- Specialty Pharmacy Benefit Management *from Express Scripts*
- Specialty Pharmacy and Distribution *from CuraScript*
- Medical Benefit Management *from Care Continuum*

We deliver flexible solutions that rein in the cost of specialty drugs, close gaps in care and make healthcare more affordable for plan sponsors and members. Because our solutions address the entire specialty landscape, we help control the many sources of specialty waste, including: 1) a lack of effective management of medically billed specialty drugs and 2) suboptimal pharmacy behaviors.

Unique in the industry, **Specialty Benefit Services** offers plan sponsors a **savings guarantee** on specialty medical drug spend and enhanced, comprehensive member care across the **entire pharmacy – medical spectrum.**

1) Effective Medical Benefit Management

Through Medical Benefit Management from Care Continuum, we provide the industry's most comprehensive range of utilization, trend and claims management tools for controlling the cost of medically billed specialty drugs including oncology medications. With our extensive experience and URAC accreditation, Care Continuum is supported by a staff of clinicians, medical professionals and a board-certified medical director.

To achieve savings on medically billed specialty drugs, we apply three management principles:

- **Utilization Management** – ensuring the safe and appropriate use of specialty medications
- **Site of Care Management** – redirecting members and medications to the lowest-cost and most clinically appropriate site of care
- **Reimbursement Management** – verifying that claims are paid accurately and at the contracted rate, and helping clients achieve a pathway to rebates

Medical Benefit Management provides value to members, physicians and plan sponsors in the following ways: Member utilization is managed to facilitate safe and appropriate care. We reduce administrative demands on physicians' offices, speed

their reimbursement and provide access to user-friendly online tools. Plan sponsors receive guaranteed savings on their specialty medical drug spend, proving our medical benefit management expertise and our alignment with the goals of plan sponsors.

2) Addressing the Specialty Pharmacy Dilemma

As noted earlier, consumer behavior and decision making stand between healthcare providers and great health outcomes, particularly within the pharmacy benefit. The result is poor health outcomes, leading in turn to hundreds of billions of dollars of unnecessary costs each year in the United States.

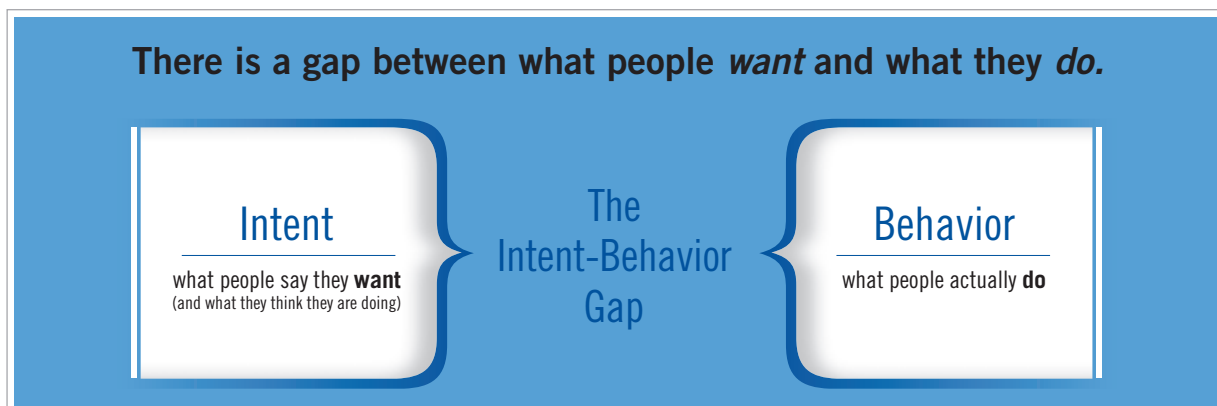
Historically, plan sponsors have had only two approaches to deal with this situation. Mandatory programs (e.g., an exclusive specialty pharmacy network) are effective in reducing waste, but limit member choice. On the other hand, certain passive programs (e.g., education) are easy to implement and deliver high member acceptance, but are only modestly effective.

Until now, plan sponsors who are unable to implement the most aggressive, mandatory programs have had to rely on the far less-effective passive programs. This has resulted in little change in consumer behavior, leading to suboptimal health outcomes and ballooning financial waste.

Identifying the Gap Between Intent and Behavior

At first blush, this problem seems intractable: patients are engaged in behaviors that lead to poor health outcomes and increased costs, but education and incentives have only modest effects. This would seem to suggest that patients and plan sponsors don't really see eye to eye on what's best. For example, plans want to save money by moving members to a specialty pharmacy, but patients tend to use retail pharmacies instead. This situation leaves plan sponsors to conclude they can either focus on better outcomes by requiring members to use a specialty pharmacy or they can focus on preserving individual choice and let people stay in retail.

Our ongoing research and program results show there is a third way. We are now convinced that – perhaps surprisingly – most patients and plan sponsors are in agreement about what they want. The issue isn't that there is a gap between what patients and plan sponsors want. Instead, the gap is between what patients *want* (intent) and what they *do* (behavior).



This insight is crucial. If there is a disconnect between intent and behavior, increased education and adjustments to financial incentives will have limited effect, a disappointing result consistent with the experience of many plan sponsors. Even more importantly, such a gap illustrates that many patients want exactly what plan sponsors want. In that case, the issue is not about convincing patients to align their behaviors with the interests of the plan sponsors, but rather to bring to life their own underlying desires. Considering the high cost of specialty drugs, plan sponsors can no longer afford a wide gap filled with suboptimal behavior.

Leveraging an Advanced Understanding of Behavior to Improve Care for Specialty Pharmacy Patients

Through our experience in working with thousands of specialty patients at our specialty pharmacy, CuraScript, we have developed innovative solutions that address the three pharmacy-related behaviors in which patients should engage: take medications as prescribed, use the lowest-cost, clinically-effective medication, and use the safest, most cost-effective delivery channel. Our programs close the gap between patients' intentions and their actions.

Keeping Specialty Patients Adherent

One of the most difficult behaviors to change involves how people take their medications. We estimated that failure to take medications as prescribed is costing the U.S. more than \$300 billion annually.

It is clear that adherence is a multifaceted problem. Possible causes include forgetfulness, procrastination (especially around refills and renewals), financial costs, concern that the medication is causing side effects, belief that the medication isn't working, and others.

For specialty patients, nonadherence may mean costly medication waste, adverse health events and medical expenses resulting from hospitalization or emergency room visits. In a recent study, nonadherent multiple sclerosis (MS) patients were found to have 35% more MS-related hospitalizations and 22% higher MS-associated medical expenses than their adherent counterparts.⁷

At CuraScript, nurses and pharmacists begin managing adherence even before a patient receives their first medication. As part of our Accreditation Commission for Health Care (ACHC) certification, each new patient at CuraScript speaks with a nurse and receives a clinical assessment. Based on this information, we build individual profiles that help us develop a deeper understanding of each patient. As a result, we tailor our clinical counseling to the needs of the individual and encourage behaviors that support adherence.

As shown in Exhibit 1, the average specialty patient who receives medications at retail achieves an adherence rate of 65%, while specialty patients who use CuraScript achieve an average adherence rate of 74% – 9% higher, due to our personalized care model and in-depth clinical programs.⁸ CuraScript patients also report increased satisfaction and education compared to those in retail, both critical factors to maintaining adherence.⁹

In addition, CuraScript offers Specialty Care Management clinical programs, designed to help patients remain adherent to their prescribed therapy and achieve positive health outcomes. Called CareLogic[®], these programs reinforce positive patient behavior by providing important access to specialized nurses and pharmacists who perform routine health assessments and deliver personalized counseling.

The programs act to remove barriers to healthcare professionals and eliminate suboptimal behavior, while proactively educating patients about their condition and the medications used to treat them. As a result, CareLogic programs help close the intent-behavior gap and build upon the improved adherence CuraScript patients experience. Patients enrolled in CareLogic programs achieve adherence rates, on average, 6% higher than patients not enrolled in the programs.¹⁰

In 2010 CuraScript expanded the range of complex conditions for which we have a CareLogic program. Program conditions include, but are not limited to bleeding disorders, cancer, hepatitis, multiple sclerosis, pulmonary arterial hypertension, rheumatoid arthritis, and psoriasis. We continue to assess the value of additional clinical programs for our plan sponsors and patients.

Specialty Step Management: Promoting Clinically Appropriate, Cost-Effective Therapies

Factor such as inertia and inattention can lead physicians and patients to choose high-cost medications that deliver no added benefit over lower-cost alternatives. To reduce waste and promote the lowest cost, clinically effective medications, we offer Specialty Step Management. Using the same tried-and-true concepts of step therapy and prior authorization that have been a great success in managing traditional medications, this program is tailored to fit the unique characteristics of specialty drugs and patients.

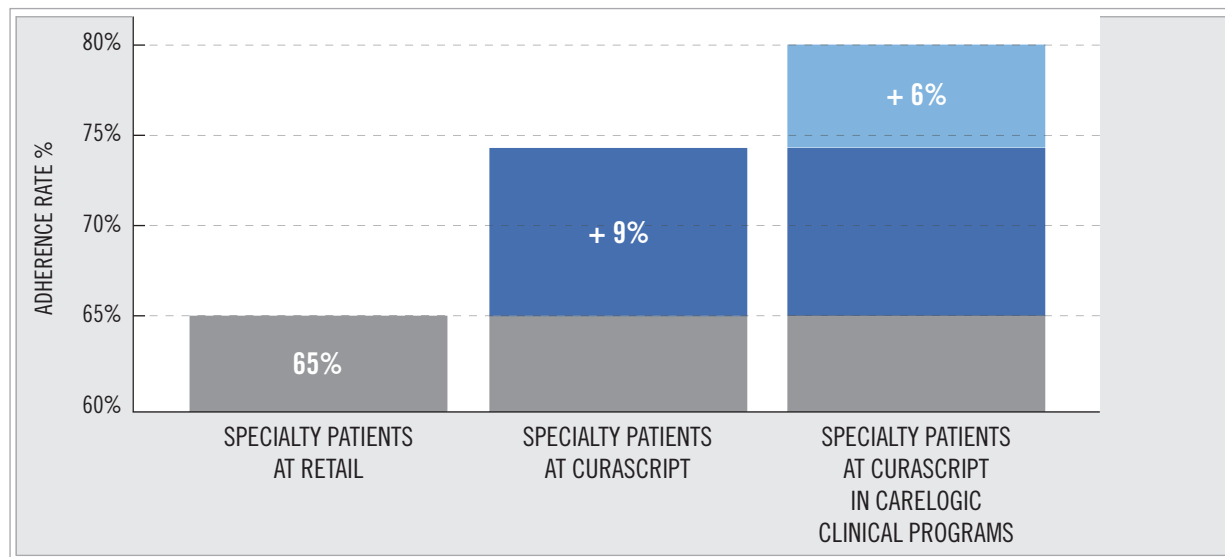
Specialty Step Management encourages formulary compliance, maximizes rebate opportunities on preferred products and is applicable regardless of the dispensing pharmacy. It may be several years before biosimilars begin to have an impact on the cost of specialty medications. However, Specialty Step Management is paving the way by training the market to choose preferred medications and moving market share, in turn driving down costs.

We believe that physicians and patients want to select lower-cost, clinically effective alternatives, and Specialty Step Management helps them act on it. This program addresses several of the most costly specialty therapy classes.

Specialty Step Management Therapy Classes

INFLAMMATORY CONDITIONS
MULTIPLE SCLEROSIS
GROWTH HORMONES
PULMONARY ARTERIAL HYPERTENSION
INFERTILITY
ERYTHROID STIMULANTS
CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME
ALPHA-1 PROTEINASE INHIBITORS
PROSTATE CANCER GNRH ANALOGS

Exhibit 1 | Improved Adherence Through CuraScript



Select Specialty, Powered by Choice: Driving Patients to the Most Cost-Effective Channel

A firm understanding of the gap between intent and behavior is critical for the development of practical programs that deliver greater effectiveness with minimal disruption to members. Using this knowledge, we've developed Select Specialty – within our Select Solutions family of programs – to drive greater use of CuraScript Specialty Pharmacy for specialty medications.¹¹

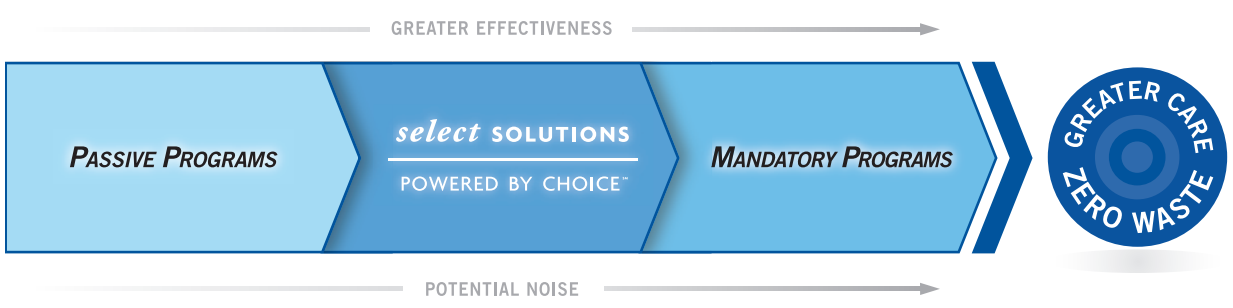
Rather than forcing all members into the optimal channel or hoping that more education will convince them to use a specialty pharmacy, Select Specialty requires members on specialty medications to choose whether to receive those medications at retail or from CuraScript. The program is voluntary, encouraging

patients to make active, informed healthcare decisions and take advantage of our comprehensive clinical care and services. Select Specialty maintains freedom of choice, while increasing the number of patients who choose CuraScript and receive our personalized care. On average, plan sponsors who implement Select Specialty see a 28% increase in the number of patients who use CuraScript.¹²

As a result, this program drives better program performance while preserving individual choice – which translates into low member disruption.

Select Specialty is effective in closing the gap between what members already want but aren't doing. It is easy to implement and, by preserving individual choice, leads to minimal noise.

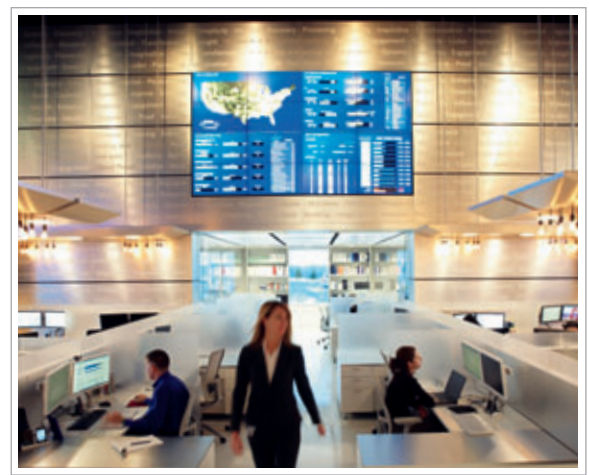
Exhibit 2 | Select Solutions Offer Greater Effectiveness with Minimal Noise



Delivering Practical Solutions: The Express Scripts Research & New Solutions Lab

Express Scripts opened the Research & New Solutions Lab in December 2010. One of the most advanced research and development facilities in healthcare, it is an embodiment of our belief that greater insights into human behavior lead to greater value for plan sponsors. Through the technology and talent at work in the Lab, we are turning data into insights and insights into proven solutions.

