Dear Friends of Express Scripts:

From the day we opened our doors in 1986, innovation has been central to our mission. We published the industry's first Drug Trend Report in 1996 and opened The Express Scripts Research & New Solutions Lab in 2010. Over the years, Express Scripts has focused on developing new ways to deliver quality care while driving waste from the healthcare system.

Our pioneering work in understanding consumer behavior relative to healthcare benefits has yielded practical, well-accepted programs that reduce waste while preserving individual choice. We’ve taken this work to the next level to create a breakthrough solution that addresses the persistent problem of nonadherence to medication therapy. Our new solution, combined with other exciting developments detailed on the following pages, makes this edition of the Drug Trend Report particularly compelling.

Now that our merger with Medco Health Solutions has been finalized, we have the potential to transform not only the pharmacy benefit management industry, but American healthcare overall. Moving forward as the new Express Scripts, we will build upon a strong clinical foundation and apply Consumerology® to make it easier for people to choose better health. We will provide even greater cost savings for members and plan sponsors, close more gaps in care, drive waste out of the system, and improve the management of high-cost specialty drugs.

As we look ahead to our next 25 years, we remain deeply committed to helping plan sponsors and patients retain a quality benefit at an affordable cost. We will continue to develop innovative ways to improve healthcare for millions of Americans.

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Chief Medical Officer

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Vice President and
Chief Scientist

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Introduction
Since our founding in 1986, Express Scripts has been committed to meeting the pharmacy needs of our plan sponsors and their members. Our core commitment to deliver benefits that achieve optimal health outcomes at the lowest net cost is still at the center of everything we do.

At every step along the way, two principles have guided our actions. First, our business model of alignment ensures that we succeed when plan sponsors and members do well. Second, we have a deep belief that our point of view should be rooted in evidence — not just opinions. These parallel guideposts lead us to concentrate on our clients’ most pressing challenges and on delivering innovative, proven solutions.

Over the past few years, our research has repeatedly demonstrated that better care and zero waste often go hand in hand: the most effective care often costs the least. Thus, the challenge is not simply to make these two goals compatible, but rather to do so in a manner that is acceptable to both members and plan sponsors. Surprisingly, we now know that the biggest gap is not between what plan sponsors want and what patients want, but rather between what patients want and what patients do. The real gap, our research has revealed, is between good intentions and observed behavior. Rather than trying to drive behavior change directly, recognizing this gap leads us toward solutions focused on activating the good intentions that most members already have.

To activate good intentions, Express Scripts leads the way in the convergence of the behavioral sciences and healthcare, an approach we call Consumerology®. This unique approach provides plan sponsors with practical solutions that deliver better health and lower cost while preserving individual choice.

Our passion for learning and innovation is also embodied in The Express Scripts Research & New Solutions Lab, which opened in December 2010. Located within The Express Scripts Technology & Innovation Center in St. Louis, the Lab’s researchers carefully investigate how patients interact with their drug therapies: what medications they take, whether they adhere to their therapies and why they behave as they do. Solutions developed in the Lab help patients act on their good intentions, leading to better outcomes. Our solutions are informed by an ongoing pipeline of pilot programs and studies rooted in the behavioral sciences.

Although we have made great strides in enhancing the pharmacy benefit over the last 25 years, we continue to believe that much work is still needed to optimize adherence, rein in specialty costs, increase utilization of more affordable pharmacies and improve quality outcomes while reducing costs for plan sponsors and public programs such as Medicare and Medicaid. We look forward to addressing these challenges as we always have — in alignment with our plan sponsors and members, based on solid scientific research and focused on practical solutions that achieve meaningful results.
Since 1986
A Legacy of Leadership and Innovation

1986
Express Scripts Founded

1987
Dispensed first home delivery prescriptions to reduce medication costs through centralization

1989
Developed first Express Scripts formulary – offering plan sponsors a clinically appropriate way to control costs

1991
Moved to 90-day prescriptions with Sanus Health Systems to further drive down member costs

1996
Began online pharmacy claims processing to integrate mail and retail claims

1999
Launched step therapy, reaffirming our dedication to providing high-quality prescription drugs at lower cost

2000
Became first major pharmacy benefit manager for Medicaid

2003
Filled our 100 millionth prescription

2004
Acquired CuraScript® to help control specialty drug costs

2008
Launched Consumerology® – the advanced application of the behavioral sciences to healthcare

2010
Opened The Express Scripts Technology & Innovation Center and The Express Scripts Research & New Solutions Lab

2011
Documented the Intent-Behavior Gap

1987
Dispensed first home delivery prescriptions to reduce medication costs through centralization

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2011
Documented the Intent-Behavior Gap
Year in Review

The pharmacy landscape in 2011 was dynamic and complex. Many patients and payers struggled to balance healthcare needs and costs with other priorities. In particular, specialty medications, while holding great promise for improved health, continued to increase in cost.

Economic recovery in the U.S. and across the globe has been slow, with many Americans facing uncertainty, unemployment and revised retirement horizons. Uncertainty remains about how the implementation of the Patient Protection and Affordable Care Act (PPACA) will unfold, even as the number of uninsured adults in the U.S. keeps increasing, recently reaching a record high of 17.1%.

Given the value we all place on health, many argue that healthcare expenditures are less discretionary than other consumer services, at least for persons covered by insurance. Although the rate of healthcare spending growth has slowed, total U.S. health spending in 2010 reached $2.6 trillion, an average of $8,402 per person and 17.9% of gross domestic product (GDP).

This slowing is likely temporary. Most health economists anticipate that as the economy improves, healthcare inflation will increase as it has done in the past.

1 THING REMAINS CLEAR

what America needs now are proven methods for providing quality care at an affordable cost.

Healthcare Reform

Both the implications and the eventual scope of the PPACA remain clouded in uncertainty, as the legislation has proven complicated and fluid. One example of its dynamic nature is how essential health benefits will be defined. A single uniform set of essential health benefits that must be offered in the individual and small-group markets was expected last year. However, on December 16, 2011, the Department of Health and Human Services submitted a proposal that would allow state officials to choose an essential health benefit template for their exchanges from certain existing insurance plans in their states. Although this proposal allows “flexibility and freedom,” it also leaves many details unresolved. The stage is set for additional administrative costs and confusion around implementation.

Debate around the PPACA remains active, as evidenced by the jettisoning of a provision for long-term care insurance. More than 25 court challenges have been filed against various parts of the law, with conflicting appellate decisions as a result. The central challenge is whether Congress has the constitutional power to require citizens to purchase health insurance or face a penalty, a feature of the law known as the individual mandate. As of this writing, the Supreme Court is slated to hear arguments on the mandate in March 2012, and a decision is expected in early summer. In addition, any shifts in the political landscape that result from the presidential and congressional elections later in 2012 could have substantial implications for the viability of the PPACA as well as for how it is implemented.

Although many of the changes provided for in the PPACA will not be put in place until 2014, others have already reshaped the healthcare industry. These include changes to the rates for Medicare providers, prescription-drug rebates for Medicare beneficiaries who have reached the “donut hole,” a requirement to cover pre-existing conditions for children, a tax credit for small businesses offering employer-sponsored insurance and extension of dependent coverage for adult children to age 26. New regulations facing group health plans and insurers for 2012 include medical loss ratio reporting, rebate payments and uniform document requirements.
Supply Chain and Retail Network Dynamics

Competition within the supply chain remains fierce as pharmaceutical manufacturers vie for market share. Double-digit trends in traditional pharmacy spend have not been seen since 2005, as our plan sponsors have increasingly embraced trend management programs (e.g., formularies, tiered copayments, step therapy programs, greater focus on home delivery). However, affected drug makers will not sit idly by as plan sponsors and their pharmacy benefit managers (PBMs) drive waste out of the system.

Recently, drug shortages have occurred more frequently – usually without warning. Affecting all segments of healthcare, particularly injectables administered in hospital or clinic settings, the frequency of drug shortages more than tripled between 2005 and 2010. The many reasons for shortages include consolidation within the industry, raw material or active pharmaceutical ingredient issues, supply chain disruptions, international sourcing, manufacturing delays and regulatory issues.

The many services that PBMs perform include negotiating competitive retail-network pricing for plan sponsors while maintaining patient access to medications. Express Scripts remains committed to ensuring that reimbursement to retail pharmacies is both competitive and commensurate with the value the network pharmacies deliver. This approach makes certain that our plan sponsors receive the most value for their pharmacy benefit dollars while ensuring sufficiently broad access for members.

Our 2011 retail-network negotiations marked another milestone in our heritage of independence from pharmacies and alignment with our plan sponsors. One retail pharmacy chain, Walgreens, was unwilling to offer rates and terms consistent with those of the market, and instead opted to leave our pharmacy network at the beginning of 2012. Although we remain open to Walgreens being part of our pharmacy network in the future, the positive reaction we received from plan sponsors and members during the process of transitioning patients to other pharmacies confirmed what our prior analyses had shown: the vast majority of the U.S. has an oversupply of pharmacies, suggesting that networks can be tightened significantly while maintaining sufficient patient access.

The frequency of drug shortages more than tripled between 2005 and 2010.

Meanwhile, the number of retail pharmacies in the country continues to grow, which means that multiple cost-effective, convenient options can be found in almost every community. Members have many choices, ranging from chain drug stores to retail pharmacies within grocery and mass retailers to independently owned community pharmacies. As demonstrated by our successful transition of members from Walgreens to other pharmacies in early 2012, most patients understand the broad access available to them.

Specialty Drugs

Concerns continue about the rising cost of specialty medications, the fastest-growing segment of drug spend. Looking at pharmacy benefits alone, 17.6% of total 2011 pharmacy costs among Express Scripts plan sponsors were for specialty medications. The real growth in specialty drug costs is somewhat hidden, however, because approximately 47% of overall specialty-medication costs are billed under medical benefits. In oncology, 78% of specialty medications are billed on the medical side.

Limited competition – exacerbated by the absence of generic alternatives and a dearth of statistically valid head-to-head comparisons – contributes to the cost of specialty agents. Effectively managing the specialty side of pharmacy benefits is increasingly complicated due to many other factors, including:

- Diminishing margins on traditional medications may lead manufacturers to seek greater profits on specialty medications.
- Patent protection on specialty medications remains highly favorable to brands.
- The number of indications is increasing for many specialty products.
- Complex, difficult-to-manage diseases often require multiple therapeutic agents.
Today, new and often more effective specialty medications are being introduced, their initiation often occurs sooner in the disease trajectory and their costs continue to rise. Plan sponsors must seek comprehensive solutions to manage specialty drug spend whether it occurs in medical benefits or on the pharmacy side of cost. In addition, programs that help patients adhere to treatment regimens are also critical, not only to achieve the best clinical outcomes associated with these medications, but also to manage overall healthcare costs.

**Personalized Medicine and Pharmacogenomics**

Personalized medicine is typically considered to be the application of genomic and molecular data to better target healthcare delivery. One aspect of personalized medicine, pharmacogenomics, examines the influence of genetic variations on drug response in individual patients. The field holds great promise, but it also comes with associated costs and many unanswered questions.