In the Lab, we study in real time how patients interact with their prescription-drug therapy: what medications they take, whether they comply with their therapy, what health outcomes result and more. These insights enable us to rapidly translate our research findings into practical applications. Using proprietary analytics and patent-pending technologies, we build products that deliver proven solutions to our plan sponsors' most pressing needs.



The Express Scripts Research & New Solutions Lab

SPECIALTY BENEFIT SERVICES

Our comprehensive solution enhances care and manages out the waste across Pharmacy and Medical.



Medical

With over half of all specialty spend billed through the medical benefit, there's no time to lose in implementing more effective controls.



Pharmacy

With unsustainable increases in specialty drug spend, there's no time to lose in addressing the underlying cause of waste-producing pharmacy behaviors.

Ineffective management contributes to specialty **medical drug-related waste:**

Utilization

Waste from inappropriate or off-label use of high-cost specialty drugs.

Site of Care

Use of the highest cost sites of care, with no added benefit or improvement in clinical care.

Reimbursement

Ineffective claims management and reimbursement practices that lead to overpayment and increased administrative demands for providers and plan sponsors.

Reduce waste and close gaps in care by more effectively managing medically billed specialty drugs. Our medical benefit management services are backed by proven programs and a savings guarantee.

Suboptimal behavior contributes to specialty **pharmacy-related waste:**

Adherence

Waste from patients who do not take medications as prescribed, resulting in unused medication, unnecessary hospital admissions, avoidable emergency room visits, additional physician visits, additional therapy and other healthcare costs.

Drug Mix

Waste associated with the use of higher-cost medications that generate no additional health benefit.

Channel

Waste from patients that use less effective and less accurate specialty drug dispensing channels, such as retail.

Close the gap between what people *want* and what they *do*, with proven solutions from Specialty Benefit Services.

Trend Overview

TREND IN REVIEW

Looking back at the last five years, two main patterns in drug trend have emerged. First, annual increases in traditional drug-cost trends have slowed, leveling off at less than 2%. Second, specialty drug-cost trends have increased tremendously, with year-over-year spending increases in the solid double digits. The estimated 55% of specialty medication costs that are billed under medical benefits is not included in our trend calculations. The methods we used to calculate trend are explained in Appendix 1.

Last year, overall drug-spend growth (including both traditional medications and specialty medications) was cut nearly in half (to 3.6% in 2010 from 6.4% in 2009). Trend for traditional drugs decreased to 1.4%, from 4.8%, in 2009, while specialty increased by 19.6%, approximately the same rate as in 2009.

2010 Drug Trends

The *2010 Specialty Drug Trend Report* is produced based on research results compiled in the *Express Scripts 2010 Drug Trend Report*. Since its inception, the *Express Scripts Drug Trend Report* has led the industry in providing the most

in-depth analysis of prescription spending patterns in the United States. In last year's report, in addition to explaining what drove trend, we examined who affected trend. In this edition we continue to explore the influence that patient behavior has on specialty drug spend.

Behavioral Factors Versus Market Factors

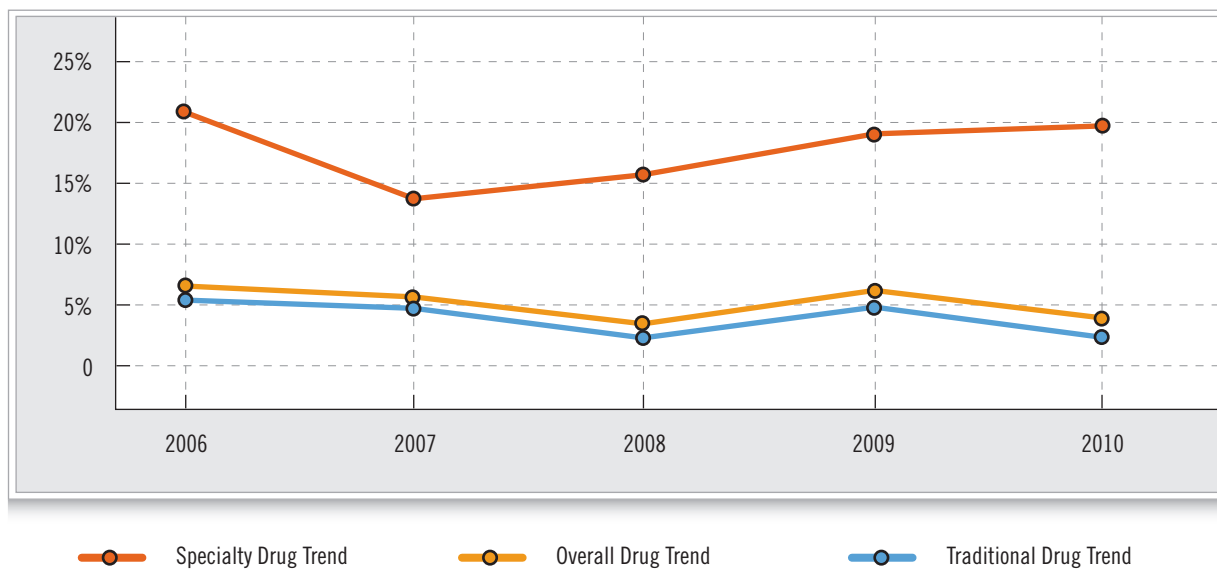
As noted in the previous section, we have identified three key areas of waste based on specific behaviors:

- **Nonadherence** – patients not taking medications as prescribed
- **Drug Mix** – patients taking more expensive medications when less-expensive options offer the same benefit
- **Channel** – patients using less-clinically effective, more-costly channels for filling prescriptions

Accordingly, we have divided components of drug trend into two groups: market factors and behavioral factors.

Market factors reflect both supply-side forces within the prescription-drug market and changes in the prevalence of disease within a population. Market factors include:

Exhibit 3 | Drug Trend – Express Scripts, 2006 to 2010



- **Prevalence** – changes in the fraction of members taking medications; the many factors influencing prevalence include lifestyle choices, physician prescribing behavior, changes in what is deemed to be appropriate care, access to healthcare, social factors and genetic predisposition, among other things
- **Cost per Unit (cost/unit)** – ingredient cost plus taxes plus administrative fees less rebates for each dispensed unit (e.g., per pill, gram, mL, etc.)
- **Units per Prescription (units/Rx)** – the number of units prescribed per fill (e.g., number of pills per prescription fill); this factor is largely driven by prescriber patterns
- **Patent Expirations** – the impact on spending from branded drug patent expirations in 2010
- **New Drugs** – the impact on spending from new branded drug entrants in 2010

Note that in our trend estimates, plan sponsor and member costs are combined. This more comprehensive approach focuses on solutions that drive out costs rather than those that simply shift financial responsibility between plan sponsor and member.

Behavioral factors focus on whether patients are taking medications, as well as on which medications they are taking. The behavioral factors that we track are:

- **Intensity** – changes in adherence to medication
- **Mix** – changes to lower-cost or higher-cost products within each drug class

A Closer Look at 2010 Trends

Exhibit 4 shows the trend components for traditional, specialty and overall medications. For both traditional and specialty drugs, upward pressure on unit cost was the most important

Exhibit 4 | PMPY Spending Trend, 2009 to 2010

		TRADITIONAL	SPECIALTY	OVERALL
TREND		1.4%	19.6%	3.6%
Market	OVERALL	1.2%	16.4%	3.0%
	Prevalence	-0.7%	7.0%	0.3%
	Cost/Unit	3.5%	9.2%	4.2%
	Units/Rx	0.2%	-0.8%	0.0%
	Patent Expirations	-1.9%	-0.1%	-1.7%
	New Drugs	0.2%	1.1%	0.3%
Behavioral	OVERALL	0.2%	3.2%	0.6%
	Intensity	1.9%	0.0%	1.7%
	Mix	-1.7%	3.3%	-1.1%

Market factors increased total spend, with upward pressure on unit cost – the key driver of trend.

Exhibit 5 | Components and Drivers of Trend for the Top 10 Specialty Therapy Classes, PBM-Adjudicated Claims Only, Ranked by 2010 PMPY Spend

Rank	Therapy Class	PMPY Spend	% of Total Specialty Spend	PMPY \$ Change from 2009	TREND		
					Market	Behavioral	Total
1	INFLAMMATORY CONDITIONS	\$37.16	28.6%	\$7.07	18.5%	5.0%	23.5%
2	MULTIPLE SCLEROSIS	\$29.80	22.9%	\$6.04	29.4%	-3.9%	25.4%
3	CANCER	\$21.81	16.8%	\$4.17	10.2%	13.4%	23.7%
4	ANTICOAGULANT	\$6.99	5.4%	\$1.00	11.2%	5.4%	16.6%
5	GROWTH DEFICIENCY	\$5.98	4.6%	\$0.90	6.5%	11.3%	17.8%
6	PULMONARY HYPERTENSION	\$4.40	3.4%	\$1.17	18.8%	17.5%	36.3%
7	RESPIRATORY CONDITIONS	\$4.04	3.1%	\$0.50	10.7%	3.4%	14.1%
8	BLOOD CELL DEFICIENCY	\$3.89	3.0%	\$0.02	-1.5%	2.0%	0.5%
9	INFERTILITY	\$3.13	2.4%	\$0.04	4.6%	-3.2%	1.3%
10	HEPATITIS C	\$2.41	1.9%	\$0.01	-5.0%	5.3%	0.3%
	Top 10	\$119.62	92.0%	\$20.92	16.5%	4.7%	21.2%
	Others	\$10.36	8.0%	\$0.39	14.9%	-11.0%	3.9%
	Total	\$129.98	100.0%	\$21.31	16.4%	3.2%	19.6%

Total specialty drug spend grew 19.6%, driven primarily by an increase in cost per unit.

driver. Patent expirations helped mitigate these increases to some degree, at least for traditional medications.

Drug-price inflation for branded products was the single most important trend driver in 2010. Pricing decisions by pharmaceutical manufacturers depend on many factors, including market inertia and lack of competition. A report from the U.S. Government Accountability Office on pricing changes for branded products from 2000 to 2008 concluded that “lack of therapeutically equivalent drugs – generics and other brand-name drugs used to treat the same condition – and limited competition may contribute to extraordinary price increases.”

Our analysis of medications dispensed for the *2010 Drug Trend Report* member sample showed that traditional generic medications *declined* in price by 10.2% while traditional brand medications *increased* in cost by 9.7% – an absolute difference of nearly 20%. In classes with limited competition, plan sponsors have few options to manage drug mix; this allows manufacturers more freedom to increase pricing. Significant growth in unit cost is particularly dramatic for the specialty therapy classes, which have the most limited generic availability and fewer clinical competitors. Accordingly, growth in unit costs was 9.2% among specialty medications compared to 3.5% within the traditional therapy classes.

Exhibit 6

Distribution of Pharmacy and Medical Specialty Spending, Ranked by Relative Change in Medical Spend
Thomson Reuters MarketScan Commercial Database, 2005-2008

Therapy Class	PHARMACY			MEDICAL			TOTAL	
	Total Spend PMPY		Relative % Change	Total Spend PMPY		Relative % Change	% Spend, 2008	
	2005	2008		2005	2008		Pharmacy	Medical
1 MULTIPLE SCLEROSIS	\$12.70	\$18.86	48.5%	\$0.52	\$2.22	326.9%	89.5%	10.5%
2 PULMONARY HYPERTENSION	\$0.86	\$1.85	115.1%	\$0.24	\$0.73	204.2%	71.8%	28.2%
3 INFERTILITY	\$2.20	\$3.01	36.8%	\$0.02	\$0.06	200.0%	98.1%	1.9%
4 BLOOD CELL DEFICIENCY	\$4.37	\$3.18	-27.2%	\$9.08	\$17.20	89.4%	15.6%	84.4%
5 RESPIRATORY CONDITIONS	\$2.39	\$3.03	26.8%	\$1.03	\$1.70	65.0%	64.0%	36.0%
6 INFLAMMATORY CONDITIONS	\$16.30	\$26.08	60.0%	\$8.47	\$13.27	56.7%	66.3%	33.7%
7 ANTICOAGULANT	\$2.46	\$4.13	67.9%	\$0.16	\$0.24	50.0%	94.7%	5.3%
8 CANCER	\$6.48	\$11.49	77.3%	\$35.27	\$48.44	37.3%	19.2%	80.8%
9 GROWTH DEFICIENCY	\$3.99	\$5.93	48.6%	\$0.55	\$0.28	-49.1%	95.5%	4.5%
10 HEPATITIS C	\$3.97	\$2.81	-29.2%	\$0.08	\$0.02	-75.0%	99.1%	0.9%
Others	\$5.63	\$7.18	27.5%	\$8.86	\$21.16	138.8%	25.4%	74.6%
Total	\$61.35	\$87.55	42.7%	\$64.28	\$105.32	63.8%	45.4%	54.6%

An estimated 55% of specialty medication spend is being billed under the medical benefit.

Specialty Drugs

Specialty drug spending in the pharmacy benefit increased by 19.6%, resulting in a 2010 PMPY cost of \$129.98 (See Exhibit 5). The top three therapy classes for PBM-adjudicated specialty claims (inflammatory conditions, MS and cancer) make up 68.3% of total pharmacy-billed specialty drug spending (compared to

66.7% in 2009), with each of the top three classes growing at rates in excess of 23%.

Not surprisingly, given the limited availability of lower-cost generic alternatives, trend for specialty drugs is mainly market driven rather than behavioral. Market forces contributed 16.4% in higher costs, with approximately 9.2% of cost growth due

to increases in cost/unit and another 7.0% due to increased prevalence. Note that increased prevalence does not necessarily reflect an increase in the prevalence of a given condition per se, but rather an increased prevalence of the use of specialty medications to treat these diseases. Behavioral factors, almost all from mix (3.3%), added only 3.2% to specialty trend increases.

Our researchers estimate that approximately 55% of total spending for specialty medication occurs on the medical side of the benefit through drugs administered in physician offices and other outpatient facilities. Therefore, based on aggregate pharmacy and medical benefit expenditures, total specialty spending may have approached \$289 PMPY for some plan sponsors in 2010. For the first time, specialty costs (in both the

pharmacy and medical benefit) comprised 25% of total drug spend and exceeded the PMPY spend in the top four traditional therapy classes.

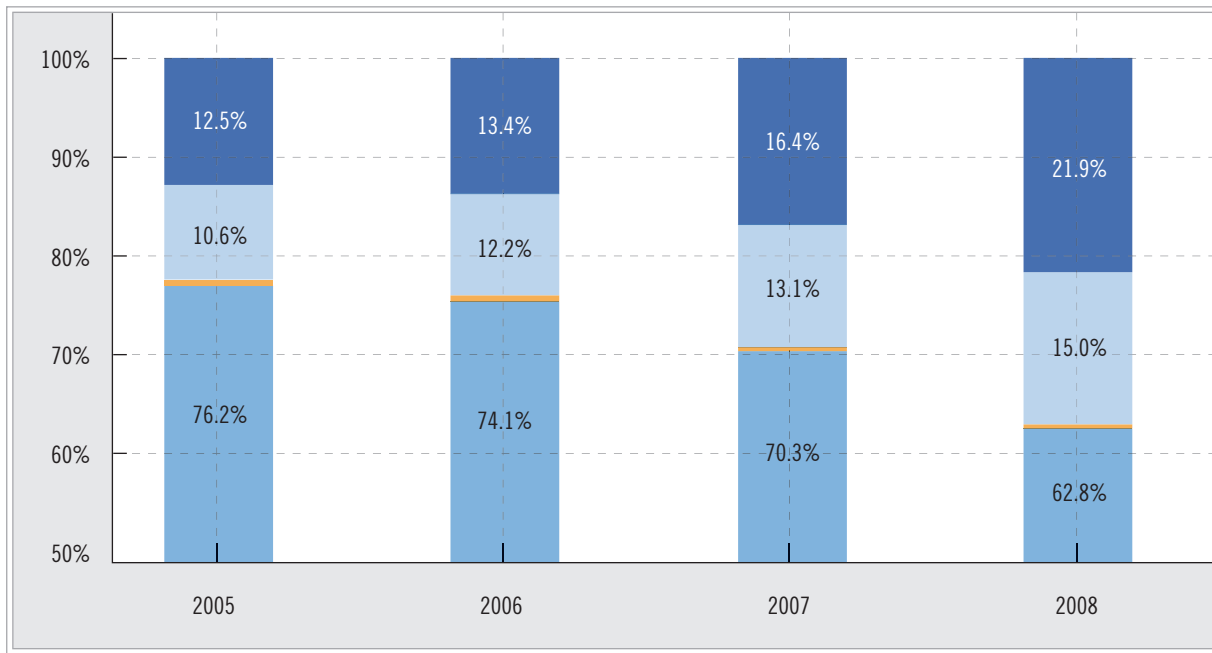
Specialty Drug Spending in the Medical Benefit

Based on our analysis of claims data from the Thomson Reuters MarketScan® Commercial Database, some of the most dramatic growth in specialty drug spending over the past several years occurred in the medical benefit (see Exhibit 6). Although it is impossible to know from these data whether the changes in spending are due to the changing prevalence of users, a change in the amount being utilized, a change in the drug mix or a change in the drug costs, there were significant differences from 2005 to 2008 in several key therapy classes. From 2005

Exhibit 7

Division of Medically Billed Specialty Drug Spend By Site of Care
Thomson Reuters MarketScan Commercial Database, 2005-2008

MEDICALLY BILLED SPECIALTY DRUG SPEND BY SITE OF CARE BETWEEN 2005 AND 2008



■ % Outpatient Care Facility ■ % Other Medical Care Facility ■ % ER/Urgent Care and Inpatient Care Facility (Combined) ■ % Doctor's Office

Specialty medical drug spend is trending to more expensive settings.

to 2008, several key therapy classes saw increases of 50% or more in medical drug spend. Inflammatory conditions rose 56.7%, while pulmonary hypertension climbed 204.2% and multiple sclerosis soared 326.9%.

For some therapy classes, the majority of specialty spend is billed through the medical benefit. In 2008, more than 80% of all cancer drug costs were billed in the medical benefit, with a PMPY cost of \$48.44, compared with a PMPY of \$11.49 in the pharmacy benefit.

The drivers of medical drug trend include the same components that affect pharmacy-billed drugs, such as drug cost and prevalence, in addition to many other complex factors. These include how well or how poorly the utilization of the drug is managed, the cost associated with different places of service or sites of care, and the reimbursement practices of health plans and providers. For instance, the cost of administering

a drug in an outpatient hospital setting can differ greatly from the cost of administering the same drug in a physician's office. Consequently, the simple shift of patients and drugs to a certain site of care can significantly impact the amount of spend. As shown in Exhibit 7, the largest shift in sites of care between 2005 and 2008 occurred out of physicians' offices and into outpatient hospital settings.

As demonstrated in Exhibit 8, the MarketScan data show a major increase in the percentage of drugs administered in outpatient hospitals from 2005 to 2008. Although trend differences emerge by region, all geographic areas show positive growth in the amount of drug spend occurring in this setting – typically the most expensive site of care. The North Central region of the U.S. saw the largest shift to an outpatient hospital setting over the three-year period.

Exhibit 8 | Percentage Increase of Medical Drug Spend in the Outpatient Hospital Setting by Region
Thomson Reuters MarketScan Commercial Database, 2005-2008

U.S. Region	Year	% Outpatient (as Percentage of Specialty Spend Billed Through Medical Benefit)	% Increase 2005-2008
NORTH CENTRAL	2005	9.9%	
	2008	25.0%	15.1%
NORTHEAST	2005	26.2%	
	2008	36.3%	10.1%
SOUTHERN	2005	8.8%	
	2008	16.9%	8.1%
WESTERN	2005	18.0%	
	2008	21.9%	3.9%
Total	2005	12.5%	
	2008	21.8%	9.3%

The percentage of drugs administered in outpatient hospitals, typically the most expensive site of care, continues to rise across the country.



Therapy Class Review:
Specialty Medications

SPECIALTY MEDICATIONS

Specialty medications are used to treat patients with chronic, serious health conditions. Complex and costly, specialty drugs usually need special storage and handling. The therapy may require frequent dosing adjustments and intensive clinical monitoring.

In 2010, spending on specialty medications grew 19.6%, with drugs used to treat inflammatory conditions, multiple sclerosis and cancer representing over 68% of the total. Specialty trend

growth was mainly due to increased cost per unit, followed by greater prevalence of use. On average, only 1% of plan sponsors' members utilized specialty drugs, yet this low rate is increasingly offset by the very high cost of treatment – on average, \$2,080 per prescription. It is also important to note that more than half of specialty medications are covered by the medical rather than the pharmacy benefit; this utilization is not reflected in our analysis.

Exhibit 9 | 2010 Key Metrics for Top 10 Specialty Therapy Classes, PBM-Adjudicated Claims Only

Rank	Therapy Class	PMPY Spend	% of Total Specialty Spend	Prevalence of Use	Cost per Adjusted Rx	Trend
1	INFLAMMATORY CONDITIONS	\$37.16	28.6%	0.22%	\$1,896.80	23.5%
2	MULTIPLE SCLEROSIS	\$29.80	22.9%	0.11%	\$2,718.78	25.4%
3	CANCER	\$21.81	16.8%	0.17%	\$2,718.29	23.7%
4	ANTICOAGULANT	\$6.99	5.4%	0.31%	\$1,086.36	16.6%
5	GROWTH DEFICIENCY	\$5.98	4.6%	0.02%	\$2,823.42	17.8%
6	PULMONARY HYPERTENSION	\$4.40	3.4%	0.01%	\$3,590.94	36.3%
7	RESPIRATORY CONDITIONS	\$4.04	3.1%	0.02%	\$2,740.33	14.1%
8	BLOOD CELL DEFICIENCY	\$3.89	3.0%	0.04%	\$2,030.22	0.5%
9	INFERTILITY	\$3.13	2.4%	0.07%	\$771.89	1.3%
10	HEPATITIS C	\$2.41	1.9%	0.02%	\$1,389.04	0.3%
	Others	\$10.37	8.0%	0.10%	\$2,063.28	3.9%
	Total	\$129.98	100.0%	1.06%	\$2,077.58	19.6%

The top three specialty classes represent 68% of total specialty spend.



Increased Utilization and Inflation Drove Trend Up

Year in Review

- Trend for the inflammatory conditions class continues to be driven by increases in utilization, reflecting both the use of these agents for broader indications and use earlier in a patient's disease course.
- In September 2010, the new American College of Rheumatology and European League Against Rheumatism joint Rheumatoid Arthritis (RA) recommendations for the management of RA with synthetic and biological disease-modifying antirheumatic drugs¹ were published. The guidelines present a new approach emphasizing the identification of patients who may benefit from early institution of disease-modifying antirheumatic drug (DMARD) therapy after a relatively short duration of symptoms. Starting patients on therapy sooner helps explain the increased prevalence and the effect it has on spend.
- Increased use of newer drugs – Stelara[®] (ustekinumab), Simponi[®] (golimumab) and Cimzia[®] (certolizumab) – significantly affected trend. Stelara is a novel, subcutaneous (SQ) biologic drug for psoriasis that requires administration by a healthcare professional. Simponi and Cimzia are long-acting subcutaneous tumor necrosis factor (TNF) inhibitors for a variety of inflammatory conditions.
- Actemra[®] (tocilizumab), a novel biologic medication that inhibits interleukin-6, was approved in January 2010 for patients with RA who do not respond to TNF inhibitors. It is administered as a monthly intravenous (IV) infusion. Actemra competes with other infused therapies such as Orencia[®] (abatacept) and Rituxan[®] (rituximab) that typically are billed under the medical benefit.
- In September 2010, Krystexxa[™] (pegloticase) was approved for the second-line treatment of chronic, symptomatic gout. Krystexxa is administered as a two-hour IV infusion every two weeks.

A Closer Look

- The typical pharmacy costs to treat inflammatory conditions exceed \$14,453 per treated member per year, an increase of more than \$500 from 2009. The increased use of very expensive medications such as Stelara appears to be driving spend higher.
- Instituting programs that ensure therapeutic appropriateness as well as preferring products according to published guidelines continue to be critical in managing trend in this class. By taking a holistic approach to manage these products at a therapy class level, this

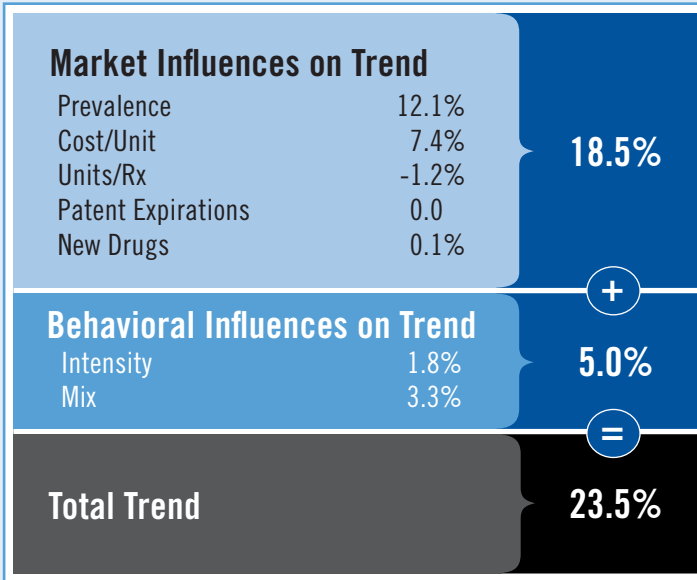
MEDICAL

Our medical benefit management services channel patients and the administration of medication to the lowest-cost and most clinically appropriate site of care.

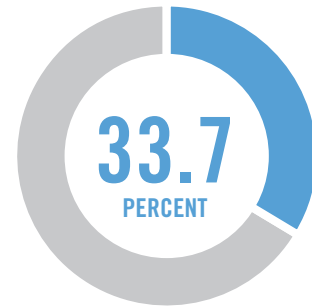
PHARMACY

Rheumatoid arthritis patients who use a specialty pharmacy have increased adherence rates and lower medical costs compared to those who receive their medications at retail.²

Our programs make it easy for the patient to select the most cost-effective channel and receive beneficial clinical support offered at CuraScript.



SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$37.16

#Rx PMPY
0.02

Prevalence
0.22%

Average Cost/Rx
\$1,896.80

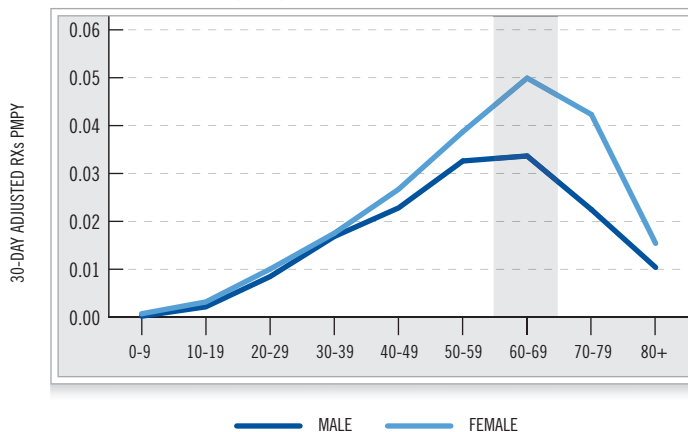
#Rx/User/Yr
7.62

process maintains member and physician satisfaction while continuing to address additional pipeline treatment options.

What's Ahead

- Benlysta® (belimumab), the first new drug to treat lupus in over 50 years, was approved in March 2011. A novel, biologic drug that inhibits B-lymphocyte stimulators, Benlysta is given as a monthly infusion for patients with systemic lupus erythematosus (SLE).
- Arcalyst® (rilonacept) and Ilaris® (canakinumab) may receive expanded indications to treat gout in the near future. Both currently are approved to treat cryopyrin-associated periodic syndromes (CAPS), rare inherited autoinflammatory conditions.
- Tofacitinib, an oral biologic with an initial indication in RA, and apremilast, which likely will gain approval for psoriasis, will enter the market within the next two or three years.

PMPY Rx Use by Age and Gender



NEW DRUGS IN MARKET

Drug	Actemra®
Approval Date	January 2010
Indication	Rheumatoid arthritis
Drug	Krystexxa™
Approval Date	September 2010
Indication	Gout



MEDICAL

Through Medical Benefit Management, we match billed services with Prior Authorizations and manage claims at the NDC level, allowing us to verify claims are paid accurately and enabling more timely reimbursement to provider offices.

PHARMACY

Newly diagnosed MS patients average 2.3 times as many physician visits and 7.5 times the outpatient pharmacy costs of their healthy counterparts.⁴

To reduce waste and promote the lowest-cost, clinically effective medications, we offer a wide range of clinical and trend programs, including Specialty Step Management.

Inflation Continued to Drive Double-Digit Trend

Year in Review

- Unit-cost growth continues at double-digit rates, fueling much of the upward overall trend in the multiple sclerosis (MS) class. For example, cost-per-unit spending on the market leader, Copaxone® (glatiramer), increased 19% in 2010.
- In 2010, utilization of MS medications was higher than in 2009. Increased use of MS medications earlier in a patient's disease course and use of new oral drugs for MS may have contributed to the increase. These factors also tend to decrease intensity, however, as patients exhibiting fewer symptoms from MS tend to be less adherent.
- In January 2010, the FDA approved Ampyra® (dalfampridine) to improve walking in the 65% to 85% of MS patients who experience walking difficulties. An oral drug that can be used alone or in combination with other MS medications, Ampyra is approved to treat symptoms of MS. It is not considered to be disease modifying.
- Gilenya™ (fingolimod), the first oral, disease-modifying medication for MS, was approved in September 2010. Gilenya is known as a sphingosine 1-phosphate receptor modulator. It works by preventing white blood cells from reaching the central nervous system where they can potentially attack the protective covering around nerve fibers. Gilenya costs nearly \$48,000 per patient for a year of treatment, considerably more than injectable drugs for MS.

A Closer Look

- New research suggests that the use of disease-modifying therapies to treat MS may prevent disease progression and subsequent increased disability and related costs. Multiple randomized controlled trials have provided evidence of significantly delayed disease progression in patients who initiate therapy early in the course of disease. National clinical authorities increasingly recommend initiation of therapy immediately after diagnosis to delay progression, and for some patients starting therapy even before a definitive clinical diagnosis has been formally established.³
- According to the *Express Scripts 2006 Drug Trend Report*, the average cost per prescription of an MS medication was \$1,470. By 2009, the average cost per prescription had increased almost 70% to \$2,465. In 2010, this cost increased to \$2,802, with annual treatment costs for MS medications approaching an average of \$25,000 per treated patient per year.