The science of pharmacogenomics aims to optimize pharmacotherapy by identifying specific genetic variants that are associated with differential effectiveness of pharmaceutical agents.

That is, the effectiveness of some drug therapies varies significantly based on specific genetic variations, and some of those variations can be detected via genetic testing. Theoretically, the use of pharmacogenomics can improve efficacy while minimizing adverse effects. However, the gene-drug relationship is highly complicated and, as with most medical technologies, each test must be evaluated carefully—test by test, indication by indication—to determine, first, whether the drug offers a net benefit and, if so, for which patients and at what cost. Although some genetic tests have passed careful, evidence-based evaluations, many have not.

As always, Express Scripts assembles the best available evidence to make informed recommendations for our plan sponsors.

We believe that **four critical questions** must be answered to determine whether a pharmacogenomic test is **clinically sound** and **cost-effective**:

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

Currently, we recommend only a subset of available pharmacogenomic tests based on the answers to the questions posed above, giving particular consideration to 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. These requirements might seem intuitive and straightforward; however, the evidence to support them is sparse (or even negative) for many pharmacogenomic tests. Exhibit 1 lists the medications for which we currently recommend testing and those lacking sufficient evidence to recommend.

Plan sponsors can manage the complicated area of pharmacogenomic testing through programs such as prior authorization, Integrated Data Services and ExpressAlliance®. We recommend pharmacogenomic testing only in areas with clear value. As new clinical evidence proves or disproves the value of additional tests, we will adjust our clinical programs accordingly.
Insights into Consumer Behavior: Mission Critical for Optimal Clinical Care

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

In the 2010 Drug Trend Report, we explained that delivering optimal health outcomes demands advanced, effective and applied understanding of consumer behavior. Frequently, what stands in the way of attaining high-quality outcomes is individual behavior. Although not the only factor, consumer behavior represents a significant, actionable barrier to excellent outcomes — outcomes that patients, clinicians and plan sponsors all want.

Improved outcomes & reduced waste are ever more important as we continue further implementation of healthcare reforms in 2014.
For 25 years, Express Scripts has worked to eliminate waste in the pharmacy benefit. We aim toward achieving optimal clinical outcomes at financially sustainable costs to plan sponsors and members.

Patients acted rationally they would engage in 3 simple pharmacy-related behaviors:

- Take medications as prescribed
- Use the lowest-cost, clinically effective medication
- Use the safest, most cost-effective delivery channel

Because many patients fail to engage in these three behaviors, the system is swamped with waste. The costs of these behavioral missteps are enormous. In 2011 alone, suboptimal pharmacy-related behavior by U.S. consumers wasted more than $408 billion—equivalent to more than $1,300 for each American. These enormous and avoidable costs provide no additional health benefits.
By the Numbers: Waste Across America

Per-Capita WASTE

HIGHEST WASTE
- Mississippi $1,504.70
- Texas $1,480.17
- Arizona $1,479.17

LOWEST WASTE
- Vermont $892.78
- Minnesota $947.53
- Maine $968.16

Colors reflect per-capita waste by state; dollar amounts represent total waste for each state in billions.

States in lowest 33.3%
- States in middle 33.3%
- States in highest 33.3%

By the Numbers: Waste Across America

INTRODUCTION

TREND OVERVIEW

THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID
A Scientific Approach to the Problem of Waste

Based on our understanding that greater insights lead to greater results, researchers at The Express Scripts Research & New Solutions Lab address plan sponsor challenges through Consumerology — the advanced application of the behavioral sciences to healthcare. Our work includes in-depth research, advanced analytics, and real-world pilot testing of solutions. In the Lab’s dedicated test-and-learn environment, we pioneered more than 45 pilots to tackle the key sources of pharmacy-related waste: where people get their medications, which medications they get, and whether they take their medications as prescribed.

408 billion in Pharmacy-Related Waste:

The simple truth is that Americans’ failure to take medications as prescribed costs the nation billions of wasted dollars annually. The need to address both the immediate costs of nonadherence and its long-term consequences has never been greater.
**INTRODUCTION**

**TREND OVERVIEW**

**THERAPY CLASS REVIEW**

**FORECAST**

**MIX WASTE: $49.8 BILLION**

**What it is:** Waste associated with the use of higher-cost medications that provide no additional health benefit compared to lower-cost options.

**What is included:** Savings could be obtained by achieving the clinical maximum generic fill rate within each therapy class, with no double-counting of mix savings already attributed to optimizing the delivery channel.

**How to eliminate it:** Programs (including step therapy, prior authorization and tiered copayment design) can help eliminate waste by encouraging the use of generics and lower-cost brands which provide the same clinical benefit as higher priced drugs. These programs also save members unnecessary excess copayment costs. Once again this year presents significant savings opportunities as many popular brand-name drugs will lose patent protection. Plan sponsors should ensure they have the necessary programs in place to capitalize on this opportunity.

**CHANNEL WASTE: $96.3 BILLION**

**What it is:** Waste that could be fully avoided if all maintenance-medication users currently in retail pharmacies moved to home delivery, if acute medications were dispensed through narrow-retail-network pharmacies and if specialty medications were distributed through optimal channels, such as CuraScript specialty pharmacy.

**What is included:** $41.1 billion of waste could be avoided through better unit pricing, lower dispensing fees in optimal channels and better management of drug mix among patients who move to home delivery. An additional $55.2 billion of waste could be avoided due to improved therapy adherence associated with the use of home delivery; this amount is attributed to both categories but not double-counted in the in the $408 billion of total waste.

**How to eliminate it:** Through effective channel-management programs, plan sponsors could eliminate waste while offering members safer, more convenient access to their medications.

**NONADHERENCE WASTE: $317.4 BILLION**

**What it is:** Waste from patients who do not take medications as prescribed, potentially resulting in unnecessary hospital admissions, avoidable emergency room visits, additional physician visits, extra laboratory tests, additional therapy and other costs.

**What is included:** The $317.4 billion reflects the total annual savings that could be achieved if all patients took medications as prescribed. Since $55.2 billion of nonadherence waste would be eliminated by optimizing channel, this amount is attributed to both categories but not double-counted in the $408 billion of total waste.

**How to eliminate it:** By investing in clinically-proven, evidence-based adherence programs that help patients take medications as prescribed, plan sponsors can help ensure optimal patient care, while eliminating nonadherence waste.
Chronic conditions affect all of us directly or indirectly. Treating chronic diseases accounts for about 75% of the healthcare dollars spent in the U.S., with two-thirds of the increase in healthcare spending since the late 1980s due to increases in the incidence and costs of chronic conditions.\(^1\) At the top of the list of chronic conditions are diabetes, high blood cholesterol and high blood pressure/heart disease.

In last year’s Drug Trend Report our analysis noted that diabetes was poised to become the largest driver of per-member-per-year (PMPY) pharmacy spend in the next few years. As shown in Exhibit 2, diabetes in fact outpaced high cholesterol for the first time in 2011, overtaking the number-one spot in PMPY spend.

A recent report from the Centers for Disease Control and Prevention (CDC) estimates that 45% of adults in the U.S. have one of the conditions treated by medications in the top three therapy classes when both diagnosed and undiagnosed prevalence is considered.\(^2\)

Already fairly common in the U.S., diabetes is becoming more common every day, with 8.3% of the population estimated to have the condition (18.8 million diagnosed and 7 million undiagnosed). An additional 79 million Americans may have pre-diabetes.\(^3\) Because age and obesity are risk factors for developing type 2 diabetes, the incidence of diabetes will continue to rise as the population ages and obesity becomes more prevalent. Anticipated increases in incidence and prevalence continue to fuel the development of new medications to treat diabetes.

Additionally, quality ratings (e.g., CMS Five-Star Quality Ratings, NCQA HEDIS scores\(^4\)) for the management of diabetes by physicians and health plans can lead to more aggressive pharmaceutical treatment. Analysis of Express Scripts data shows that the use of diabetic medications (e.g., prevalence) increased only slightly in 2011 as compared to 2010. Increased trend was driven largely by wider use of newer diabetes medications.

### Exhibit 2

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>Prevalence of Use</th>
<th>Average Cost Per Rx</th>
<th>Trend</th>
<th>%</th>
<th>PMPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$81.12</td>
<td>10.1%</td>
<td>5.4%</td>
<td>$87.35</td>
<td>7.0%</td>
<td>45.6%</td>
<td>$37.02</td>
</tr>
<tr>
<td>2</td>
<td>High Blood Cholesterol</td>
<td>$78.38</td>
<td>9.7%</td>
<td>12.2%</td>
<td>$58.84</td>
<td>2.5%</td>
<td>52.5%</td>
<td>$41.16</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$62.84</td>
<td>7.8%</td>
<td>16.1%</td>
<td>$28.18</td>
<td>-9.5%</td>
<td>32.7%</td>
<td>$20.52</td>
</tr>
</tbody>
</table>
drugs such as glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors. No new generics have been approved recently to offset the cost of new drugs in this category.

High blood cholesterol, which held the number-one spot in pharmacy spend for a decade, affects one in every six American adults (16.3%). Individuals with high blood cholesterol have twice the risk of heart disease—a major cause of death in the U.S. and a major driver of healthcare costs. Elevated low-density lipoprotein cholesterol (LDL) can be treated effectively. However, of the estimated 71 million adults with high LDL, fewer than half (48%) were treated and only one-third (33.2%) had their LDL controlled. Lipitor® (atorvastatin), the most popular brand medication to treat high cholesterol, lost patent protection in late November 2011. Generic versions of Lipitor, which were introduced too late in 2011 to have a significant impact on trend for the year, are expected to have a pronounced and favorable effect on costs in this category in 2012. Enhanced health plan quality measures for cholesterol management, anticipated in 2012, are likely to fuel increased use of statin medications over the next few years.

High blood pressure is among the most common chronic conditions. Approximately one-third of U.S. adults—76.4 million individuals—have elevated blood pressure. More than half of those diagnosed with high blood pressure fail to reach adequate levels of control. The abundance of generics in the category, especially among angiotensin-converting enzyme (ACE) inhibitors, offset utilization trends in 2011. The first generic angiotensin receptor blocker (ARB), which was approved in 2010, also contributed to reduced costs. As with diabetes and high blood cholesterol, new quality measures are in place for evaluating cholesterol treatment. The scheduled 2012 release of The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) is expected to increase awareness of and influence treatment decisions for high blood cholesterol in coming years.

The conditions treated by the top three traditional therapy classes have several things in common. First, they often treat comorbid conditions in the same patient. About one in eight Americans (13%) has two of the three conditions; almost 3% live with diabetes, high cholesterol and high blood pressure.

Second, all three conditions share a common key risk factor: excess body weight. Today, adults of normal weight are in the minority: only 35.3% of the adult U.S. population is of normal weight. Of even greater concern, the obesity rate for children in the U.S. has tripled since the mid-1970s. As a result, chronic conditions such as type 2 diabetes, high blood cholesterol and high blood pressure, once found almost exclusively in older adults, are now increasingly common in younger adults and children. Consider that one national study found that nearly one-third of eighth graders were pre-diabetic. Serious implications for the future health of our nation are easy to see.