INTRODUCTION

TREND OVERVIEW

THE THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID

Market Influences on Trend

Prevalence	10.0%	} 29.4%
Cost/Unit	16.8%	
Units/Rx	0.0	
Patent Expirations	0.0	
New Drugs	2.7%	

+

Behavioral Influences on Trend

Intensity	-4.0%	} -3.9%
Mix	0.0	

=

Total Trend 25.4%

SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$29.80

#Rx PMPY
0.01

Prevalence
0.11%

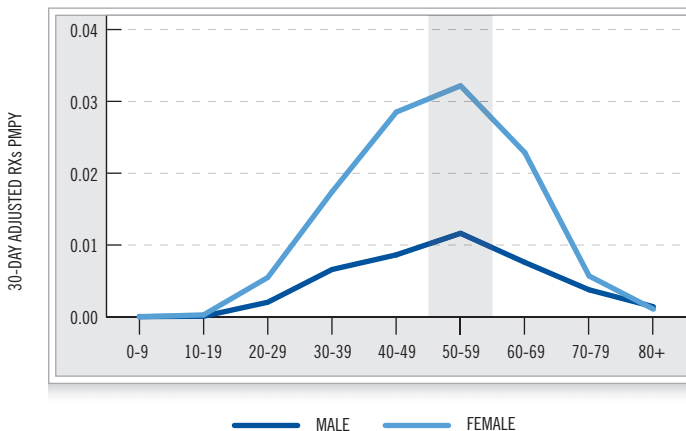
Average Cost/Rx
\$2,718.78

#Rx/User/Yr
8.87

What's Ahead

- Several other oral, disease-modifying medications are expected to join Gilenya on the market within the next year or two. Dimethyl fumarate, cladribine, laquinimod and teriflunomide are also in late-phase development for MS.
- Some of the novel oral MS therapies may be used alone, while others may be used in combination with injectable MS medications already on the market.
- Currently available injectable, biologic drugs that are indicated for other conditions may expand into the MS market in the near future. Lemtrada™ (alemtuzumab), currently marketed as Campath® to treat chronic lymphocytic leukemia, and a new SQ formulation of Zenapax® (daclizumab), a transplant medication, may gain FDA approval to treat MS.

PMPY Rx Use by Age and Gender



NEW DRUGS IN MARKET

Drug	Ampyra®
Approval Date	January 2010
Indication	Multiple sclerosis
Drug	Gilenya™
Approval Date	September 2010
Indication	Multiple sclerosis



MEDICAL

We provide improved management of medically billed oncology medications through evidence-based medical guidelines and more effective claims reimbursement systems.

PHARMACY

Reasons for patients not adhering to their prescribed oral cancer medications include disease complexity, poor communication, use of retail pharmacies, higher copayments, patient perceptions and motivations.⁷

Our clinical programs improve adherence by providing personalized counseling and proactively educating patients about their conditions and the medications used to treat them.

Rising Prices Fueled Cancer Medication Trend

Year in Review

- The nearly 11% increase in the cost/unit for cancer medications was a major trend driver in the class. Some higher-utilized medications such as Gleevec® (imatinib mesylate) and Lupron Depot® (leuprolide acetate for depot suspension) have had both cost/unit and utilization increases contributing to trend growth.
- The increase in cancer medication utilization is primarily due to the increased use of oral cancer medications. Non-oral (typically infused) cancer medications are often billed under the medical benefit.
- In 2010, several oral cancer medications including Tykerb® (lapatinib), Tarceva® (erlotinib), Tassigna® (nilotinib), Spyrcele® (dasatinib) and Afinitor® (everolimus) received expanded approvals allowing for their use earlier in treatment protocol or for new indications.
- Use of Revlimid® (lenalidomide) as a first-line treatment option in patients with multiple myeloma increased 47% in 2010 compared to 2009.
- In April 2010, Provenge® (sipuleucel-T) was approved to treat hormone-refractory prostate cancer. It was the first therapeutic vaccine to treat cancer. Typically, vaccines are used to prevent disease. Provenge is given as a series of three intravenous infusions, which totals \$93,000 for the treatment course. Currently Provenge is primarily billed under the medical benefit.
- Two other infused cancer medications that primarily fall to the medical benefit were approved in 2010. Jevtana® (cabazitaxel) was approved in June to treat hormone-refractory prostate cancer and Halaven™ (eribulin) was approved in November to treat advanced breast cancer.

A Closer Look

- The cost of cancer care is on the rise. The total cost of cancer care in the U.S. could reach between \$158 and \$173 billion by 2020,⁵ a 27% to 39% increase over 2010. The aging U.S. population, improved diagnostics, longer survival and new therapies will all contribute to the increased cost to treat cancer.
- Pharmacogenomics will play an important role in the treatment of cancer. Manufacturers are able to target very specific groups of patients who are most likely to respond to the medication. Tests that help identify appropriate patients for treatment will frequently accompany the medication and may be required via FDA-approved product labeling. The FDA currently has 21 approved oncology drugs with pharmacogenomic information on their labels.⁶
- Pharmacogenomic tests have already been incorporated into nationally

Market Influences on Trend

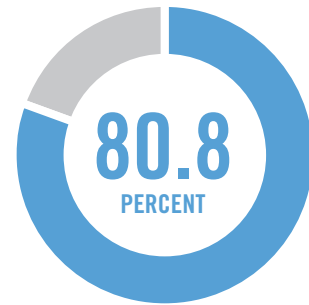
Prevalence	0.9%	} 10.2%
Cost/Unit	10.4%	
Units/Rx	-1.3%	
Patent Expirations	0.0%	
New Drugs	0.2%	

Behavioral Influences on Trend

Intensity	5.3%	} 13.4%
Mix	8.1%	

Total Trend **23.7%**

SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$21.81

#Rx PMPY
0.01

Prevalence
0.17%

Average Cost/Rx
\$2,718.29

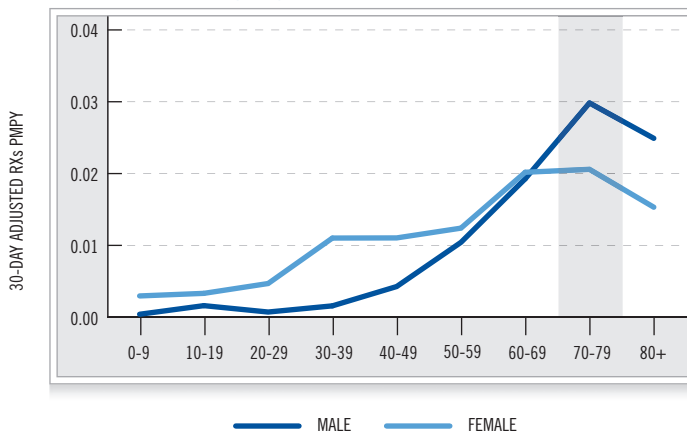
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4.08

recognized cancer clinical practice guidelines such as those of the National Comprehensive Cancer Center (NCCN).⁸ Examples of pharmacogenomic tests recommended by NCCN guidelines to select candidates for drug therapy include the Her2 test for Herceptin[®] (trastuzumab), used to treat breast cancer, and the Philadelphia Chromosome test to identify candidates for Sprycel[®] (dasatinib), for example, used to treat chronic myelogenous leukemia (CML).⁹

What's Ahead

- The cancer pipeline is extensive, accounting for approximately half of all specialty drugs in development.
- Oral drugs will continue to have a greater impact on pharmacy benefit spend. Crizotinib for certain patients with non-small cell lung cancer and ridaforolimus for bone and soft tissue sarcomas are among the oral cancer drugs that may be approved within the next year.
- Zictifa[™] (vandetanib) is an oral, targeted therapy that was approved in April 2011 for patients with advanced medullary thyroid cancer.

PMPY Rx Use by Age and Gender



NEW DRUGS IN MARKET

Drug	Provenge [®]
Approval Date	April 2010
Indication	Prostate cancer
Drug	Jevtana [®]
Approval Date	June 2010
Indication	Prostate cancer
Drug	Halaven [™]
Approval Date	November 2010
Indication	Breast cancer

INDUSTRY FACT

In a 2008 survey, more than **one million older adults** were estimated to have **drug interactions with anticoagulants.**

Increase in Prevalence Drove Trend

Year in Review

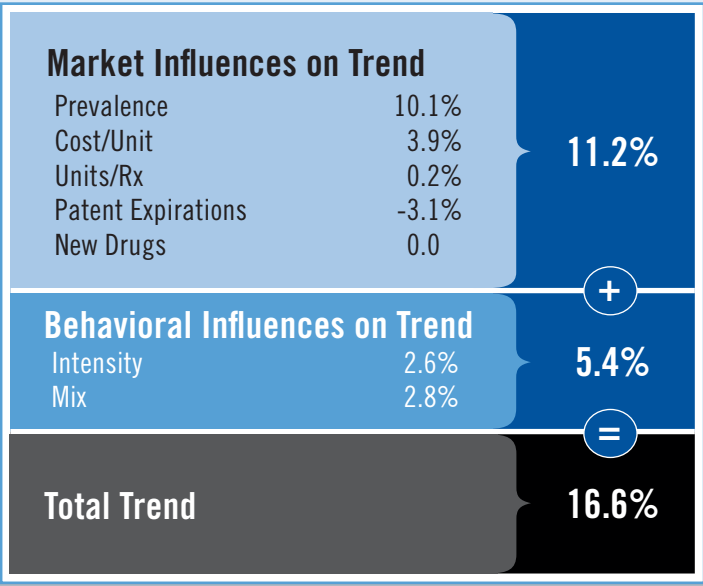
- In 2010, the big story for the anticoagulant therapy class was the July launch of a generic to the category-dominating branded Lovenox® (enoxaparin). Although the full impact of cost savings was delayed by quality issues with syringes shortly after the generic launch, a lower-cost alternative has helped to moderate trend in this class.
- Both cost per unit and utilization of anticoagulants were slightly higher in 2010 compared to 2009.
- Increased use of Arixtra® (fondaparinux) may reflect positive clinical data. For Fragmin® (dalteparin), an additional approval for longer-term use in the treatment of deep vein thrombosis (DVT) may have contributed to increased use.

A Closer Look

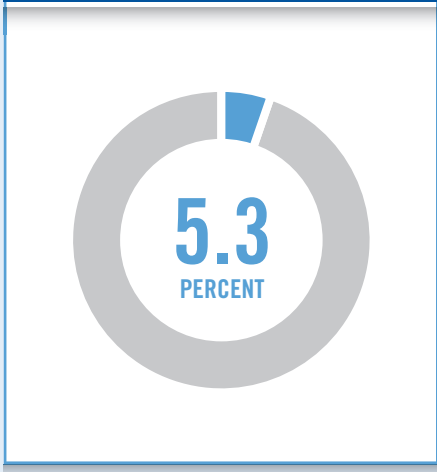
- Because more than 87% of members in this category receive a course of treatment involving two or less prescriptions and are often on the medication for only a short time, it can be difficult to predict utilization at the plan level.
- More than 70% of members with a prescription for Lovenox receive only one dose of medication.
- The use of Innohep® (tinzaparin) has fallen to nearly zero following the pattern of rapid decline seen year over year since the December 2008 warning that it was associated with a higher death rate among elderly patients with kidney conditions.

What's Ahead

- The cost trend for anticoagulants is expected to lower as the use of generic enoxaparin continues to grow. An additional generic version of Lovenox, which may compete in this market in 2011, could help to bring down trend in the class.
- Trend growth may also slow over the next several years as more oral anticoagulants enter the market. Oral anticoagulants are typically filled at retail and mail-order pharmacies, not specialty pharmacies.
- Pradaxa® (dabigatran) was approved in October 2010 to prevent stroke in patients with atrial fibrillation. In 2011, it may be approved to prevent clots in patients who have had hip or knee replacement surgery, possibly competing with the injectable anticoagulants for these patients.
- Other oral anticoagulants in late-phase development include Xarelto®



SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$6.99

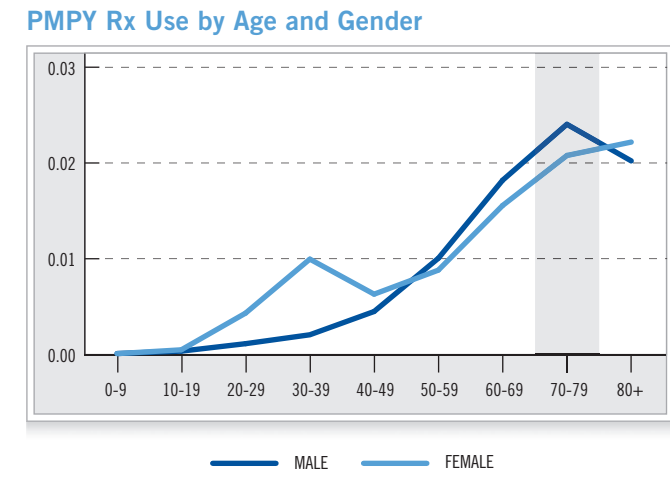
#Rx PMPY
0.01

Prevalence
0.31%

Average Cost/Rx
\$1,086.36

#Rx/User/Yr
1.76

- (rivaroxaban), Eliquis™ (apixaban), edoxaban and otamixaban.
- In 2011, semuloparin, a next-generation Lovenox that is more effective with no increased risk of bleeding, may be approved.
- Idrabiotaparinux, a long-acting anticoagulant that is administered once weekly by subcutaneous (SQ) injection, may reach the market in 2012.



NEW DRUGS IN MARKET

Drug	Generic enoxaparin
Approval Date	July 2010
Indication	Anticoagulant

INDUSTRY FACT

Teens have the **highest rates of nonadherence** to growth hormone therapy, demonstrating the need to assist in **developing strategies for adherence.**

Both Market and Behavioral Factors Drove Trend

Year in Review

- In 2010, drug trend for growth-deficiency medications was driven by increased utilization, particularly the use of Genotropin® (somatropin), which increased 42.5%.
- The impact from newer somatropin formulations, Nutropin AQ® NuSpin™ and Norditropin® FlexPro®, contributed to increased trend in this class.

A Closer Look

- The average age of users declined to 20.6 years from the average of 22.0 seen in the previous two years.
- Research suggests that adherence in this therapy class may vary in medications with different routes of administration. Among pediatric patients using traditional needle and syringe methods of administration, 13.4% miss at least half of prescribed doses of medication, compared to only 6% of patients using needle-free delivery systems.
- Programs that promote formulary compliance along with an assessment of appropriate use are crucial in managing this class. Abuse potential continues to be an issue, but clinical criteria are able to detect and mitigate unapproved use. With costs exceeding \$21,000 per patient per year, managing inappropriate use is critical.

What's Ahead

- Two new long-acting human growth hormone formulations are expected to enter the market in 2012. Declage™ and ALTU-238 are both administered once weekly by subcutaneous injection.

Market Influences on Trend

Prevalence	8.3%	} 6.5%
Cost/Unit	4.6%	
Units/Rx	-6.5%	
Patent Expirations	0.0	
New Drugs	0.0	

+

Behavioral Influences on Trend

Intensity	6.7%	} 11.3%
Mix	4.6%	

=

Total Trend **17.8%**

SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$5.98

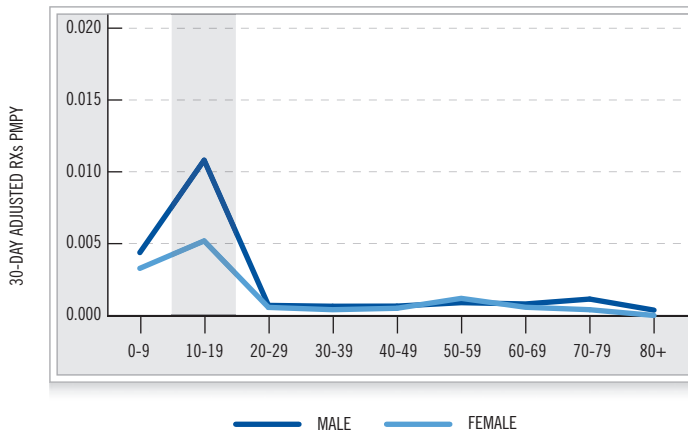
#Rx PMPY
0.002

Prevalence
0.02%

Average Cost/Rx
\$2,823.42

#Rx/User/Yr
7.49

PMPY Rx Use by Age and Gender



INDUSTRY FACT

Proactively assessing patients with pulmonary arterial hypertension for risk of nonadherence is critical to **reduce the costs** related to poor treatment management.