Third, as with most chronic conditions, diabetes, high cholesterol and high blood pressure have significant behavioral components, in both risk factors for developing them and protocols for managing them once they are diagnosed. In terms of prevention, the World Health Organization (WHO) reports that eliminating just three behavioral risk factors—being overweight or obese, getting insufficient exercise and smoking—would prevent 80% of heart disease, stroke and diabetes and 40% of cancer cases. Once a patient is diagnosed, however, prescription-drug therapy is often a major component of care. Self-care is particularly important with chronic conditions. Estimates are that more than 95% of diabetes care is conducted by the patient. Behavior is central to this type of care—making decisions and finding ways to implement healthy behaviors within the context of other goals, priorities and demands of daily life.

Fourth, medications that are effective in controlling diabetes, high cholesterol and high blood pressure can help reduce healthcare costs when taken as prescribed. Adherence to prescribed drug therapy is one of the most important self-care behaviors for maintaining or improving health and preventing disease progression for patients with chronic conditions. But despite the benefits of taking medications as prescribed, adherence rates are far from ideal—behavior that is both costly and dangerous. Our research estimates that the national cost of nonadherence for these three conditions alone exceeds $105.8 billion per year.
45.1% of adults in the U.S. have **one or more** of the conditions treated by medications in the top 3 therapy classes.

<table>
<thead>
<tr>
<th>Therapy Class</th>
<th>Total Affected (%)</th>
<th>Adults Affected (%)</th>
<th>Children Affected (%)</th>
<th>Undiagnosed/Prediagnosed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>45.2%</td>
<td>8.0%</td>
<td>0.2%</td>
<td>37.0%</td>
</tr>
<tr>
<td>High Blood Cholesterol</td>
<td>32.7%</td>
<td>16.2%</td>
<td>8.5%</td>
<td>8.0%</td>
</tr>
<tr>
<td>High Blood Pressure/Heart Disease</td>
<td>45.1%</td>
<td>33.5%</td>
<td>3.6%</td>
<td>8.0%</td>
</tr>
</tbody>
</table>
There are common behavioral components both in risk factors for developing and in protocols for managing these 3 diseases.

**Did you know?**

**Weight** is a key risk factor.
- 63.1% of adults are overweight or obese.²²

**Adherence** is critical for managing these diseases.
- 39% of those in the top 3 are nonadherent.³¹

**What can be done?**

If people stop smoking, lose weight and exercise more, 80% of these diseases can be prevented.³⁴

If we improve adherence in the top 3, $105.8 billion of waste can be eliminated.³⁵

The **OLD** methods DON'T work. It's time to look at this in a **NEW** way...
Nonadherence is a national issue: patients who fail to take medications as prescribed have higher healthcare costs. They often suffer from unnecessary complications, including heart attacks, strokes, heart failure, peripheral vascular disease, amputations, retinopathy, end-stage renal disease and vision loss. As noted earlier, we estimate that failure to take medications as prescribed costs the U.S. approximately $317 billion annually. Nearly $106 billion of this annual cost is due to nonadherence to medications for diabetes, high cholesterol and high blood pressure/heart disease.

Nonadherence to medication therapy is one of the most costly and difficult challenges facing plan sponsors. Nonadherence arises from multiple sources, including clinical concerns, financial issues and behavioral reasons; it cannot be solved with a one-size-fits-all approach. Moreover, although the healthcare system has historically relied on pharmacy claims data to detect nonadherence, these data do not provide insight into the unique cause of each patient’s nonadherence. Another limitation is that pharmacy-claims data can alert us to nonadherence only after the fact. To address these issues, Express Scripts researchers have directed considerable efforts to seeking answers to questions about nonadherence. We firmly believe that this ongoing work has set the stage for new solutions capable of effectively confronting the challenge of nonadherence.

Do Patients Intend to Take Medications as Prescribed?

Published research about the value of adherence most often falls within one of two primary categories: studies that provide supporting evidence for the clinical or economic value of adherence or those that demonstrate that patient beliefs about medications impact adherence. However, little research has evaluated the importance that patients place upon adherence to prescribed medications. To remedy this knowledge gap, we designed a study to help us understand the perceived value of medication taking and medication adherence, as well as the relative importance of adherence compared to other health behaviors.

For this study, we conducted an online survey of more than 40,000 randomly selected Americans age 18 or older who were currently taking a medication used to treat at least one chronic condition. We asked participants how they valued taking medication relative to other health behaviors. In view of the pressures from the poor economy, we also set out to measure the impact of economic stress on health behaviors, including medication adherence.

The results from our survey show that Americans highly value medication adherence as an important health behavior. Over 81% of survey respondents agreed that skipping medications is bad for them, and more than 90% agreed that taking medications as prescribed is important for their health.

When survey participants ranked the importance of several health behaviors, medication adherence was valued as the most important, followed by avoiding smoking and eating a healthy diet.

### Exhibit 3: Most Important Health Behavior, All Respondents

<table>
<thead>
<tr>
<th>Health Behavior</th>
<th>0%</th>
<th>5%</th>
<th>10%</th>
<th>15%</th>
<th>20%</th>
<th>25%</th>
<th>30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taking medication as prescribed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoiding smoking</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Eating a healthy diet</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Getting enough sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Getting enough exercise</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoiding overeating</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Getting an annual flu shot</td>
<td></td>
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</tr>
</tbody>
</table>
We also examined a number of other factors that might affect participants’ views on medication adherence: the medications the respondent was taking, whether the medication was for a symptomatic condition or an asymptomatic condition, whether the medication was a traditional medication or a specialty medication, and the degree to which the respondent was concerned about the economic environment. In all but one case, being adherent to medication therapy was ranked as the most important behavior. The exception was among patients who were taking medications for high cholesterol. They ranked avoiding smoking and eating a healthy diet to be of similar importance to taking their medication as prescribed. In short, patients of all types – regardless of their concerns about the economy (which was used as a proxy for their economic condition) – rated adherence as an extremely important behavior. This study makes clear that most people intend to take their medications as prescribed.

Are Patients Aware of Their Own Nonadherence?

If Americans value taking their medications as prescribed, why aren’t they doing it more regularly? Despite the benefits of taking medications as prescribed, research suggests that adherence rates may be lower than 50% in some cases. A tantalizing hint emerges when we examine the level of adherence that patients believe they maintain. Our survey asked participants what percentage of time they took medications as prescribed. Self-reported adherence behavior was high; 85.2% reported taking their medications as prescribed at least 80% of the time. But if more than 85% of a national sample of adults taking chronic medications report being adherent to therapy, why are actual adherence rates much lower?

In a separate study of Express Scripts members, we set out to assess whether self-reported adherence differed from actual adherence. We asked these members questions such as whether they ever missed doses of medication, how often they missed a dose, and what percentage of time they took their medications as prescribed. From their answers, we computed a perceived medication possession ratio (perceived MPR). Medication possession ratio is a commonly used measure of adherence that is estimated by dividing the days’ supply of medication that a patient has on hand by the number of days for which medication should be available to that patient. The results from our member survey were strikingly similar to the results of our national survey – most people report that they are adherent.

When we compared perceived adherence to the patients’ actual MPR, what we found was remarkable. First, almost all patients overestimate their adherence. Second, and perhaps most important, the degree of overestimation is greatest for patients with the lowest adherence.

For example, patients in the least-adherent group in the survey of Express Scripts members had an average actual MPR of 24.3%. The average perceived MPR reported by patients in this group, however, was 90.6%. We therefore found a staggering 66% gap between perceived MPR and actual MPR.

Using Predictive Models to Identify Patients at Risk for Nonadherence

This situation is vexing, because it means that patients are unaware of the adherence problems they face, and, by extension, their doctors are often also unaware. Although we could use pharmacy claims data to identify patients who refill their prescriptions late (and therefore probably are nonadherent), we would have to wait until well after the problem had occurred to detect the issue.

In 2010 we developed high-performing predictive models for estimating the chance of future nonadherence among patients taking medications to treat diabetes, high cholesterol and high blood pressure/heart disease. These proprietary models identify specific patterns and characteristics that reliably indicate in advance whether an individual member is at increased risk for nonadherence. Specifically, using hundreds of variables, the models generate a score — the Express Scripts Adherence IndexSM — indicating the likelihood that the patient will be adherent over the next 12 months. Our models have been proven through repeated validation using different patient samples and data from different time periods.
To determine whether our predictive models are more accurate than the patient’s own perceptions of adherence, we further analyzed results for the least-adherent participants in our member survey. We compared each nonadherent member’s perceived MPR to the individual’s Express Scripts Adherence Index score. We found that only 10.1% of these members correctly believed they were nonadherent. In contrast, the Express Scripts Adherence Index predicted that 88.1% of these patients would be nonadherent. In short, the Express Scripts Adherence Index was 8.7 times more accurate than the members themselves (Exhibit 4).

**What Is Causing Patients to Be Nonadherent?**

Our research identified **three** interlocking findings:

- Patients overwhelmingly view adherence to medication therapy as being among the most important of their health behaviors.
- Patients significantly overestimate their own adherence to medication therapy.
- Our predictive models offer a powerful alternative for identifying, in advance, patients who are at increased risk of nonadherence.

**However, two questions remained:**

- Why are patients nonadherent to medication therapy?
- What is the relative frequency of those causes?

These are critical questions because the possible causes of nonadherence are numerous, and each comes with a different implication for improvement of adherence. Causes of nonadherence include simply forgetting to take medicines, delaying refills, neglecting to renew expiring prescriptions on time, questioning effectiveness, being concerned about possible side effects, resisting being “medicalized” and worrying over a number of other issues including costs and side effects.

To determine the relative frequency of these causes—and how best to address them—we are conducting a large pilot that includes more than 600,000 members from dozens of plan sponsors and nearly 130,000 interventions to date. The goal is to categorize the causes of nonadherence in real-world settings. The preliminary results are shown in Exhibit 5. In contrast to the common belief that patients are nonadherent due to cost or clinical concerns, we found that over two-thirds of nonadherence was due to inattention and procrastination—39% of nonadherent patients simply forget to take their medications, 10% procrastinated on getting their refills and 20% did not renew their prescriptions on time. Taken together, forgetting to take medications, failing to get medications refilled and procrastinating on prescription renewals account for most nonadherence.
As observed in our survey research, although most patients want to be adherent, those who aren’t adherent are unaware of the problem. Such findings lead us to believe that the main driver of nonadherence can best be described by the intent-behavior gap—the difference between what people want to do and what they actually do.

This divide between what people want to do and what they actually do can be attributed to the “50-bits” problem. The human brain processes information at a rate of about 10 million to 12 million bits per second; the conscious part of the brain, however, processes only about 50 bits per second. Therefore, people are wired for inattention and inertia. We tend to focus our 50 bits on things that are either pressing or pleasurable. For many patients, remembering to take medicine as prescribed, ordering refills or calling the doctor for a prescription are neither pressing nor pleasurable. Although most patients intend to take their medications as prescribed and often believe they are adherent, the truth is they need help to activate their good intentions.

Patient Education Is Not Enough

With their promises of lower cost and better outcomes for people living with chronic conditions, disease-management programs offered hope to many plan sponsors. Over the last several years, however, formal evaluations of these programs have shown disappointing results. A recent Congressional Budget Office (CBO) report that looked at disease-management and care-coordination programs for Medicare beneficiaries found that these programs overall did not create net savings after program costs were included. Although education-based programs increased the percentage of participants who reported being taught self-management skills, they had little or no effect on actual behavior as measured by patient-reported adherence to prescribed self-care regimens.

Our studies led us to an approach completely different from typical patient education. First, we recognize that the majority of patients already understand the importance of adherence. Furthermore, we now know that most nonadherent patients fail to recognize the issue. Although we understand the value of education, we know it will have little effect for the most likely causes of nonadherence: inattention and procrastination.

To test this, we studied the impact of inexpensive reminder devices that emit an audible signal when it is time for patients to take their medication. In this pilot study, use of this device increased the fraction of patients who became adherent to therapy by 6.25% over controls. Targeting these devices to patients at mid-range risk, based on the Express Scripts Adherence Index, doubled this effect. For most nonadherent patients, less-expensive and more-effective interventions (e.g., daily reminders) are more likely to be successful than the interventions that are central to disease-management programs.
Treating Nonadherence as a Medical Condition

Although our studies had given us a much deeper understanding of nonadherence, the path to a practical solution was not yet clear. Knowing that the biggest breakthroughs sometimes occur when the problem is reframed, we took a step back and looked to success stories in overall healthcare.

Over the past 10 years, significant medical progress has reduced disability and death from the top three most devastating diseases: heart disease, cancer and stroke. Although many factors contributed to these gains, one that stands out is the increased use of effective screening programs for diseases (e.g., hypertension, colorectal cancer).

Successful screening hinges on two interlinking factors:

- Identification of at-risk individuals early in the course of a disease (before overt symptoms are observed).
- Use of interventions that are more effective earlier in the disease course.

Reflecting on the success of screening for many medical conditions, we started to reframe nonadherence as if it were a medical condition. In other words, if we treated nonadherence as a disease, what might we do differently?

One solution was immediately clear: we should screen for nonadherence.

Screening for Nonadherence

Put simply, just as medical screenings make it possible to detect health issues before they are well advanced, detecting nonadherence before it starts provides unprecedented opportunities to improve health outcomes and reduce waste.

Screening for nonadherence requires two capabilities:
1. Identify patients who are at risk for nonadherence
2. Deliver effective interventions to those at risk

Our predictive models provide the first capability by identifying members who are at risk for nonadherence. To deliver the second – an intervention structured for the at-risk individual – we developed a proprietary set of questions to identify the likely adherence obstacles facing the individual patient. By combining our predictive models and our tailored interventions, we have created a screening and intervention tool for nonadherence.

This new program – to be released later in 2012 – is called ScreenRx.
Express Scripts is focused on creating more efficient and effective healthcare solutions to help patients deal with the challenges of managing their health. These new solutions are designed to make better health decisions easy, natural and intuitive.

**Introducing Our Breakthrough Adherence Solution: ScreenRx**

ScreenRx is our proprietary adherence solution that combines early detection with tailored interventions. Avoiding or lessening nonadherence before it starts improves long-term health for patients and can lower costs for plan sponsors.

To focus initial ScreenRx efforts where they are most needed, Express Scripts has identified the most critical disease states that benefit from improved adherence. Evidence shows that five nationally prevalent conditions—asthma, diabetes, high cholesterol, high blood pressure/heart disease and osteoporosis—cause significant increases in medical spend for plan sponsors.

Through the use of our predictive models, ScreenRx combines clinical and behavioral factors to accurately detect which individual patients are at risk of not taking medications as prescribed, up to one year in advance. Once these at-risk patients are detected, we perform diagnostic outreaches to identify adherence obstacles for each individual. Finally, we leverage our understanding of human behavior to tailor interventions for patients who are at risk for nonadherence.

For the 69% whose nonadherence is due to behavior-related issues, we offer customized interventions and personalized services such as:

- Dose reminders (e.g., timers)
- Renewal reminders (e.g., messaging on prescription bottles)
- Transition to the Express Scripts Pharmacy (which reduces refill procrastination)
- Auto refills of medications (which reduce the need for patient action)

For the 16% of patients for whom cost is a potential barrier, we help identify lower-cost delivery channels and lower-cost medications. Only 15% of patients are nonadherent due to clinical factors. With ScreenRx, we identify these patients and offer individualized consultation with a pharmacist.

The distribution of causes of nonadherence—69% due to inattention and inertia, 16% due to cost and 15% due to clinical concerns—turns existing interventions such as copay waivers and disease management on their heads. Rather than assuming that most adherence is an active decision by patients (e.g., drug too costly, causes side effects, may not be working), ScreenRx recognizes that most nonadherence can be addressed more effectively and at a lower cost by helping patients remember to take their medications on time and by reducing procrastination on refills and renewals. By recognizing at-risk patients with clinical concerns up front, we direct the most-expensive and most time-consuming interventions to the small fraction of patients that presents the greatest degree of risk. Balanced solutions, such as ScreenRx, are what plan sponsors are asking for—programs that provide optimal clinical care for patients and greater savings for plan sponsors.

**Plan sponsors should judge claims of the effectiveness of adherence programs very carefully: failure to compare an adherence intervention to a proper control group inevitably overestimates the effectiveness of the intervention.**

Breakthrough adherence programs such as ScreenRx are critical to ensuring optimal patient care. When coupled with other types of solutions designed to meet the needs of a specific plan sponsor, optimal care and lower costs can be achieved. We highlight some of our other solutions on the following pages.
Nonadherence: the $317 billion problem

There is $408 billion in total pharmacy-related waste. Of this waste, $317 billion is due to nonadherence.

Eliminating nonadherence can cover the cost of healthcare for 44.8 million Americans.
Adherence matters to people.

46% of Americans have chronic conditions requiring long-term use of maintenance medications.

90% of those with chronic conditions say taking medication as prescribed is important for their health.

So why are people nonadherent?

Our research shows that there is a gap between many patients’ perceived adherence and their actual adherence.

89% of nonadherent people report that they are adherent.

The Perception Gap

Patient-Specific Obstacles

<table>
<thead>
<tr>
<th>BEHAVIORAL</th>
<th>COST</th>
<th>CLINICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>39% missed dose</td>
<td>16% cost</td>
<td>15% clinical</td>
</tr>
<tr>
<td>20% late renewal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10% late refill</td>
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</tbody>
</table>
Rethinking Nonadherence

Taking a cue from the success of screening for medical conditions, we started to think about nonadherence in a new way.

We asked, if we treat nonadherence as a condition, what might we do differently?

One solution was clear: we should screen for nonadherence.
ScreenRx detects future risk for nonadherence and tailors interventions for individual patients.

**EARLY RISK DETECTION**

Just as medical screenings make it possible to detect health issues before they are well-advanced, detecting nonadherence before it starts provides unprecedented opportunities to improve health outcomes and reduce waste.

- Proprietary predictive models
- Up to 98% accuracy in predicting nonadherence up to one year in advance

**TAILORED INTERVENTIONS**

Nonadherence springs from multiple causes and cannot be solved with a one-size-fits-all solution. ScreenRx uses a personalized approach to overcome patient-specific obstacles.

- Predictive data paired with customized interventions and personalized clinical services
Enhancements to Select Solutions, Powered by Choice™

In 2011, Express Scripts introduced several enhancements to our family of Select Solutions products. Select Solutions programs identify each member’s underlying intent and then make acting on those preferences as easy as possible for the individual. This approach drives better program performance while preserving individual choice.

Select Network – Copay Differential: Select Network is a choice-based solution that drives out waste in the retail channel. Plan sponsors may choose between two programs: with and without a copayment differential. Select Network allows members to opt out before being automatically enrolled in a network of pharmacies that offer reduced rates. Introduced in 2011, Select Network – Copay Differential adds a financial incentive to use more cost-effective pharmacies. The estimated plan-sponsor savings for Select Network are up to $13 PMPY.

Select Home Delivery – Opt Out: Select Home Delivery (SHD) is a choice-based solution that requires members to choose either the Express Scripts Pharmacy or remain at retail with no financial penalty for their maintenance prescriptions. Introduced in 2011, our SHD – Opt Out approach gives members 60 days to opt out of the exclusive use of the Express Scripts Pharmacy, generating estimated savings of up to $30 PMPY.

Select Step Therapy – Comprehensive: For plan sponsors without current step therapy programs, the Comprehensive version of Select Step Therapy allows members to opt out before implementation of a step therapy program. Select Step Therapy – Comprehensive results in nearly 100% participation, a higher generic fill rate and 2.6 times greater savings in the first year than similar plans not participating in this program.

Select Step Therapy – Focused: For plan sponsors who have step therapy with grandfathering in place, Select Step Therapy offers a choice-based solution to generate additional savings by reducing grandfathering. Plan sponsors piloting the focused version of step therapy realized a 22% overall increase in annual ingredient savings for their targeted step therapy modules.

The Express Scripts Pharmacy Delivers Greater Patient Care

The Express Scripts Pharmacy is the most reliable path between patients and their medication. Through best-in-class pharmacy technology and ongoing innovation, we provide solutions that deliver greater safety, lower costs and optimal clinical care. In fact, our research shows that members who use the Express Scripts Pharmacy have up to 8% higher adherence than those who use retail – demonstrating yet another way to tackle the problem of nonadherence.

Dispensing accuracy for the Express Scripts Pharmacy: 99.99+%  
Average dispensing accuracy for a retail pharmacy: 98.30% 
Our pharmacies eliminate 2 million drug errors each year as a result of our improved accuracy vs. retail.
The Future of Retail Pharmacy Networks

The U.S. now has about twice as many pharmacies as grocery stores. When it comes to filling prescriptions, there is clearly an oversupply of pharmacy access. Not every pharmacy must be included in a plan sponsor’s retail network to ensure sufficient access.

Our successful transition of Walgreens utilizers to more cost-effective pharmacies with minimal member noise demonstrated a new way to eliminate waste through proven channel management strategies. We strongly believe that plan sponsors need choice-based retail solutions that balance the needs for lower costs, pharmacy access and improved clinical outcomes.

For release in early 2013, Express Advantage Network™ is a new choice-based solution that combines tiered retail networks with member engagement and cost sharing to achieve greater savings for plan sponsors with minimal member noise. With Express Advantage Network, members will still have access to an open network of pharmacies but at higher copayments. This approach offers plan sponsors a new option for lowering costs, improving health outcomes and preserving member choice.

ExpressAlliance®: Coordinating Member Care

ExpressAlliance provides solutions for a highly fragmented healthcare system by improving coordination of care and optimizing adherence. By combining our data expertise with our pharmacist consultation services, ExpressAlliance supports total health management strategies for our plan sponsors.

Through best-in-class clinical targeting and coordination with a plan sponsor’s other health-management vendors, we add the pharmacy expertise needed for effective clinical interventions. ExpressAlliance goes beyond data integration by enabling pharmacists to consult directly with nurse advisors, significantly improving the quality of patient outreach. Gaps in care are closed, duplication of health services is prevented and health outcomes are improved.