Medication Spend for Pulmonary Hypertension Increased Significantly

Year in Review

- Double-digit increases in both unit cost and utilization contributed to significant spend growth for pulmonary hypertension medications in 2010. The class jumped from Specialty Spend Rank 10 in 2009 to Rank 6 in 2010. Factors affecting spend in this class include increased combination use of medications and increased use of oral dosage forms that are billed under the pharmacy benefit.
- In 2010, Tyvaso[®], an inhaled formulation of the prostaglandin treprostinil, captured market share from Ventavis[®] (iloprost), another inhaled prostaglandin that is dosed more frequently than Tyvaso. The number of Ventavis prescriptions decreased 57% in 2010 compared to 2009.
- Increased use of newer, oral drugs also drove up trend in this class. Use was greater for the phosphodiesterase type-5 (PDE5) inhibitor Adcirca[®] (tadalafil, the same drug as Cialis[®]) compared to Revatio[®] (sildenafil, the same drug as Viagra[®]).

A CLOSER LOOK

- Combination therapy is common in existing clinical practice although support for combination studies has been largely empirical or derived from small-scale observational studies.¹⁰ Several double-blind randomized controlled trials investigating combination therapy have been published. These trials reinforce the importance of well-designed and adequately powered studies for the evaluation of combination therapy.¹¹
- A milestone was crossed with the development of a more robust utilization management strategy for the most common therapy classes that treat pulmonary hypertension. This program ensures the most appropriate, lowest-cost option is attempted first, thereby managing drug spend.
- Express Scripts has created step therapy programs to encourage formulary utilization within chemical classes.

Market Influences on Trend

Prevalence	6.2%	} 18.8%
Cost/Unit	11.4%	
Units/Rx	1.1%	
Patent Expirations	0.1%	
New Drugs	0.0	

+

Behavioral Influences on Trend

Intensity	11.1%	} 17.5%
Mix	6.4%	

=

Total Trend 36.3%

SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$4.40

#Rx PMPY
0.001

Prevalence
0.01%

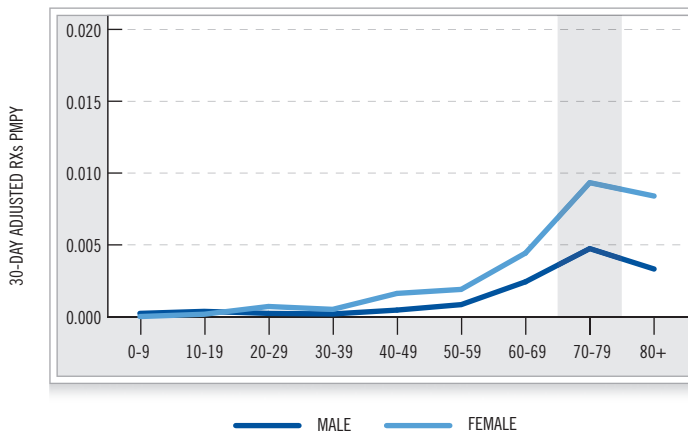
Average Cost/Rx
\$3,590.94

#Rx/User/Yr
9.07

What's Ahead

- An oral tablet formulation of treprostinil may be approved in 2012.
- Other oral pulmonary hypertension medications including macitentan and riociguat may enter the market in 2012.
- In 2012, Gleevec® (imatinib), an oral cancer medication, may receive an expanded indication to treat pulmonary hypertension.

PMPY Rx Use by Age and Gender



INDUSTRY FACT

Adolescents with cystic fibrosis demonstrate greater adherence to medication when symptoms flare but need **education** to help them **maintain adequate adherence** during times of wellness.

Market Factors Drove Trend Up

Year in Review

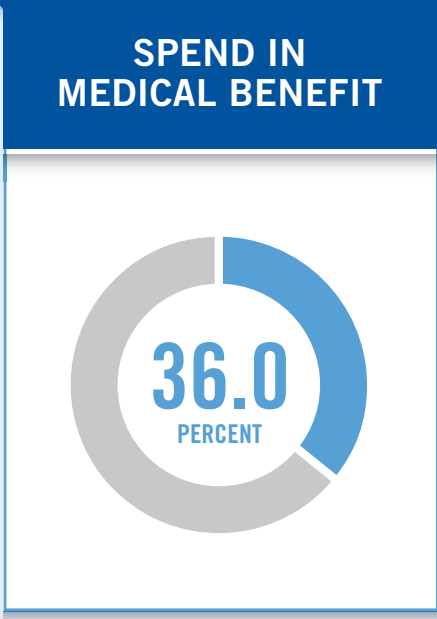
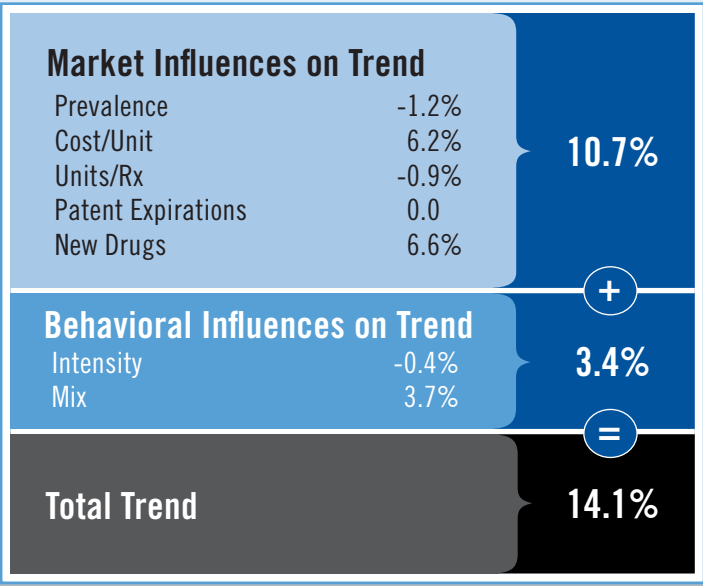
- This class includes specialty drugs to treat cystic fibrosis (CF), alpha-1 antitrypsin (AAT) deficiency and allergic asthma.
- Use of the class leader, Xolair® (omalizumab) for allergic asthma, was down from 2009.
- The launch of Prolastin®-C (alpha1-proteinase inhibitor), a more potent formulation of Prolastin® that requires half the volume and infusion time, contributed to higher trend in this class. This medication is used to treat AAT deficiency.
- In February 2010, Cayston® (aztreonam lysinate for inhalation), gained FDA approval to treat CF lung infections. Similar to TOBI® (tobramycin inhalation solution), Cayston is an antibiotic inhaled through a specialized nebulizer device. Although TOBI is inhaled only twice a day (compared to three times a day for Cayston), each TOBI treatment takes 15 minutes, whereas Cayston administration takes only two to three minutes.
- Glassia™, an alpha-1-proteinase inhibitor to treat AAT deficiency, was launched in late October 2010. It is another infused medication similar to Aralast™, Prolastin® and Zemaira®.

A Closer Look

- Medications used to treat CF made up more than 51% of market share for respiratory medications dispensed in 2010, followed by asthma (35.4%) and AAT deficiency (12.8%).
- Alpha-1-proteinase inhibitors continue to show significant cost per unit increases. The deployment of a preferred product approach will create additional competition in the market, mitigate cost inflation and maintain quality therapy for patients.

What's Ahead

- VX-770, an inhaled medication that improves mucus clearance in patients with CF, may reach the market in 2011.
- Ataluren is an oral drug that treats the underlying disease in patients with CF due to defects in DNA that lead to incomplete protein production. Such mutations play a role in inherited diseases such as CF. A pharmacogenomic test will be used to identify appropriate candidates for treatment with ataluren, which is expected to be approved in 2012.

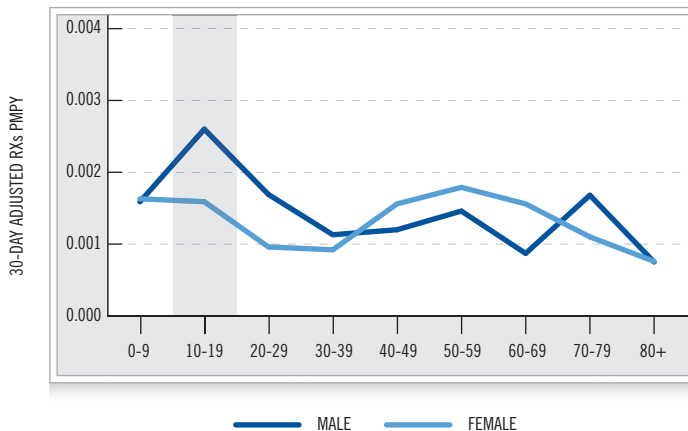


KEY FACTS

- Cost PMPY **\$4.04**
- #Rx PMPY **0.001**
- Prevalence **0.02%**
- Average Cost/Rx **\$2,740.33**
- #Rx/User/Yr **6.77**

- Aeroquin™ (levofloxacin) and Arikace™ (amikacin) are inhaled antibiotics that decrease pseudomonas lung infections. They may compete with TOBI and Cayston in 2012.
- Idiopathic pulmonary fibrosis (IPF), a condition affecting 250,000 Americans, is characterized by scarring of lung tissue. The approval of Pirfenidone™, an oral drug in development for the treatment of IPF, was expected in 2010. However, the FDA is requiring additional studies. Pirfenidone may reach the U.S. market in 2012 and would be the first medication approved to treat this disease.

PMPY Rx Use by Age and Gender



NEW DRUGS IN MARKET

Drug	Cayston®
Approval Date	February 2010
Indication	Cystic fibrosis
Drug	Glassia™
Approval Date	July 2010
Indication	Alpha-1-antitrypsin deficiency

INDUSTRY FACT

Synchronizing the timing of chemotherapy and erythropoiesis-stimulating agents to occur during the same outpatient oncology visit may provide convenience and lower healthcare costs.

Decreased Utilization Contributes to a Nearly Flat Trend

Year in Review

- The majority of spend for blood cell deficiency medications is billed under the medical benefit.
- In 2010, the nearly 10% decrease in utilization of erythropoiesis-stimulating agents (ESAs) – Aranesp® (darbepoetin alfa), Epogen® (epoetin alfa) and Procrit® (epoetin alfa) – contributed to negative trend for this category. ESAs are losing market share due to safety concerns and reduced Medicare reimbursement to prescribers. This accounts for most of the 7.9% reduction in prevalence for blood cell deficiency medications in 2010.
- Overall class trend would have been much lower if the use of Nplate® (romiplostim) and Promacta® (eltrombopag) to treat idiopathic thrombocytopenic purpura (ITP) had not increased significantly.
- Although Mozobil® (plerixafor) typically is billed under the medical benefit, its increased use also had an effect on pharmacy trend. Mozobil is used in combination with Neupogen® (filgrastim) to mobilize stem cells for transplantation.

A Closer Look

- ESA use has been on the decline following labeling changes in March 2007 that identified cardiovascular risks.¹² In 2007, utilization of ESAs dropped nearly 20%, with subsequent drops each year compared to the previous year: 20.8% in 2008, 16.3% in 2009 and 9.9% in 2010.
- In 2010, the American Society of Clinical Oncology/American Society of Hematology updated their clinical practice guideline on the use of epoetin darbepoetin in adult patients with cancer. For patients undergoing myelosuppressive chemotherapy who have hemoglobin levels less than 10g/L, the recommendations are that the side effects (e.g., thromboembolism, shorter survival) and benefits (e.g., increase in hemoglobin, decreased transfusions) should be weighed. In addition, clinicians are advised to use the lowest dose possible to avoid transfusions. Clinicians are also cautioned to avoid use of ESAs in cancer patients not receiving chemotherapy, except for those with lower-risk myelodysplastic syndromes.

Market Influences on Trend

Prevalence	-7.9%	-1.5%
Cost/Unit	5.2%	
Units/Rx	1.1%	
Patent Expirations	0.0	
New Drugs	0.1%	

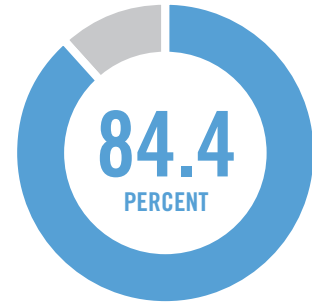
Behavioral Influences on Trend

Intensity	-2.1%	2.0%
Mix	4.1%	

Total Trend

0.5%

SPEND IN MEDICAL BENEFIT



KEY FACTS

Cost PMPY
\$3.89

#Rx PMPY
0.002

Prevalence
0.04%

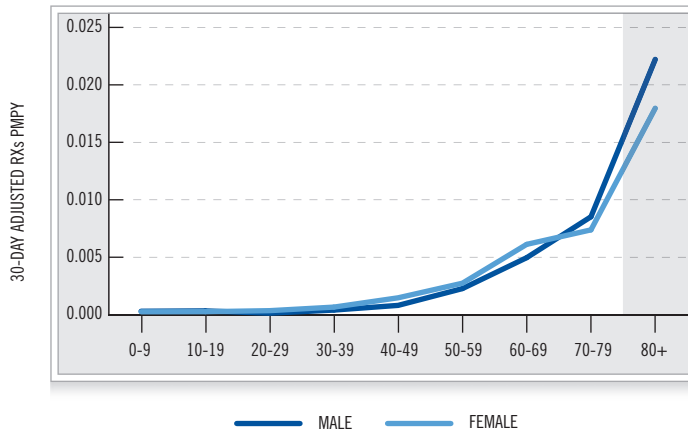
Average Cost/Rx
\$2,030.20

#Rx/User/Yr
4.01

What's Ahead

- Neuroval™ (filgrastim), a biosimilar medication to Neupogen, may reach the U.S. market in 2011. These medications increase white blood cells to help fight infections in patients taking certain chemotherapeutics.
- Hematide™ (peginesatide) is a synthetic peptide-based ESA that may be approved for anemia in 2012.

PMPY Rx Use by Age and Gender



INDUSTRY FACT

Pregnancy rates are diminished after two cycles of medication-only fertility treatment.

Rising Cost per Unit Tempered by Favorable Mix, Lower Use

Year in Review

- In 2010, trend for infertility agents was essentially flat, with an approximately 5% increase in cost/unit balanced by a nearly 4% decrease in utilization.
- Certain manufacturers significantly raised prices on their infertility portfolios compared to others.
- Increases in the cost and use of Menopur® (menotropins) contributed to trend growth in the class.

A Closer Look

- The decrease in utilization of fertility drugs is due to a number of factors including an increase in the percentage of women opting for in-vitro fertilization (IVF), a therapy that produces a higher pregnancy success rate than intrauterine insemination.
- Also contributing to a decrease in intensity of use were utilization management programs implemented by plan sponsors through the Express Scripts Freedom Fertility Pharmacy™, where 39% of fertility prescriptions through Express Scripts are dispensed.
- In addition, physicians are reducing the average number of eggs sought for retrieval in an IVF cycle and therefore are reducing the amount of follicle-stimulating hormone (FSH) medication administered per IVF patient.
- Increased frequency of fertility treatment cycles using donor eggs or previously frozen eggs and embryos also limits medication requirements.
- Men may be prescribed fertility agents for rare conditions such as hypogonadotropic hypogonadism to increase sperm production.