Specialty Benefit Services: Complex Conditions Need an End-To-End Solution

Although inflation, rising utilization and new specialty drugs will keep drug spend climbing, Express Scripts Specialty Benefit Services can help by managing specialty utilization under both pharmacy benefits and medical benefits, in all sites of care and during any phase of treatment.

Plan sponsors no longer are forced to choose between limiting increases in specialty drug spend and improving care for specialty patients. Specialty Benefit Services helps plan sponsors eliminate waste while optimizing patient outcomes. Furthermore, we support specialty providers by reducing their administrative costs. The results are increased efficiencies and enhanced care across the entire healthcare delivery system.

Using many of the same utilization, trend, channel and reimbursement management tools that have proven successful for the pharmacy benefit, we manage medications billed in the medical benefit.

Unique in our industry, Specialty Benefit Services offers:

- Specialty Medical Benefit Management from Care Continuum™, an Express Scripts company
- Specialty Pharmacy Benefit Management, a core service of Express Scripts
- Specialty Pharmacy and Distribution from CuraScript® the Express Scripts specialty pharmacy, and from CuraScript Specialty Distribution™ (CuraScript SD)

Better Care, Lower Costs

Quality care for specialty patients — who face some of the most complex, costly and challenging issues in healthcare — has important implications not only for health outcomes but also for overall health spend. Especially for patients in critical-care areas such as oncology, transplant, bleeding disorders, pulmonary hypertension and intravenous immunoglobulin, nonadherence to therapy can lead to expensive, dangerous
adverse health events. In fact, keeping one transplant patient adherent to anti-rejection therapy can avoid more than $19,190 in wasteful medical costs per year.\textsuperscript{33}

Our specialty pharmacy, CuraScript, starts every patient on a path to better adherence by providing an initial health assessment – a primary feature in our accreditation from the Accreditation Commission for Health Care. We ensure patients receive education about their conditions and medications. Throughout the course of their therapy, we provide patients with ready access to clinical experts, including regular clinical assessments to ensure they have no obstacles to taking their medications as their doctors have prescribed. Among our cancer patients taking Gleevec\textsuperscript{®} (imatinib), 63\% achieved an MPR of 90\% or better compared to 53\% who used retail pharmacies. (Exhibit 6)

Compared to other drug-delivery channels, including retail pharmacies, CuraScript offers patients more personalized clinical support from experts in specific diseases, frequent clinical touch points, extensive monitoring, greater resources and education about diseases and the medications used to treat them. As a result, we support our patients, particularly those new to specialty therapy, with the resources they need to make informed decisions. Our industry-leading adherence results document the difference. As shown in Exhibit 7, CuraScript patients enrolled in Oncology Care, a program proven to help cancer patients stay on therapy, achieved adherence rates 12\% higher than those for similar patients who received their medications through retail. Adherence was measured by MPR.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Exhibit_6.png}
\caption{Exhibit 6 \quad Medication Possession Ratio (MPR) of Patients Taking Gleevec\textsuperscript{®}}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Exhibit_7.png}
\caption{Exhibit 7 \quad Adherence: CuraScript and Oncology Care versus Retail\textsuperscript{34,35}}
\end{figure}
Managing Patients and Costs Across the Pharmacy-Medical Spectrum

Another important element of a comprehensive set of specialty solutions is the ability to manage patients regardless of where they receive medications: home, doctor’s office, hospital, clinic or any other location. Providing consistent, coordinated care across all treatment locations allows us to treat the specialty patient, not just the pharmacy-drug utilizer. Patients benefit through better coordination of care. Plan sponsors benefit through better visibility to the most clinically sound and cost-effective channels.

Because we manage patients and drugs across all sites of care, we can focus on driving out wasteful spend entirely, not simply shifting unnecessary costs from the pharmacy benefit to the medical benefit or vice versa. Our site-of-care management programs achieve savings for plan sponsors while ensuring patients receive the care they need from the healthcare practitioner best suited to deliver it. Based on plan sponsor and patient preferences, we direct each patient to the most cost-effective and clinically appropriate site of care for the administration of each drug. For example, when clinically appropriate, we encourage drug administration to occur in a physician’s office or in a patient’s home rather than through an outpatient hospital setting, typically the most expensive site of care.

Regardless of the site of care or where the drug is administered, our utilization-management tools ensure patient safety and protect against the inappropriate use of high-cost drugs. Our prior authorization, quantity management and clinical policy management programs in both the pharmacy and medical benefit afford plan sponsors an improved level of control over specialty medications.

We also deliver cost savings and improved rebates through our ability to prefer medications in both pharmacy and medical benefits. One such program on the pharmacy side, Specialty Step Management, delivered plan sponsor savings of up to 10% on overall specialty spend in 2011.

Supporting Specialty Providers

Our end-to-end solution allows us to serve not only patients and plan sponsors, but other providers as well. By managing the specialty drugs billed in both pharmacy and medical benefits, we better support clinicians who care for specialty patients. By alleviating the many administrative demands on specialty provider practices, our services allow providers to focus on delivering care to patients. Aligning with physicians’ offices helps maintain quality care for patients while preserving appropriate physician reimbursement.

Complementing CuraScript, our specialty pharmacy, we also offer direct medication distribution services to physician offices through our wholly owned subsidiary, CuraScript Specialty Distribution (SD). Providing physician practices access to essential therapies preserves and enhances in-office care for specialty patients. CuraScript SD also focuses on reducing wasteful costs. Our Total Account Management approach improves the efficiency of specialty practices through dedicated support for everything from revenue-cycle management and inventory controls to rebate management and volume aggregation.

We also offer physician offices ExpressPAth™, a web-based provider portal that allows providers and their designated office staff to request prior authorization (PA) online. A user-friendly system, ExpressPAth gives providers an easy solution to manage PAs for drugs in both pharmacy benefits and medical benefits.

Our reimbursement practices speed and simplify payments to providers. And, through our large buying power, we can obtain wide access to medications and the best pricing on many specialty drugs. As a result, we also administer a competitive provider fee schedule that can generate savings for plan sponsors while maintaining reimbursement levels for physicians.
Express Scripts 2011 Drug Trend Report

Medicare and Medicaid: The Only Constant Is Change

Six years ago, the nation was focused on ensuring that the Medicare population had access to prescription medications. The focus has shifted, however, due to rising healthcare costs, the influx of baby boomers to the Medicare program and uncertain economic conditions. Now, the Centers for Medicare & Medicaid Services (CMS) mandates a more careful approach to the management of healthcare costs. To that end, CMS introduced Five-Star Quality Ratings (star ratings) for health-plan services. CMS evaluates each health plan on several key measures, including some that reflect how well prescription medications are used. Express Scripts can assist our plan sponsors in achieving high star ratings in pharmacy-related categories.

In the Medicare population, the Express Scripts approaches to adherence and affordability are working. Not only do the adherence levels of our patients exceed CMS targets, health plans that have implemented our trend programs also have been better able to control costs while preserving member coverage.

Medicaid has been the financial safety net for many Americans since its inception in mid-1965. Changes over the past 25 years have caused it to grow into the nation’s largest health-related funding source for patients with limited incomes. Providing coverage to the elderly, low-income families and the disabled, the program has seen its enrollment increase dramatically since the recession began in 2008. The PPACA has also paved the way for another dramatic increase in the number of Medicaid beneficiaries due to the expansion of eligibility requirements.

Managing pharmacy benefits for more than 4 million (or 7% of) Medicaid recipients in managed care plans, Express Scripts understands the factors that drive prescription-drug trend in Medicaid. We help plan sponsors contain pharmacy spend through lower-cost brand and generic utilization, which ensures clinically effective care. We also leverage the use of less-expensive, clinically superior delivery channels, such as home delivery, that increase medication adherence. Our fraud, waste and abuse programs help better manage pharmacy benefit budgets through proactive investigations and collaborative consultations.

Public policy changes as well as changes in demographics and in CMS requirements contribute to the cost and utilization of prescription drugs by the Medicare and Medicaid populations. Express Scripts is committed to driving out waste and achieving better health outcomes by maximizing pharmacy benefits for both rapidly growing groups.

Greater Insights, Greater Solutions

In the face of a particularly difficult year for many Americans, Express Scripts continued to apply effectively what we’ve learned over a quarter century: high-quality care and low-cost medications are not diametrically opposed but rather go hand in hand.

We have spent years studying human behavior as it pertains to taking medication. Our solutions focus on patients who are at risk and intervene with choice-based designs that activate the good intentions that patients already have.

With Express Scripts, plan sponsors can choose from a proven, research-based suite of products and services to meet their specific needs. By becoming part of the solution, plan sponsors are helping to eliminate pharmacy waste and reduce healthcare spending across the country.
Trend in Review

Over the last five years, one main pattern in pharmacy spend has emerged: growth in the year-over-year spend per member per year (PMPY) has slowed (Exhibit 8). From 3.6% in 2010, the overall trend fell to 2.7% in 2011, the lowest percentage observed since Express Scripts began tracking trend. After several years of increase, specialty trend eased slightly in 2011, to 17.1% (down from 19.6%), although the increase still represented a substantial year-on-year cost growth for plan sponsors. (Note: The estimated 47% of specialty medication costs that are billed under medical benefits is not included in our trend calculations.) Trend for traditional drugs fell to a record low of 0.1%, with downward pressures associated with a higher generic fill rate offsetting other factors. The methods we used to calculate trend are explained in Appendix 2.

2011 Drug Trends

As for previous years, the Express Scripts 2011 Drug Trend Report continues to lead the industry in providing the most in-depth analysis of prescription spending patterns in the U.S. This year’s Drug Trend Report continues to focus on waste – situations in which patients and plan sponsors spent more but realized no incremental health benefit in return.
Behavioral Factors Versus Market Factors

As noted previously, we have identified three key areas of waste that are created by specific patient behaviors:

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

Accordingly, we have divided the 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:

- **Prevalence** — changes in the fraction of members taking medications; the many factors influencing prevalence include members’ lifestyle choices, prescribing behavior of physicians, changes in views about what care is deemed appropriate care, access to healthcare, social factors and genetic predisposition
- **Cost per Unit (cost/unit)** — ingredient cost plus taxes plus administrative fees less rebates for each dispensed unit (e.g., pill, gram, mL)
- **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 2011
- **New Drugs** — the impact on spending from new branded-drug entrants in 2011

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

**Behavioral factors** focus on whether patients are taking medications as prescribed, 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

Although we do not track the effect of channel use (e.g., use of home delivery from the Express Scripts Pharmacy instead of retail for maintenance medications) for year-over-year trends, channel use is important. The direct savings from home delivery are significant, and additional benefits are realized from the improved drug mix and better therapy adherence found in patients who move from retail to home delivery.

In addition to reporting the effects of member behaviors on trend (i.e., year-over-year change in spend), we also estimate the overall waste due to pharmacy-related behaviors. Overall waste typically far exceeds the behavioral elements of trend because a substantial amount of waste persists year after year.