What's Ahead

- Makena™ (hydroxyprogesterone caproate, formerly named Gestiva™) is a progesterone product for the prevention of preterm birth. Approved by the FDA in February 2011, it is given as a weekly intramuscular

Market Influences on Trend		4.6%
Prevalence	-2.2%	
Cost/Unit	6.7%	
Units/Rx	0.2%	
Patent Expirations	0.0	
New Drugs	0.0	
		+
Behavioral Influences on Trend		-3.2%
Intensity	-1.6%	
Mix	-1.6%	
		=
Total Trend		1.3%

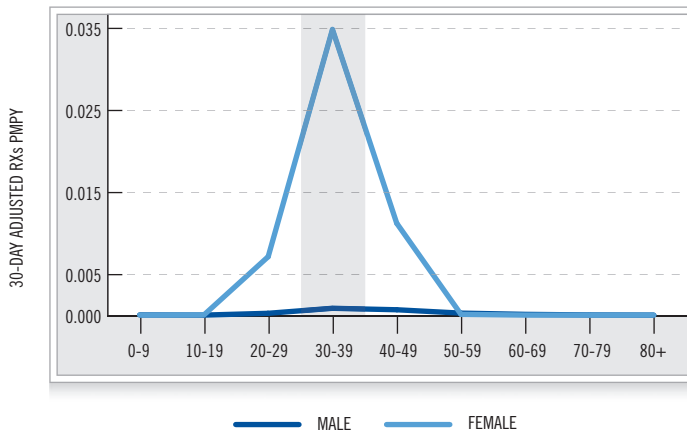
SPEND IN MEDICAL BENEFIT



(IM) injection beginning at week 16 to week 20 until week 37 in women with a history of preterm birth.

- Corifollitropin alfa is a long-acting FSH that may be approved in 2013. It is given as one injection per cycle compared to daily injections with currently available follitropin beta.
- A patch containing gonadotropin-releasing hormone may be approved in 2014.

PMPY Rx Use by Age and Gender



KEY FACTS

Cost PMPY
\$3.13

#Rx PMPY
0.004

Prevalence
0.07%

Average Cost/Rx
\$771.89

#Rx/User/Yr
4.66

INDUSTRY FACT

As hepatitis C regimens become **more complex**, adherence will be extremely important for **successful treatment** and to **prevent resistant mutations** due to suboptimal dosing.

Decreased Prevalence Flattens Trend

Year in Review

- Trend for hepatitis C medications was driven by a nearly 13% decrease in overall utilization (prevalence and intensity combined).
- Overall trend for the class would have been much lower had it not been for double-digit increases in the cost/unit of many hepatitis C medications.
- The drop in utilization may reflect an ongoing reduction in the incidence of untreated infection, patients awaiting the approval of more effective regimens or other factors.¹³
- Perhaps the most significant factor driving down utilization in this class is that many patients and prescribers were waiting for new hepatitis C medications to be approved in 2011 and added to the current standard of care.¹⁴

A Closer Look

- Pegasys® (peginterferon alfa-2a) was the most widely dispensed hepatitis C medication in both 2009 and 2010.
- An estimated 3.6 million Americans have hepatitis C but most do not know they are sick, resulting in a mere 2% receiving treatment. Those patients who are aware of their infection may have been waiting for the approval of new oral medications in May 2011. These medications will serve as an important adjuvant to current therapy.
- New oral protease inhibitors that received FDA approval in May 2011 show promising viral cure rates when added to the current standard of care (pegylated interferon and ribavirin).
- Clinical trials have shown viral cure rates with the new three-drug combination to more than double those of the current two-drug combination.¹⁵

What's Ahead

- FDA approvals of oral protease inhibitors telaprevir and boceprevir will increase treatment efficacy and may shorten therapy treatment course as well but will also increase side effects such as anemia. Specialty pharmacy patient management programs are critical to achieve the desired outcomes.

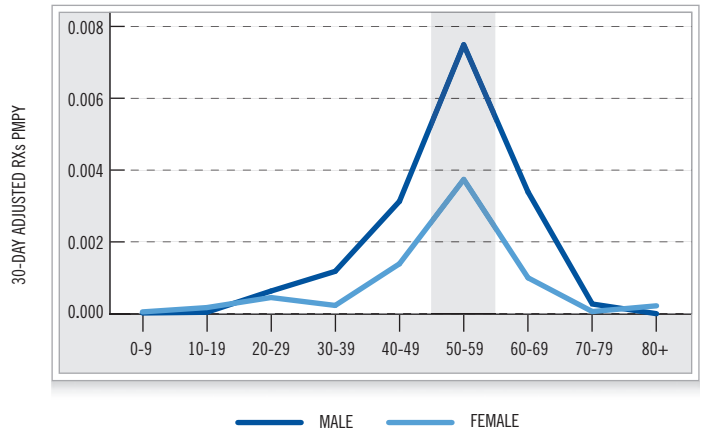
Market Influences on Trend		-5.0%
Prevalence	-15.0%	
Cost/Unit	10.0%	
Units/Rx	-0.1%	
Patent Expirations	0.1%	
New Drugs	0.0	
Behavioral Influences on Trend		+ 5.3%
Intensity	2.1%	= 0.3%
Mix	3.3%	
Total Trend		

SPEND IN MEDICAL BENEFIT



- Several other types of oral, direct-acting antiviral medications are in development for hepatitis C.
- Newer interferons such as PEG-interferon-lambda and Locteron®, a longer-acting interferon alpha-2b that would be used less frequently than current interferons, may be approved in the next two to three years.

PMPY Rx Use by Age and Gender



KEY FACTS

Cost PMPY
\$2.41

#Rx PMPY
0.002

Prevalence
0.02%

Average Cost/Rx
\$1,389.04

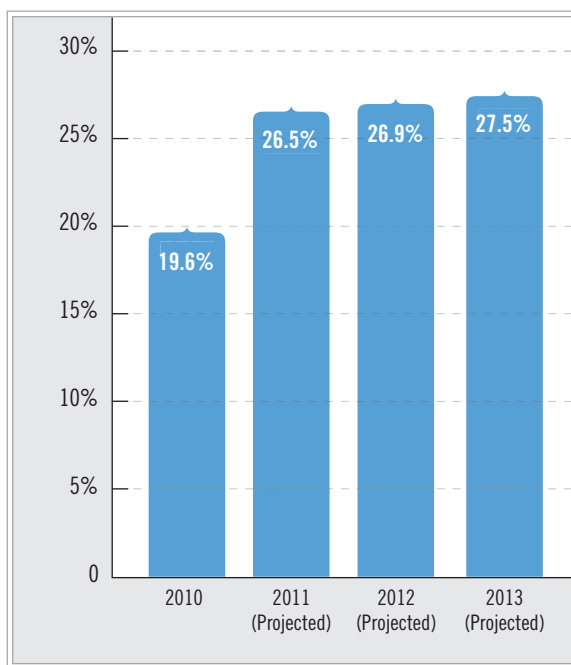
#Rx/User/Yr
9.30

Forecast

SPECIALTY FORECAST

In contrast to the traditional market in which lower-cost generics have slowed year-over-year growth in spend, the portion of specialty trend covered under pharmacy benefits is expected to expand about 27% annually over the next three years. The two major components of trend – cost/unit and utilization – will contribute about equally to growth. Therefore, we predict that the per-member-per-year (PMPY) spend for specialty medications in the pharmacy benefit alone will more than double over the same period, from \$129.98 in 2010 to \$266.03 by 2013.

Exhibit 10 Specialty Drug Trend, 2010 (Actual) and 2011 to 2013 (Projected)



This specialty forecast section focuses only on medications covered by pharmacy benefits. To better quantify the proportion of total specialty spend captured within medical benefits, Express Scripts analyzed data from the Thomson Reuters MarketScan®

Commercial Database. In 2008, approximately 45% of all specialty spend was covered under pharmacy benefits, with the remaining 55% under medical benefits. Considering the current drug pipeline and understanding payer strategies, we anticipate that utilization and expense will rise in both the pharmacy and the medical benefit.

We anticipate that specialty cost per prescription will increase annually between 13% and 15%. The main drivers will be brand inflation and, to a lesser extent, drug mix. Looking ahead, we believe that brand-name unit price increases will hover in the high single-digit to low double-digit range through 2013. When they reach the market, biosimilars will increase competition within several specialty therapy classes. Their introductions will allow new utilization management strategies that should mitigate the consistent price-per-unit hikes seen recently for many specialty medications.

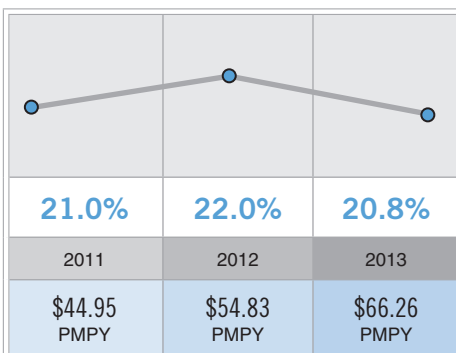
Utilization for specialty drugs also will continue to grow (around 12% per year) over the next three years, primarily due to approval of novel therapies for currently unmet needs. Innovation across many specialty therapy classes has led to the discovery of novel biologic drugs that significantly broaden treatment options for certain conditions. In addition, many oral medications are in development to treat conditions – such as rheumatoid arthritis, multiple sclerosis, cancer and hepatitis C – which now are treated mostly by infused or injected drugs. Significant uptake of oral specialty medications will affect the pharmacy benefit directly. Utilization also will grow as new and existing products are used for a wider range of conditions.

Through 2013, the top three specialty therapy classes – inflammatory conditions, multiple sclerosis and cancer – will continue to account for approximately two-thirds of specialty-drug spend under pharmacy benefits. In contrast, the remaining one-third of specialty spend is fragmented across a wide range of medications. These relatively small therapy classes are susceptible to significant trend swings as new drugs or indications are approved.

1

INFLAMMATORY CONDITIONS

TREND

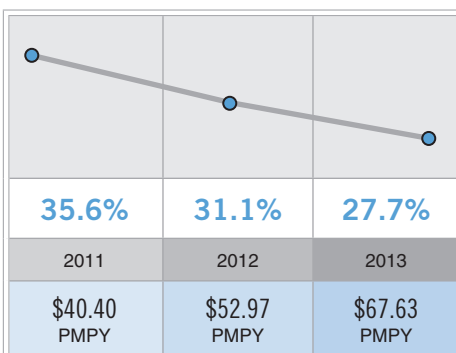


Sustained growth is expected in the inflammatory conditions therapy class as new drugs and new indications for existing drugs increase utilization. Unit costs of many medications may increase in anticipation of new, oral competitors. Oral drugs for inflammatory conditions are expected to begin affecting the market in 2012 and 2013.

2

MULTIPLE SCLEROSIS

TREND

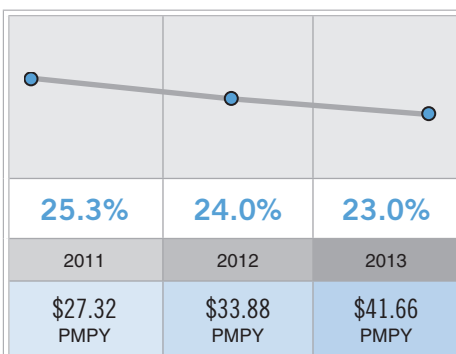


New oral drugs for multiple sclerosis (MS) are expected to drive up utilization in the class as they probably will be used earlier in therapy, to control symptoms, and in combination with other MS medications. Continued unit price hikes across the class are anticipated for the next several years.

3

CANCER

TREND

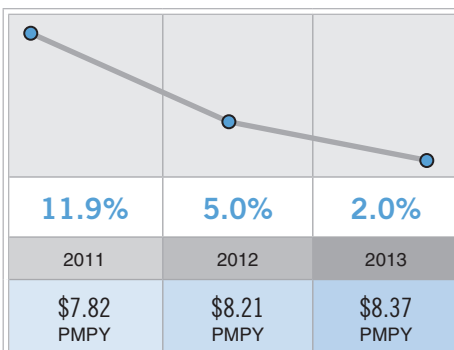


As treatments have improved, cancer is becoming more of a chronic condition with longer-term drug use that fuels increased utilization. An increased use of oral drugs, shifting cost from medical benefits to pharmacy benefits, is expected for the foreseeable future. Double-digit increases in class spend are likely to continue as well.

4

ANTICOAGULANTS

TREND

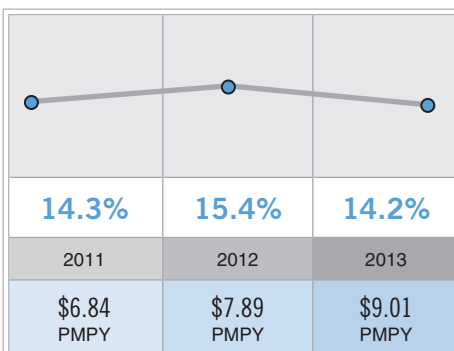


Generics to Lovenox®, the market-leading anticoagulant, were launched in mid-2010 with another possible in the second half of 2011. These alternatives will decrease cost/unit and slow trend growth in the class. Pradaxa® and other new oral anticoagulants that are still in development will pull prescriptions away from the specialty market as they are offered under the traditional prescription-drug benefit.

5

GROWTH DEFICIENCY

TREND

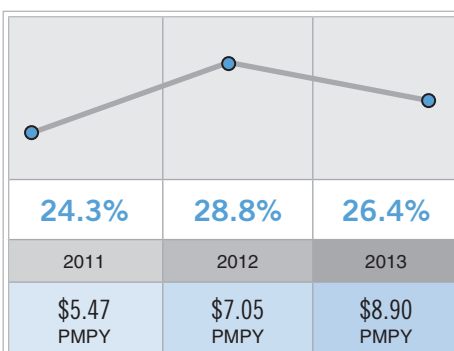


Moderate growth is expected in the class due to increases in both cost/unit and utilization. Two new long-acting growth hormones that are on track to enter the market in 2012 also will contribute to increased utilization.

6

PULMONARY HYPERTENSION

TREND



New oral drugs for pulmonary hypertension, which are expected to enter the market in 2012, will drive significant positive utilization trend and a medical-to-pharmacy benefit shift in the class. Oral agents will be much more convenient for patients than the complicated inhaled drugs that they replace, as well. Inflation and combination therapy using more than one drug at a time also will contribute to projected growth rates.

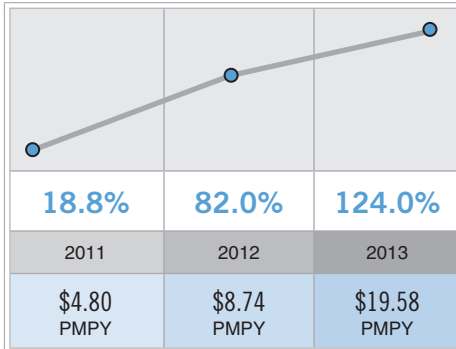
2011 to 2013 Forecast for the Top 10 Specialty Therapy Classes

CONTINUED

7

RESPIRATORY CONDITIONS

TREND

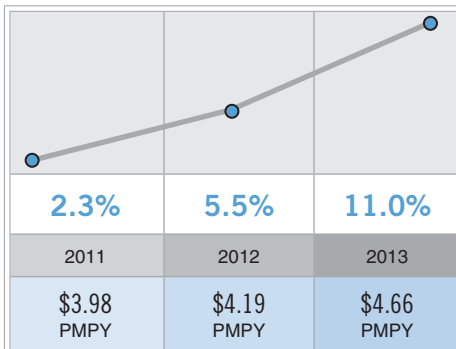


The potential approval of pirfenidone in mid-2012 will be the primary driver of very large trend growth expected in the class. If approved, it will be the first medication to treat the devastating condition of idiopathic pulmonary fibrosis. In addition, several investigational new oral and inhaled drugs for cystic fibrosis also will increase utilization for several years after they reach the market.

8

BLOOD CELL DEFICIENCY

TREND

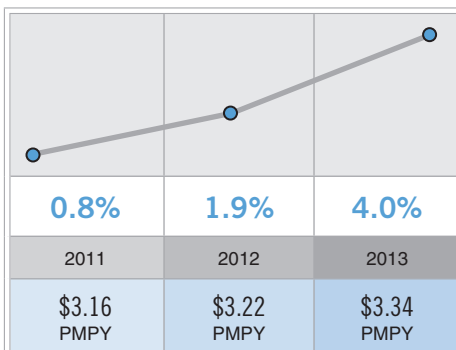


Decreases in the utilization of erythropoiesis-stimulating agents due to safety concerns are expected to continue for a few more years. Offsetting the decrease will be increases in cost/unit. The possible approval of Neutroval®, a biosimilar to Neupogen®, in 2011 will mitigate some of the increases in spend, but use of expensive new drugs for idiopathic thrombocytopenic purpura will increase both cost/unit and utilization in the class.

9

INFERTILITY

TREND

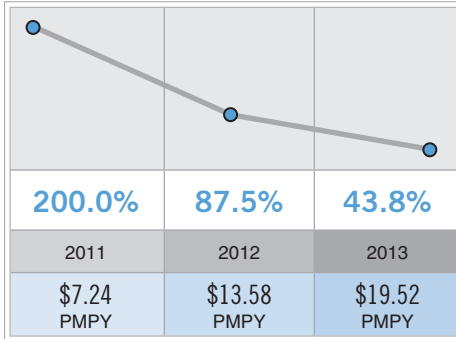


Trend for infertility medications is expected to be modestly positive, with decreased utilization balanced by increased cost/unit. Makena™, a new intramuscular medication to prevent preterm birth, was approved in 2011. Makena, as well as a new long-acting follicle-stimulating hormone that may be approved in 2013, could contribute to positive trend in the class.

10

HEPATITIS C

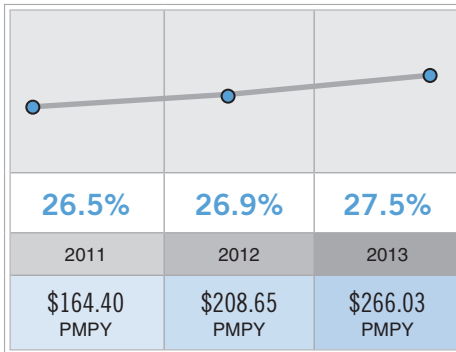
TREND



Approved by the FDA in May 2011, new oral protease inhibitors, boceprevir and telaprevir, will increase treatment efficacy in this class dramatically. Their influence will be felt for the next several years as they fill a significant unmet need from patients postponing the current standard of care (pegylated interferon and ribavirin). They may shorten therapy treatment course but cause increased side effects, such as anemia, underscoring the need for specialty pharmacy patient management programs. Significant increases in both utilization and cost/unit are expected for the class.

TOTAL

TREND



Medicare/Medicaid

MEDICARE

Exhibit 12 | Medicare Trend vs Commercial Trend for Key Specialty Therapy Classes, PBM-Adjudicated and Medicare Part D Claims Only

SPECIALTY				
Rank	Therapy Class	Medicare Trend	Commercial Trend	Difference
1	PULMONARY HYPERTENSION	44.6%	36.3%	8.3%
2	MULTIPLE SCLEROSIS	21.0%	25.4%	-4.4%
3	CANCER	16.5%	23.7%	-7.2%
4	ANTICOAGULANT	12.4%	16.6%	-4.2%
5	INFLAMMATORY CONDITIONS	10.1%	23.5%	-13.4%
6	RESPIRATORY CONDITIONS	8.9%	14.1%	-5.2%
7	BLOOD CELL DEFICIENCY	-5.4%	0.5%	-5.9%
8	GROWTH DEFICIENCY	-18.1%	17.8%	-35.9%
	Top 10	13.2%	21.2%	-8.0%
	Others	6.1%	3.9%	2.2%
	Total	12.7%	19.6%	-6.9%

Medicare Specialty Trend

The term “specialty drug” generally refers to high-cost medications used to treat complex and costly conditions. Because specialty medications are often injected or infused and involve unique monitoring or handling, using them requires additional education and support. Although our analyses are based on this more global understanding of specialty drugs, we recognize that Medicare defines any drug whose cost exceeds a predetermined threshold per month (currently set at \$600) as a specialty medication.

For the next three years, specialty spend is expected to grow at rates of 20% or more, far outpacing trend for traditional drugs. Some specialty medications are more expensive because they are adjudicated under Medicare Part B, which covers medical services, rather than under Part D, the prescription-drug benefit. In 2009, \$5.3 billion dollars was spent on specialty drugs processed through Medicare Part B.¹ Many of these medications could be covered under prescription-drug plans, which employ utilization management strategies to effectively control spend.

As shown in Exhibit 13, the top 10 Medicare specialty therapy classes made up 93.7% of total specialty spending in 2010. Ranking of the top 10 classes is led by drugs used to treat cancer

(with about one-third of total specialty spend for Medicare), inflammatory conditions and multiple sclerosis (together amounting to about another one-third of total spend). These three classes alone accounted for nearly \$2 of every \$3 spent for specialty drugs.

Among the top 10 specialty therapy classes, drugs used to treat pulmonary hypertension saw the largest increase in overall trend at 44.6%, followed by osteoarthritis, which grew 33.5%. The class that saw the largest decrease in overall trend was hepatitis C at -26.2%. The generic fill rate for Medicare specialty drugs was 9.6% in 2010.

Medicare’s top three specialty therapy classes represent more than two-thirds of total specialty spending.

Exhibit 13

Components and Drivers of Trend for the Top 10 Medicare Specialty Therapy Classes, Ranked by 2010 PMPM Spend, Medicare Part D Claims Only

Rank	Therapy Class	PMPM Spend	% of Total Specialty Spend	PMPM \$ Change from 2009	Trend		
					Total	Utilization	Cost
1	CANCER	\$5.40	32.6%	\$0.76	16.5%	5.8%	10.7%
2	INFLAMMATORY CONDITIONS	\$2.87	17.3%	\$0.26	10.1%	3.4%	6.7%
3	MULTIPLE SCLEROSIS	\$2.00	12.0%	\$0.35	21.0%	9.6%	11.4%
4	BLOOD CELL DEFICIENCY	\$1.41	8.5%	-\$0.08	-5.4%	-14.0%	8.6%
5	PULMONARY HYPERTENSION	\$1.27	7.7%	\$0.39	44.6%	28.1%	16.5%
6	ANTICOAGULANTS	\$1.14	6.9%	\$0.13	12.4%	10.1%	2.2%
7	BONE CONDITIONS	\$0.56	3.4%	\$0.00	0.4%	-2.9%	3.4%
8	IMMUNE SERUMS	\$0.44	2.7%	\$0.06	15.4%	28.6%	-13.2%
9	HEPATITIS C	\$0.25	1.5%	-\$0.09	-26.2%	-20.9%	-5.2%
10	OSTEOARTHRITIS	\$0.18	1.1%	\$0.05	33.5%	22.3%	11.2%
	Top 10	\$15.52	93.7%	\$1.81	13.2%	4.7%	8.5%
	Others	\$1.04	6.3%	\$0.06	6.1%	-9.5%	15.5%
	Total	\$16.55	100.0%	\$1.86	12.7%	2.9%	9.8%

Exhibit 14 | Top 10 Medicare Specialty Drugs, Ranked by 2010 PMPM Spend, Medicare Part D Claims Only

Rank	Drug Brand Name	Therapy Class	PMPM Spend	% of Total Specialty Spend	PMPM \$ Change from 2009	Trend		
						Total	Utilization	Cost
1	ENBREL®	INFLAMMATORY CONDITIONS	\$1.35	8.2%	\$0.01	0.9%	-3.8%	4.7%
2	REVLIMID	CANCER	\$1.30	7.8%	\$0.28	27.9%	26.6%	1.4%
3	HUMIRA®	INFLAMMATORY CONDITIONS	\$1.09	6.6%	\$0.11	11.1%	4.2%	6.9%
4	GLEEVEC	CANCER	\$0.90	5.5%	\$0.13	17.3%	5.0%	12.3%
5	COPAXONE	MULTIPLE SCLEROSIS	\$0.83	5.0%	\$0.22	36.6%	14.9%	21.7%
6	PROCRIT	BLOOD CELL DEFICIENCY	\$0.74	4.5%	-\$0.12	-13.9%	-17.1%	3.2%
7	LOVENOX	ANTICOAGULANT	\$0.70	4.2%	-\$0.14	-16.8%	-17.6%	0.8%
8	TRACLEER®	PULMONARY HYPERTENSION	\$0.59	3.6%	\$0.17	41.1%	24.3%	16.8%
9	LUPRON DEPOT	CANCER	\$0.55	3.3%	\$0.02	4.5%	6.8%	-2.3%
10	TARCEVA	CANCER	\$0.50	3.0%	\$0.05	11.8%	2.0%	9.9%
	Top 10		\$8.56	51.7%	\$0.75	9.6%	-5.4%	15.0%
	Others		\$7.99	48.3%	\$1.12	16.3%	13.9%	2.4%
	Total		\$16.55	100.0%	\$1.86	12.7%	2.9%	9.8%

Top Medicare Specialty Therapy Classes

CANCER

Trend for the cancer therapy class was 16.5%, reflecting a 10.7% increase in the cost per prescription and a 5.8% increase PMPM in utilization. Increased prescription cost resulted in part from a 1.1% decrease in the generic fill rate (GFR). The top

two drugs by cost, Revlimid (lenalidomide) and Gleevec (imatinib), accounted for 24.0% and 16.7% of overall cancer spend, respectively.

TOP FIVE MEDICARE SPECIALTY DRUGS BY MARKET SHARE

LUPRON DEPOT	19.3%
METHOTREXATE	14.5%
GLEEVEC	10.9%
XELODA®	9.8%
REVLIMID	9.0%

TREND 16.5%

Cost PMPM	\$5.40
#Rx PMPM	0.002
GFR 2010	18.7%
Average Cost/Rx	\$2,757.85

INFLAMMATORY CONDITIONS

The 2010 Medicare trend for inflammatory conditions was 10.1%, which stemmed from a 6.7% increase in cost per prescription and a 3.4% increase in utilization PMPM. Lack of generics meant GFR was not a significant driver of trend in this class.

The top two most costly drugs, Enbrel (etanercept) and Humira (adalimumab), accounted for 47.1% and 38.1% of overall inflammatory condition spend, respectively.

TOP FIVE MEDICARE SPECIALTY DRUGS BY MARKET SHARE

ENBREL	49.7%
HUMIRA	39.1%
REMICADE®	5.5%
SIMPONI	2.3%
CIMZIA	1.9%

TREND 10.1%

Cost PMPM	\$2.87
#Rx PMPM	0.0016
Average Cost/Rx	\$1,832.79

MULTIPLE SCLEROSIS

The overall Medicare multiple sclerosis (MS) trend in 2010 was 21.0%, reflecting an 11.4% increase in cost per prescription and a 9.6% increase in the number of prescriptions filled PMPM. The GFR was not a significant driver of trend in this class as

almost no generics are available. Copaxone (glatiramer) and Avonex® (interferon beta-1a), the two most expensive drugs in the class, accounted for 41.4% and 22.8% of overall MS spend, respectively. They also ranked first and second in market share.

TOP FIVE MEDICARE SPECIALTY DRUGS BY MARKET SHARE

COPAXONE	36.7%
AVONEX	22.4%
REBIF®	14.0%
BETASERON®	12.8%
TYSABRI®	4.2%

TREND 21.0%

Cost PMPM	\$2.00
#Rx PMPM	0.0007
Average Cost/Rx	\$2,717.23

BLOOD CELL DEFICIENCY

In 2010, Medicare blood cell deficiency trend decreased 5.4%. This shift was driven by a 14% decrease in PMPM utilization, partially offset by an 8.6% increase in the cost per prescription.

The GFR did not change. The top two drugs by cost, Procrit (epoetin alfa) and Neupogen (filgrastim), accounted for 52.9% and 17.0% of overall blood cell deficiency spend, respectively.

TOP FIVE MEDICARE SPECIALTY DRUGS BY MARKET SHARE

PROCIT	65.0%
ARANESP	19.0%
NEUPOGEN	8.8%
NEULASTA®	2.5%
LEUKINE®	1.0%

TREND -5.4%

Cost PMPM	\$1.41
#Rx PMPM	0.0012
GFR 2010	0.1%
Average Cost/Rx	\$1,136.74

PULMONARY HYPERTENSION

The overall Medicare trend for pulmonary hypertension drugs in 2010 was 44.6%. This steep increase was due to a 16.5% increase in the cost per prescription and a 28.1% increase in the number of prescriptions filled PMPM, with no change in the

GFR due to lack of generic options. Accounting for 46.6% of cost in the class, Tracleer (bosentan) was by far the most costly, followed by Revatio (sildenafil) with 18.0% of overall pulmonary hypertension spend.

TOP FIVE MEDICARE SPECIALTY DRUGS BY MARKET SHARE	
REVATIO	45.3%
TRACLEER	30.6%
LETAIRIS®	11.0%
REMODULIN®	3.2%
TYVASO	1.9%

TREND 44.6%	
Cost PMPM	\$1.27
#Rx PMPM	0.0003
Average Cost/Rx	\$3,914.99

MEDICAID

We are pleased to debut a supplement discussing costs and utilization of specialty drugs in managed Medicaid plans. Future editions of the *Specialty Drug Trend Report* will provide deeper insight into this important, rapidly growing component of the pharmacy landscape.

The recession drastically increased financial pressure on states, demanding deep cuts in Medicaid spending while simultaneously exerting upward pressure on Medicaid enrollment. In addition, the Patient Protection and Affordable Care Act (PPACA) is expected to increase Medicaid enrollment to almost 62 million by 2014. This represents an estimated 29% increase over estimated enrollment under non-PPACA rules.¹ In addition, Medicaid patients typically require more aggressive care than non-Medicaid patients, most likely as a result of neglected routine medical care prior to becoming eligible for Medicaid.