**A Closer Look at 2011 Trend**

The components of overall trend are outlined in Exhibit 9, along with breakdowns for traditional drugs and specialty drugs. Despite a 17.1% increase in total specialty trend, overall trend in 2011 (2.7%) was the lowest in the history of the Drug Trend Report, thanks to almost no change in traditional spend (i.e., nearly flat trend).

In general, market factors moved trend upward. However, patent expirations showed negatives across the board; this is expected to continue as a number of widely used brand drugs lose patent protection in 2012. Following the pattern of the last few years, the single market factor driving positive trend was cost per unit due to price increases. Compared to 2010, the percentage increase in cost per unit slowed a little for specialty drugs but nearly doubled for traditional drugs. This finding for 2011 was not unexpected, because manufacturers continued to put price pressure on the market for products
nearing loss of patent protection. New drugs made a considerable impact on specialty trend as well, with nine new medications for cancer introduced during the year.

By contrast, behavioral influences for traditional medications – primarily greater use of generics – drove trend down more than 4%. (Note that greater adherence – which is in general desirable – leads to a positive increase in intensity, an offsetting factor.) Mix was not as favorable for specialty medications, leading to a 3.0% decrease in the behavioral elements of overall trend.

Upward pressure on unit costs was the key driver of trend in 2011.

Traditional Medications

The top 15 traditional therapy classes are shown in Exhibit 10. Together, they made up nearly three-quarters of traditional drug spend. For the top 15 classes, a 4.5% decrease attributed to behavioral factors nearly offset all of the 4.9% increase from market influences. Adding trend for the other traditional classes brought the total trend to only 0.1%. At $804.27, total PMPY spend for traditional drugs was only slightly higher ($0.86) in 2011 than in 2010.

For the first time, drugs to treat diabetes surpassed all other traditional classes to become the first-ranked class by PMPY spend. In 2011, PMPY cost for diabetes drugs jumped more than $5 to reach $81.12 and accounted for 10.1% of total PMPY spend for traditional drugs. High cholesterol drugs, now in the second spot on the list, were not far behind at $78.38 and 9.7%, respectively. Both top classes had increases in total spend (i.e., positive trend). However, several other traditional classes, especially high blood pressure/heart disease and ulcer disease, saw considerably decreased spend as a result of heavy generic use. This downward trend is likely to continue into 2012 as a number of highly prescribed brand medications such as Lexapro® (escitalopram), Plavix® (clopidogrel), Seroquel® (quetiapine) and Singulair® (montelukast) – each with well over $2.5 billion in annual sales – are scheduled to lose patent protection.
## Components and Drivers of Trend for the Top 15 Traditional Therapy Classes, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Market</th>
<th>Behavioral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$ 81.12</td>
<td>10.1%</td>
<td>$5.27</td>
<td>8.3%</td>
<td>-1.3%</td>
<td>7.0%</td>
</tr>
<tr>
<td>2</td>
<td>High Blood Cholesterol</td>
<td>$ 78.38</td>
<td>9.7%</td>
<td>$1.89</td>
<td>7.1%</td>
<td>-4.7%</td>
<td>2.5%</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$ 62.84</td>
<td>7.8%</td>
<td>-$6.58</td>
<td>-1.3%</td>
<td>-8.1%</td>
<td>-9.5%</td>
</tr>
<tr>
<td>4</td>
<td>Depression</td>
<td>$ 53.83</td>
<td>6.7%</td>
<td>-$1.67</td>
<td>1.3%</td>
<td>-4.3%</td>
<td>-3.0%</td>
</tr>
<tr>
<td>5</td>
<td>Asthma</td>
<td>$ 50.55</td>
<td>6.3%</td>
<td>$1.85</td>
<td>9.1%</td>
<td>-5.3%</td>
<td>3.8%</td>
</tr>
<tr>
<td>6</td>
<td>Ulcer Disease</td>
<td>$ 38.93</td>
<td>4.8%</td>
<td>-$4.38</td>
<td>-3.6%</td>
<td>-6.5%</td>
<td>-10.1%</td>
</tr>
<tr>
<td>7</td>
<td>Attention Disorders</td>
<td>$ 35.35</td>
<td>4.4%</td>
<td>$5.96</td>
<td>26.0%</td>
<td>-5.7%</td>
<td>20.3%</td>
</tr>
<tr>
<td>8</td>
<td>Infections</td>
<td>$ 32.83</td>
<td>4.1%</td>
<td>-$2.72</td>
<td>-1.8%</td>
<td>-5.9%</td>
<td>-7.7%</td>
</tr>
<tr>
<td>9</td>
<td>Mental/Neurological Disorders</td>
<td>$ 31.37</td>
<td>3.9%</td>
<td>$1.07</td>
<td>5.9%</td>
<td>-2.4%</td>
<td>3.5%</td>
</tr>
<tr>
<td>10</td>
<td>Pain</td>
<td>$ 30.27</td>
<td>3.8%</td>
<td>-$0.58</td>
<td>-3.1%</td>
<td>1.2%</td>
<td>-1.9%</td>
</tr>
<tr>
<td>11</td>
<td>Seizures</td>
<td>$ 23.40</td>
<td>2.9%</td>
<td>$1.14</td>
<td>7.9%</td>
<td>-2.8%</td>
<td>5.1%</td>
</tr>
<tr>
<td>12</td>
<td>Blood Modifying</td>
<td>$ 20.73</td>
<td>2.6%</td>
<td>$1.63</td>
<td>11.0%</td>
<td>-2.4%</td>
<td>8.6%</td>
</tr>
<tr>
<td>13</td>
<td>Contraceptives</td>
<td>$ 20.68</td>
<td>2.6%</td>
<td>$1.19</td>
<td>7.7%</td>
<td>-1.6%</td>
<td>6.1%</td>
</tr>
<tr>
<td>14</td>
<td>Allergies</td>
<td>$ 17.15</td>
<td>2.1%</td>
<td>-$2.66</td>
<td>0.5%</td>
<td>-13.9%</td>
<td>-13.4%</td>
</tr>
<tr>
<td>15</td>
<td>Skin Conditions</td>
<td>$ 16.54</td>
<td>2.1%</td>
<td>$0.86</td>
<td>8.9%</td>
<td>-3.4%</td>
<td>5.5%</td>
</tr>
<tr>
<td></td>
<td><strong>Top 15</strong></td>
<td><strong>$593.95</strong></td>
<td><strong>73.8%</strong></td>
<td><strong>$2.29</strong></td>
<td><strong>4.9%</strong></td>
<td><strong>-4.5%</strong></td>
<td><strong>0.4%</strong></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td><strong>$210.32</strong></td>
<td><strong>26.2%</strong></td>
<td><strong>-$1.43</strong></td>
<td><strong>2.4%</strong></td>
<td><strong>-3.1%</strong></td>
<td><strong>-0.7%</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>$804.27</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>$0.86</strong></td>
<td><strong>4.3%</strong></td>
<td><strong>-4.2%</strong></td>
<td><strong>0.1%</strong></td>
</tr>
</tbody>
</table>
The high blood cholesterol class was influenced somewhat by the introduction of a generic for Lipitor® (atorvastatin), the best-selling drug in the world. Released in late November, the first generic has exclusive market rights until May 2012. We anticipate that the subsequent launch of multiple additional generics will affect cost in the class considerably.

Behavioral trends for all other traditional classes were negative for 2011, with the exception of the pain class, which showed a small increase.

Many other classes, however, experienced significant increases caused by market factors. At 20.3%, attention disorders, the only class to have a trend exceeding 9%, reflected the effect of drug shortages. Increased demand and scarcity of the ingredients for drugs to treat attention disorders resulted in short supplies of some brands and most generics for amphetamine salts and methylphenidate, the mainstays of attention-disorder therapy. In some cases, the lack of available generics forced prescriptions to be filled with brands. Most of the other shortages experienced in 2011 were for injectable drugs used in hospital settings.

Specialty Drugs

In 2011, four specialty classes – inflammatory conditions, multiple sclerosis (MS), cancer and HIV – accounted for nearly 70% of spend for specialty drugs covered by pharmacy benefits. The top three classes have held their spots for several years.

Specialty Drugs

In 2011, four specialty classes – inflammatory conditions, multiple sclerosis (MS), cancer and HIV – accounted for nearly 70% of spend for specialty drugs covered by pharmacy benefits. The top three classes have held their spots for several years.

One change we made in compiling the 2011 Drug Trend Report was to combine oral medications used to treat HIV and transplant patients with injectable medications in the specialty drug category. This change moved the HIV class to number four and transplant drugs to number eight in PMPY spend. As new drugs enter the market and movement occurs between drugs billed under the medical benefit and the pharmacy benefit, Express Scripts reevaluates our therapy classes and shifts therapies between the traditional and specialty categories as appropriate.

Unlike the traditional classes, most specialty classes had increases in spend for both market factors and behavioral factors. Transplant was the only specialty class in the top 10 that had negative market trend, due to increasing use of class-leading generics tacrolimus and mycophenolate, which together have more than 50% of market share. New oral drugs for cancer and MS shifted spend into pharmacy benefits, away from the medical side. Drugs that had been introduced in 2010 gained utilization to increase overall spend in the respiratory conditions class 17.6% in 2011.

Affected most dramatically was hepatitis C. Two new oral drugs released in May, Incivek™ (telaprevir) and Victrelis™ (boceprevir), represent a true breakthrough for patients with hepatitis C. Incivek has a 12-week protocol, and Victrelis has a protocol of 24, 32 or 44 weeks, depending on the patient’s response as therapy progresses. For previously untreated patients, either drug, in combination with interferon and ribavirin, produces a 70% to 80% response rate. Retreatment for patients who did not respond adequately to prior therapy has a wider range of responses, from about 30% to greater than 80%. The cost of these new drugs is significant, however, ranging from $24,000 to $50,000 per round of treatment. Additionally, both must be used in combination with the previous drug therapy for hepatitis C, which caused the cost per unit in the class to soar more than 190%. Trend for the class was a dramatic 194.8%, despite a -29.6% behavior-related trend.

Please see Exhibit 11 for detailed information on the components of trend for the top 10 specialty classes in 2011.
**Exhibit 11** Components and Drivers of Trend for the Top 10 Specialty Therapy Classes, PBM-Adjudicated Claims Only, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Specialty Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Market</th>
<th>Behavioral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammatory Conditions</td>
<td>$40.70</td>
<td>23.7%</td>
<td>$6.13</td>
<td>17.4%</td>
<td>0.3%</td>
<td>17.7%</td>
</tr>
<tr>
<td>2</td>
<td>Multiple Sclerosis</td>
<td>$32.89</td>
<td>19.2%</td>
<td>$5.56</td>
<td>18.2%</td>
<td>2.1%</td>
<td>20.3%</td>
</tr>
<tr>
<td>3</td>
<td>Cancer</td>
<td>$25.20</td>
<td>14.7%</td>
<td>$3.42</td>
<td>7.0%</td>
<td>8.7%</td>
<td>15.7%</td>
</tr>
<tr>
<td>4</td>
<td>HIV</td>
<td>$18.08</td>
<td>10.5%</td>
<td>$0.84</td>
<td>3.2%</td>
<td>1.7%</td>
<td>4.9%</td>
</tr>
<tr>
<td>5</td>
<td>Growth Deficiency</td>
<td>$6.72</td>
<td>3.9%</td>
<td>$0.42</td>
<td>9.6%</td>
<td>-3.0%</td>
<td>6.6%</td>
</tr>
<tr>
<td>6</td>
<td>Anticoagulants</td>
<td>$6.42</td>
<td>3.7%</td>
<td>$0.31</td>
<td>0.0%</td>
<td>5.1%</td>
<td>5.1%</td>
</tr>
<tr>
<td>7</td>
<td>Hepatitis C</td>
<td>$6.34</td>
<td>3.7%</td>
<td>$4.19</td>
<td>224.3%</td>
<td>-29.6%</td>
<td>194.8%</td>
</tr>
<tr>
<td>8</td>
<td>Transplant</td>
<td>$5.63</td>
<td>3.3%</td>
<td>-$0.10</td>
<td>-1.9%</td>
<td>0.2%</td>
<td>-1.7%</td>
</tr>
<tr>
<td>9</td>
<td>Respiratory Conditions</td>
<td>$4.65</td>
<td>2.7%</td>
<td>$0.69</td>
<td>11.9%</td>
<td>5.7%</td>
<td>17.6%</td>
</tr>
<tr>
<td>10</td>
<td>Pulmonary Hypertension</td>
<td>$4.23</td>
<td>2.5%</td>
<td>$0.11</td>
<td>3.1%</td>
<td>-0.5%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Top 10</td>
<td></td>
<td>$150.86</td>
<td>88.0%</td>
<td>$21.57</td>
<td>14.7%</td>
<td>2.0%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td>$20.65</td>
<td>12.0%</td>
<td>$3.45</td>
<td>5.8%</td>
<td>14.2%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>$171.51</td>
<td>100.0%</td>
<td>$25.01</td>
<td>13.6%</td>
<td>3.4%</td>
<td>17.1%</td>
</tr>
</tbody>
</table>
### Exhibit 12

Distribution of Pharmacy and Medical Specialty Spending, Ranked by Relative Change in Medical Spend, Thomson Reuters MarketScan® Commercial Database, 2006-2010

<table>
<thead>
<tr>
<th>Therapy Class</th>
<th>PHARMACY</th>
<th></th>
<th>MEDICAL</th>
<th></th>
<th>TOTAL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2006</td>
<td>2010</td>
<td>% Change</td>
<td>2006</td>
<td>2010</td>
<td>% Change</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>$14.48</td>
<td>$27.56</td>
<td>90.3%</td>
<td>$0.49</td>
<td>$2.91</td>
<td>493.9%</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>$1.17</td>
<td>$2.95</td>
<td>152.1%</td>
<td>$0.59</td>
<td>$1.08</td>
<td>83.1%</td>
</tr>
<tr>
<td>Inflammatory Conditions</td>
<td>$18.80</td>
<td>$34.59</td>
<td>84.0%</td>
<td>$10.16</td>
<td>$16.14</td>
<td>58.9%</td>
</tr>
<tr>
<td>Respiratory Conditions</td>
<td>$2.83</td>
<td>$4.01</td>
<td>41.7%</td>
<td>$1.37</td>
<td>$1.94</td>
<td>41.6%</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>$3.00</td>
<td>$5.28</td>
<td>76.0%</td>
<td>$0.26</td>
<td>$0.36</td>
<td>38.5%</td>
</tr>
<tr>
<td>Cancer</td>
<td>$9.00</td>
<td>$15.44</td>
<td>71.6%</td>
<td>$41.10</td>
<td>$53.44</td>
<td>30.0%</td>
</tr>
<tr>
<td>Transplant</td>
<td>$5.77</td>
<td>$5.87</td>
<td>1.7%</td>
<td>$0.20</td>
<td>$0.24</td>
<td>20.0%</td>
</tr>
<tr>
<td>Growth Deficiency</td>
<td>$5.13</td>
<td>$7.70</td>
<td>50.1%</td>
<td>$0.47</td>
<td>$0.22</td>
<td>-53.2%</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>$3.48</td>
<td>$2.15</td>
<td>-38.2%</td>
<td>$0.06</td>
<td>$0.02</td>
<td>-66.7%</td>
</tr>
<tr>
<td>HIV</td>
<td>$10.19</td>
<td>$19.10</td>
<td>87.4%</td>
<td>$0.09</td>
<td>$0.01</td>
<td>-88.9%</td>
</tr>
<tr>
<td><strong>Top 10</strong></td>
<td><strong>$73.85</strong></td>
<td><strong>$124.65</strong></td>
<td><strong>68.8%</strong></td>
<td><strong>$54.79</strong></td>
<td><strong>$76.36</strong></td>
<td><strong>39.4%</strong></td>
</tr>
<tr>
<td>Others</td>
<td>$13.27</td>
<td>$16.84</td>
<td>26.9%</td>
<td>$36.94</td>
<td>$49.46</td>
<td>33.9%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$87.12</strong></td>
<td><strong>$141.49</strong></td>
<td><strong>62.4%</strong></td>
<td><strong>$91.73</strong></td>
<td><strong>$125.82</strong></td>
<td><strong>37.2%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pharmacy</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Spend, 2010</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>90.4%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>73.2%</td>
<td>26.8%</td>
</tr>
<tr>
<td>Inflammatory Conditions</td>
<td>68.2%</td>
<td>31.8%</td>
</tr>
<tr>
<td>Respiratory Conditions</td>
<td>67.4%</td>
<td>32.6%</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>93.6%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Cancer</td>
<td>22.4%</td>
<td>77.6%</td>
</tr>
<tr>
<td>Transplant</td>
<td>96.1%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Growth Deficiency</td>
<td>97.2%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>99.1%</td>
<td>0.9%</td>
</tr>
<tr>
<td>HIV</td>
<td>99.9%</td>
<td>0.1%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>62.0%</strong></td>
<td><strong>38.0%</strong></td>
</tr>
</tbody>
</table>
Specialty Drug Spending in the Medical Benefit

An analysis of national data that combines pharmacy spend and medical spend for specialty medications is shown in Exhibit 12. Using information for 2006 through 2010 from the Thomson Reuters MarketScan® Commercial Database, Express Scripts researchers and analysts determined that approximately 47% of U.S. specialty drug spend was in medical benefits for 2010. Individual therapy classes differ greatly, however, with the hepatitis C and HIV classes at nearly 100% pharmacy spend while more than 77% of spend for cancer treatment remained in medical benefits.

All of the top 10 classes in the analysis showed increases in total PMPY medical spend, with trend for four classes exceeding 25%.

The cancer treatment class was up the most (77.6%), but trend for both hepatitis C and HIV drugs was less than 1%. The percentage decrease for HIV in medical spend was essentially balanced by a nearly equal increase on the pharmacy side. For hepatitis C, however, spend under both benefits dropped significantly – nearly 40% in pharmacy and more than 66% in medical.

Contrary to the Express Scripts objective to have patients receive specialty medications in the most cost-effective location (e.g., patient homes or physician offices), our analysis of MarketScan data determined a gradual decrease in the use of patient homes and physician offices, lower-cost places to receive medications. Coinciding was increasing utilization of much more-costly outpatient sites for administration of specialty medications covered by medical benefits. Exhibit 13 shows the increase between 2006 and 2010.

Although most Americans may assume that specialty patients are treated in hospitals, specialty drugs administered in emergency rooms and inpatient facilities combined accounted for less than 18% of the total covered spend under medical benefits in 2010.
As detailed in Exhibit 14, medically billed specialty drugs are much more likely to be administered as outpatient procedures. In fact, the percentage of medically billed specialty drugs administered as outpatient procedures doubled in five years, increasing more than 10 percentage points across all four major regions of the country.

### Exhibit 14

Percentage Point Increase of Medical Drug Spend in the Outpatient Hospital Setting by Region, Thomson Reuters MarketScan Commercial Database, 2006-2010

<table>
<thead>
<tr>
<th>U.S. Region</th>
<th>Year</th>
<th>% Outpatient (as Percentage of Specialty Spend Billed Through Medical Benefit)</th>
<th>Percentage Point Increase 2006-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>North Central</td>
<td>2006</td>
<td>13.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>31.7%</td>
<td>18.3</td>
</tr>
<tr>
<td>Northeast</td>
<td>2006</td>
<td>31.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>43.7%</td>
<td>12.0</td>
</tr>
<tr>
<td>Southern</td>
<td>2006</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>22.1%</td>
<td>10.9</td>
</tr>
<tr>
<td>Western</td>
<td>2006</td>
<td>16.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>26.8%</td>
<td>10.7</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>2006</td>
<td>14.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>28.8%</td>
<td>13.9</td>
</tr>
</tbody>
</table>

### Member Share

Between 2010 and 2011, overall copayments made by patients were essentially flat (drop of $0.14 per copayment), as shown in Exhibit 15. Importantly, this stability occurred despite increases in copayments for nonformulary brands ($2.15 for traditional medications and $6.35 for specialty medications). The key is that as patients shift from nonformulary medications to lower-cost options, their copayments drop. By carefully working with their account teams, Express Scripts clients have been able to adjust individual copayments up while allowing patients to share in the savings that come with the use of clinically sound, lower-cost alternatives.
## Exhibit 15  
Member Share of Total Cost 2010-2011

<table>
<thead>
<tr>
<th></th>
<th>TRADITIONAL</th>
<th></th>
<th>SPECIALTY</th>
<th></th>
<th>TOTAL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Mix (Generic and Brand)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Member Share of Total Cost</td>
<td>22.1%</td>
<td>21.6%</td>
<td>0.5%</td>
<td>3.3%</td>
<td>3.1%</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Average Copayment</td>
<td>$11.83</td>
<td>$11.66</td>
<td>-$0.17</td>
<td>$51.85</td>
<td>$54.60</td>
<td>$2.74</td>
</tr>
<tr>
<td><strong>Generics Only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Member Share of Total Cost</td>
<td>25.3%</td>
<td>25.8%</td>
<td>0.5%</td>
<td>6.5%</td>
<td>5.6%</td>
<td>-0.9%</td>
</tr>
<tr>
<td>Average Copayment</td>
<td>$6.43</td>
<td>$6.54</td>
<td>$0.11</td>
<td>$17.99</td>
<td>$21.79</td>
<td>$3.80</td>
</tr>
<tr>
<td><strong>Formulary Brands Only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Member Share of Total Cost</td>
<td>18.2%</td>
<td>17.4%</td>
<td>-0.8%</td>
<td>3.1%</td>
<td>2.8%</td>
<td>-0.3%</td>
</tr>
<tr>
<td>Average Copayment</td>
<td>$21.77</td>
<td>$23.17</td>
<td>$1.40</td>
<td>$57.04</td>
<td>$61.70</td>
<td>$4.66</td>
</tr>
<tr>
<td><strong>Nonformulary Brands Only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Member Share of Total Cost</td>
<td>27.8%</td>
<td>26.4%</td>
<td>-1.3%</td>
<td>4.7%</td>
<td>4.2%</td>
<td>-0.5%</td>
</tr>
<tr>
<td>Average Copayment</td>
<td>$34.15</td>
<td>$36.30</td>
<td>$2.15</td>
<td>$74.87</td>
<td>$81.22</td>
<td>$6.35</td>
</tr>
</tbody>
</table>
Traditional Medications

The top 15 traditional therapy classes represented 73.8% of total 2011 PMPY spend. As predicted in last year’s Drug Trend Report, medications used to treat diabetes jumped ahead of high cholesterol to take the top spot on the list of traditional drugs for the first time. High blood pressure/heart disease held the third spot, as in previous years. The top three therapy classes alone accounted for nearly half the total PMPY spend for traditional drugs.