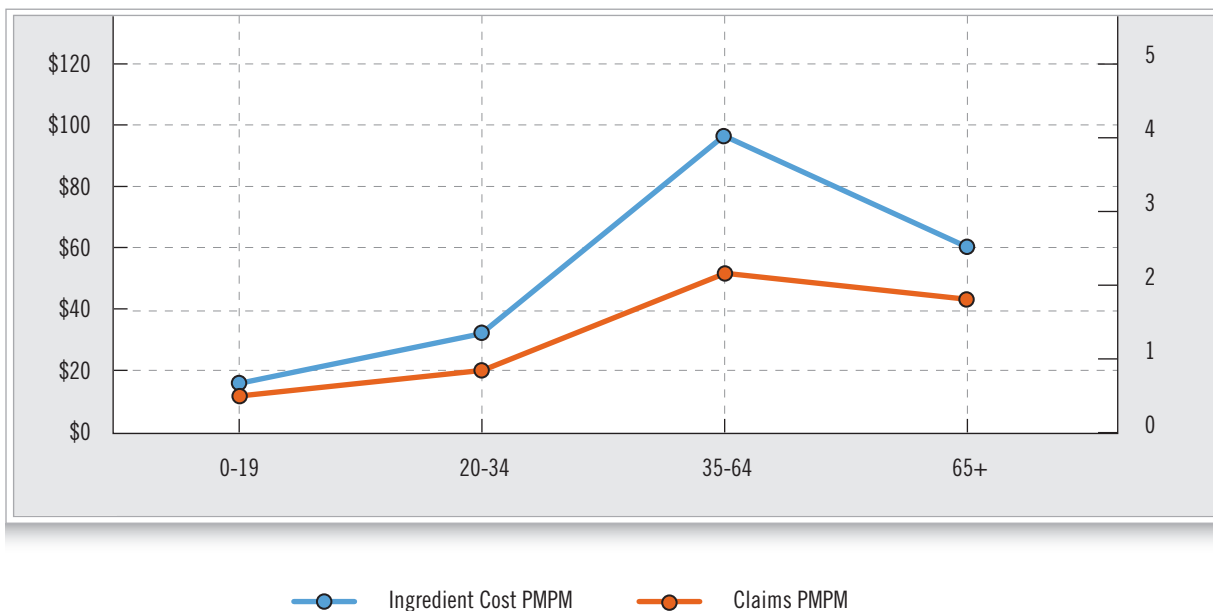
Managing the pharmacy benefit in Medicaid provides an important opportunity for containing costs. The passage of the PPACA balanced federally mandated rebates between fee-

for-service (FFS) and managed care plans. The combination of budget pressures with the PPACA changes caused many states to examine how a managed care model would affect both savings and health outcomes.

A recent study by The Lewin Group found considerable evidence that managed care organizations manage the pharmacy benefit more efficiently than FFS programs. The 2010 national average cost per prescription in Medicaid managed care was \$31.55, compared to \$56.84 in state-administered programs.²

In combination with our parent company, we manage 4.3 million Medicaid managed care lives in multiple states. As the industry leader in understanding the factors that drive drug trend, we can leverage our expertise to benefit our clients and their beneficiaries. We help our Medicaid clients manage pharmacy spend while promoting evidence-based clinical care. We are committed to aligning with plan sponsors and providing insights that help them navigate the complexities of changing Medicaid requirements and regulations.

Exhibit 15 | 2010 Medicaid PMPM Ingredient Cost and Utilization by Age Group



Medicaid Spend

During 2010, the overall PMPM ingredient cost for Medicaid was \$27.35. The average number of PMPM claims was 0.65, and the ingredient cost per claim was \$42.12.

Although several member characteristics play large roles in Medicaid costs and utilization, age is of particular interest – especially given the wide age range of patients covered by Medicaid programs. As Exhibit 15 illustrates, PMPM ingredient costs and utilization for 2010 differ considerably by age group.

Children (Ages 0-19)

Specialty utilization in children – mostly prescriptions for medications used to treat growth deficiency, inflammatory conditions, hemophilia and some rare disorders (such as enzyme deficiencies) – was lower than in any other age group. Costs related to the specialty medications used to treat respiratory syncytial virus (RSV) began to decline in 2010 after the American Academy of Pediatrics issued new guidelines that reduced the total number of recommended doses most children should receive.

Young Adults (Ages 20-34)

Specialty medications most often were used by beneficiaries in this age group to treat hepatitis and inflammatory conditions. Typically, utilization of medications for multiple sclerosis (MS) also begins in this age group. The use of MS drugs is expected to grow as new oral therapies are introduced to the market.

Mid-Adults (Ages 35-64)

In this age range, specialty drugs and medications to treat HIV drove costs. The specialty medications used most often in this age category include those indicated for cancer, inflammatory disorders, MS and blood cell deficiency along with anticoagulants.

Seniors (Age 65 and older)

Sometimes, individuals age 65 and older qualify for dual eligibility under both Medicaid and Medicare Part D prescription drug plans. Understandably, Medicaid utilization by these dual-eligible members is lower, because only a portion of their pharmacy care falls under Medicaid (usually drugs that are excluded from Medicare, such as over-the-counter medications and benzodiazepines). Members who are not dual-eligible more closely resemble the low-income subsidy (LIS) members enrolled in Medicare Part D.

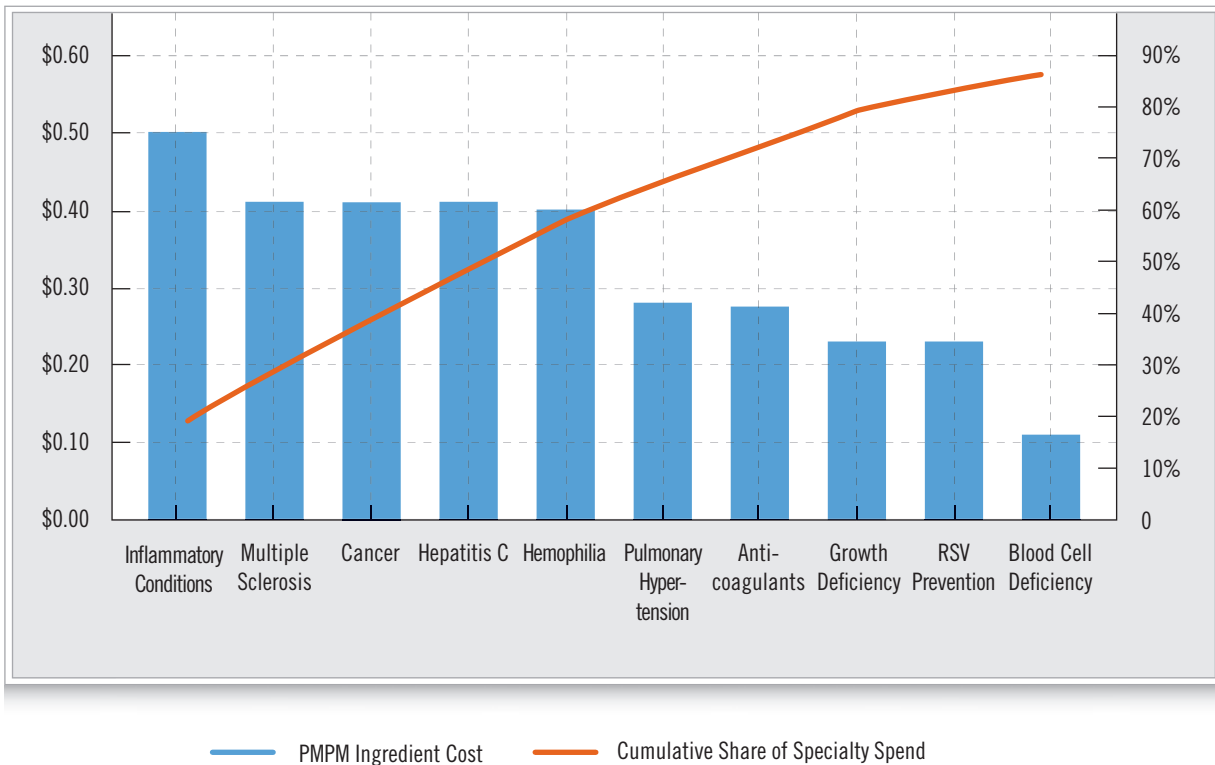
Seniors using Medicaid tend to have multiple comorbidities, as evidenced by utilization of 1.72 PMPM claims and a PMPM cost of \$60.42, both of which are high despite dual responsibility for care. In 2010, the most expensive therapy classes for them included medications used to treat cancer, diabetes and high blood pressure/heart disease.

Medicaid Specialty Therapy Class Review

Most specialty drug costs in Medicaid are associated with inflammatory conditions, multiple sclerosis, cancer and hepatitis C. As shown in Exhibit 16, these four conditions accounted for 45% of specialty costs in 2010. Therapy classes with the highest utilization were hepatitis C, inflammatory conditions and anticoagulants.

The total Medicaid PMPM ingredient cost for specialty medications was \$3.82. Because most specialty therapy classes do not have many available generics, formulary positioning is important in determining the top drugs in each category. Most Medicaid plans utilize closed formularies. However, in 2010 the cancer, hepatitis C, anticoagulant and endocrine disorders therapy classes had a combined GFR of 37%, compared to the low overall GFR for specialty medications (15%).

Exhibit 16 | 2010 Medicaid Specialty PMPM Ingredient Cost and Contribution to Spend



Top Medicaid Specialty Drugs

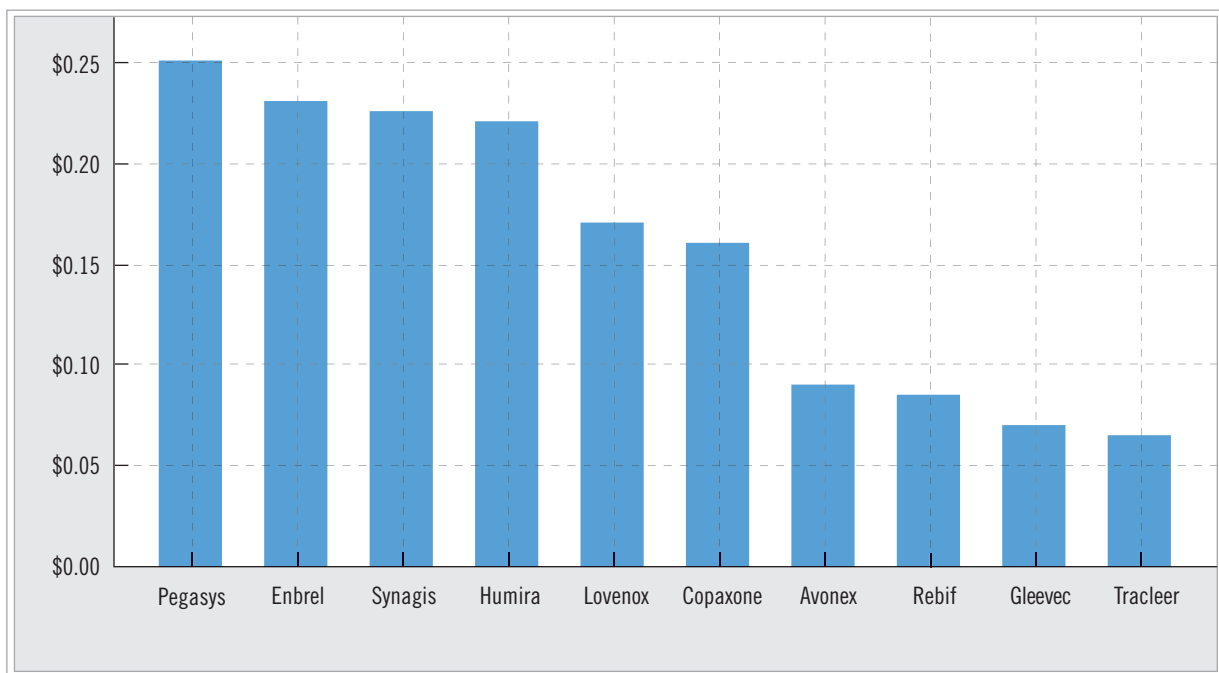
Exhibit 17 depicts the top 10 specialty medications for Medicaid in 2010. Pegasys® (peginterferon alfa-2a), used to treat hepatitis C, was the most expensive. It was followed closely by Enbrel, used to treat inflammatory conditions; Synagis® (palivizumab), for RSV prevention; and Humira, also for inflammatory conditions. Because Medicaid specialty medications represent just 1.7% of claims but about 14% of costs, plans often work closely with specialty pharmacy providers to improve medication adherence and clinical outcomes, as well as to access the most competitive pricing. Increasingly, plans are examining spend for specialty medications that fall under medical claims and are looking for partners to manage that growing cost.

Looking Ahead

Working together with plan sponsors, we are committed to providing better care with less waste for Medicaid members.

Particularly as we move closer to 2014 and the further implementation of the PPACA, innovative and clinically relevant solutions will be needed to reduce waste. Providing financially sustainable Medicaid coverage depends on it.

Exhibit 17 | 2010 PMPM Cost for the Top 10 Medicaid Specialty Drugs



Notes/Appendices

NOTES

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APPENDICES

Appendix 1: Methods for Calculating Trend: 2010 Specialty Drug Trend Report

Prescription-drug use for a random sample of approximately four million members who had prescription-drug coverage in both 2009 and 2010 were analyzed for the *2010 Specialty Drug Trend 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. Members used Express Scripts for retail and home-delivery pharmacy services as well as CuraScript for specialty prescriptions. Prescription counts were converted to equivalent quantities that would have been dispensed through retail pharmacies to allow for varying benefit structures and adjust for differential home-delivery usage rates.

Nonprescription medications (except diabetic supplies) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings are not included in this analysis. Calculations also excluded claims for Medicaid recipients and for Medicare beneficiaries receiving prescription-drug benefits through Medicare Part D plans, Managed Medicare Prescription Drug Plans (PDPs) or Medicare Advantage Prescription Drug Plans (MAPDs). Note, however, that pharmacy cost and utilization trends for Medicare and Medicaid are reported separately in a supplement.

Cost includes ingredient costs, taxes and administrative fees minus rebates.

Utilization was determined on a per-member-per-year (PMPY) basis. It was calculated by dividing the total number of 30-day adjusted prescriptions by the total number of member-years for all members. A member-year is the total number of months of eligibility for all members in the sample divided by 12. Prevalence of use for each drug class was calculated as the number of members taking medications in the class divided by the total number of members (both utilizers and nonutilizers) in the sample. The average number of prescriptions per-user-per-year (#Rx PUPY) is the total number of 30-day adjusted prescriptions divided by the total number of user years. A user-year is determined by adding the number of months of eligibility for all sample members who had at least one claim for a given drug class and then dividing the total by 12. Please note: all calculations are done allowing up to nine decimal points but are rounded down to one or two decimals in most cases for easier reading; therefore, dollar and percentage calculations may appear slightly off due to rounding.

Appendix 2: Methods for Calculating Trend: 2010 Specialty Drug Trend Report Medicare and Medicaid Supplements

Prescription-drug use for a random sample of approximately 650,000 Medicare members and 2.15 million Medicaid members who had prescription-drug benefits through Medicaid, Medicare Part D plans, Managed Medicare Prescription Drug Plans (PDPs) or Medicare Advantage Prescription Drug Plans (MAPDs) in 2010 was analyzed for the *2010 Specialty Drug Trend Report Medicare and Medicaid supplements*. Members used Express Scripts for retail and home-delivery pharmacy services as well as CuraScript for specialty prescriptions. Prescription counts were converted to equivalent quantities that would have been dispensed through retail pharmacies to allow for varying benefit structures and adjust for differential home-delivery usage rates.

Nonprescription medications (except diabetic supplies) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings are not included in this analysis.

Cost includes ingredient costs, taxes and administrative fees. Rebates are not a component of cost.

Utilization was determined on a per-member-per-month (PMPM) basis. It was calculated by dividing the total number of 30-day adjusted prescriptions by the total number of member-months for all members. Prevalence of use for each drug class was calculated as the number of members taking medications in the class divided by the total number of members (both utilizers and nonutilizers) in the sample. The average number of prescriptions per user per month (#Rx PUPM) is the total number of 30-day adjusted prescriptions divided by the total number of user-months. Please note: all calculations are done allowing up to nine decimal points but are rounded down to one or two decimals in most cases for easier reading; therefore, dollar and percentage calculations may appear slightly off due to rounding.



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