Trend for traditional drugs fell to a record low of 0.1%, with downward pressures associated with a higher generic fill rate offsetting other factors. Although, allergy medications had the largest decrease in trend (10.1%), ulcer medications had a double-digit decrease in trend for the second year in a row. Medications used to treat attention disorders had the largest increase in spend, (20.3%) due to upward pressure from both cost and utilization.
### Therapy Class Review: Traditional Medications

Exhibit 16: 2011 Key Metrics for Top 10 Traditional Therapy Classes, Including Pharmacy-Related Waste, Ranked by PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>Prevalence of Use</th>
<th>Average Cost/Rx</th>
<th>Trend</th>
<th>Pharmacy-Related Waste</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$ 81.12</td>
<td>10.1%</td>
<td>5.4%</td>
<td>$ 87.35</td>
<td>7.0%</td>
<td>45.6% $37.02</td>
</tr>
<tr>
<td>2</td>
<td>High Blood Cholesterol</td>
<td>$ 78.38</td>
<td>9.7%</td>
<td>12.2%</td>
<td>$ 58.84</td>
<td>2.5%</td>
<td>52.5% $41.16</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$ 62.84</td>
<td>7.8%</td>
<td>16.1%</td>
<td>$ 28.18</td>
<td>-9.5%</td>
<td>32.7% $20.52</td>
</tr>
<tr>
<td>4</td>
<td>Depression</td>
<td>$ 53.83</td>
<td>6.7%</td>
<td>10.4%</td>
<td>$ 56.37</td>
<td>-3.0%</td>
<td>32.4% $17.43</td>
</tr>
<tr>
<td>5</td>
<td>Asthma</td>
<td>$ 50.55</td>
<td>6.3%</td>
<td>8.4%</td>
<td>$113.71</td>
<td>3.8%</td>
<td>0.0% $ 0.00</td>
</tr>
<tr>
<td>6</td>
<td>Ulcer Disease</td>
<td>$ 38.93</td>
<td>4.8%</td>
<td>8.4%</td>
<td>$ 60.23</td>
<td>-10.1%</td>
<td>48.5% $18.88</td>
</tr>
<tr>
<td>7</td>
<td>Attention Disorders</td>
<td>$ 35.35</td>
<td>4.4%</td>
<td>2.6%</td>
<td>$171.24</td>
<td>20.3%</td>
<td>6.0% $ 2.13</td>
</tr>
<tr>
<td>8</td>
<td>Infections</td>
<td>$ 32.83</td>
<td>4.1%</td>
<td>38.5%</td>
<td>$ 33.85</td>
<td>-7.7%</td>
<td>38.9% $12.78</td>
</tr>
<tr>
<td>9</td>
<td>Mental/Neurological Disorders</td>
<td>$ 31.37</td>
<td>3.9%</td>
<td>1.7%</td>
<td>$224.35</td>
<td>3.5%</td>
<td>31.8% $ 9.98</td>
</tr>
<tr>
<td>10</td>
<td>Pain</td>
<td>$ 30.27</td>
<td>3.8%</td>
<td>18.0%</td>
<td>$ 40.31</td>
<td>-1.9%</td>
<td>58.2% $ 17.61</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>$308.82</td>
<td>38.4%</td>
<td>54.8%</td>
<td>$ 49.02</td>
<td>0.2%</td>
<td>28.3% $ 87.37</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>$804.27</td>
<td>100.0%</td>
<td>67.5%</td>
<td>$ 53.97</td>
<td>0.1%</td>
<td>32.9% $264.88</td>
</tr>
</tbody>
</table>
Diabetes

YEAR IN REVIEW

• Increased overall trend was driven by the increased use of newer, higher-cost subclasses of diabetes drugs – glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors.

• Although metformin’s utilization continues to increase, competition among its numerous generic manufacturers actually caused a cost decrease in 2011.

• After its approval in 2010, a GLP-1 agonist, Victoza® (liraglutide), continues to capture market share from Byetta® (exenatide). Victoza is a once-daily injection compared to twice-daily Byetta.

• Utilization of thiazolidinediones (glitazones), Actos® (pioglitazone) and Avandia® (rosiglitazone) decreased sharply due to serious safety concerns. Due to cardiovascular concerns, Avandia now must be prescribed through the Avandia-Rosiglitazone Medicines Access Program,™ launched November 18, 2011. Additionally, Actos is under review by the Food and Drug Administration (FDA) due to potential added risks of bladder cancer. Many members previously taking a glitzone moved to DPP-4 Inhibitors and metformin.

A CLOSER LOOK

• According to the American Diabetes Association, only about 75% of the 25.8 million Americans with diabetes have been diagnosed; approximately 7 million are undiagnosed and untreated. Additionally, 79 million others may have pre-diabetes.\(^1\)

• The incidence of diabetes will continue to rise as the population ages and obesity becomes even more prevalent.

• As utilization for drugs to treat diabetes continues to rise, implementing appropriate strategies such as ScreenRx and ExpressAlliance to manage cost trend while maximizing outcomes will be critical for successful long-term management.

• Growth for GLP-1 agonists continues despite some suggestions that they may increase the risk of pancreatitis. The Express Scripts prior authorization program for GLP-1 agonists ensures their appropriate use.

WHAT’S AHEAD

• Once-weekly Bydureon™ (exenatide extended release) was approved by the FDA in late January 2012.

• The pipeline mainly consists of new GLP-1 agonists – such as Lyxumia® (lixisenatide), which could be approved in 2013 – and DPP-4 inhibitors – such as Nesina® (alogliptin), currently under review by the FDA, with an action date of April 25, 2012.

• Degludec and DegludecPlus, an ultra-long-acting basal insulin and its combination product, should be reviewed by the FDA by July 29, 2012. Both glitazones lose patent protection in 2012. Settlement agreements may make generics to Avandia available early in the year. Generics to Actos are expected in mid-August 2012. However, the safety concerns may curtail these generic releases.
INTRODUCTION

TREND OVERVIEW

THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID

INTRODUCTION

TREND OVERVIEW

THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID

Top Drugs: Market Share

- **metformin**: 28.0%
- **OneTouch® Ultra® Test Strips**: 11.1%
- **Lantus® (insulin glargine)**: 6.4%
- **Actos® (pioglitazone)**: 6.0%
- **glipizide**: 5.8%

Behavioral Influences on Trend

- Intensity: -0.8%
- Mix: -0.5%

Total Trend: 7.0%

PHARMACY-RELATED WASTE

41% of patients are **NONADHERENT** to medication therapy

** saved opportunity**

- **$ Channel**: $20.84
- **$ Mix**: $16.18

** $37.02 PMPY = 45.6% of PMPY SPEND**

Key Drug Information

- **05.03 Tradjenta™ (linagliptin)**
- **09.30 metformin extended release (generic Fortamet® - limited supply)**
- **10.07 Juvisync™ (sitagliptin and simvastatin)**

BY THE #S

- **$81.12**: Cost PMPY
- **0.9**: #Rx PMPY
- **5.4%**: Prevalence
- **$87.35**: Average Cost/Rx
- **14.91**: #Rx/User/Year

DIABETES
High Blood Cholesterol

Waste accounts for more than half of class spend

YEAR IN REVIEW

- Overall class trend was a modest 2.5%, as decreased utilization (-1.6%) was more than offset by increased cost trend (4.1%).
- HMG-CoA reductase inhibitors (statins), the mainstay of treatment, held over 70% of market share.
- Crestor® (rosuvastatin) drove much of trend, with increases in both cost and utilization.
- In late November 2011, the first generic to Lipitor® (atorvastatin) became available. Although 2011 class trend was affected, greater impact will occur in 2012.
- Study results released in 2011 questioned whether adding Trilipix® (fenofibric acid) and Niaspan® (niacin extended release) to other cholesterol-lowering therapy has any effect on cardiovascular (CV) outcomes.
- Similarly, the ENHANCE and SEAS Trials failed to support improved CV outcomes from Zetia® (ezetimibe), suggesting that market share for it and its combination, Vytorin® (ezetimibe and simvastatin), will decrease.

A CLOSER LOOK

- Elevated blood cholesterol is a major risk factor for coronary heart disease (CHD). Annually, 785,000 Americans have a first heart attack and 470,000 have another.  

WHAT’S AHEAD

- Full adherence to the National Cholesterol Education Program Adult Treatment Panel III (Adult Treatment Panel III) guidelines could prevent 20,000 heart attacks and 10,000 deaths a year from CHD, saving $2.8 billion in healthcare costs.  
- The recent availability of atorvastatin, a high-potency generic statin, presents plan sponsors with numerous options to capitalize on the cost savings provided by generics in this class.

- Adult Treatment Panel IV, expected in 2012, will increase awareness of controlling high cholesterol, likely increasing statin use.
- Additional manufacturers will launch atorvastatin after generic exclusivity expires in late May 2012.
- Fluvastatin and fluvastatin extended release (generics for Lescol® and Lescol® XL) are anticipated in June.
- The combination of atorvastatin and ezetimibe should be reviewed by the Food and Drug Administration (FDA) in 2012, but litigation likely will delay its availability.
- With a July 2012 action date, AMR101 is an omega-3 fatty acid that will compete with Lovaza® (omega-3-acid ethyl esters), if approved.
- Kynamro® ( mipomersen), a unique once-weekly self-injected medication, inhibits apolipoprotein-B (apo-B). Mipomersen could be marketed in 2012 for treating homozygous familial hypercholesterolemia.
### Market Influences on Trend

<table>
<thead>
<tr>
<th>Influence</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>-1.4%</td>
</tr>
<tr>
<td>Cost/Unit</td>
<td>8.9%</td>
</tr>
<tr>
<td>Units/Rx</td>
<td>-0.3%</td>
</tr>
<tr>
<td>Patent Expirations</td>
<td>-0.1%</td>
</tr>
<tr>
<td>New Drugs</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

### Behavioral Influences on Trend

<table>
<thead>
<tr>
<th>Influence</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Mix</td>
<td>-4.4%</td>
</tr>
</tbody>
</table>

### Total Trend

- 7.1% increase
- 2.5% overall trend

### Behavioral Influences on Trend

<table>
<thead>
<tr>
<th>Influence</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Mix</td>
<td>-4.7%</td>
</tr>
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</table>

### Behavioral Influences on Trend

<table>
<thead>
<tr>
<th>Channel</th>
<th>Mix</th>
</tr>
</thead>
<tbody>
<tr>
<td>$18.05</td>
<td>$23.11</td>
</tr>
</tbody>
</table>

#### Savings Opportunity

- **$41.16 PMPY**
- **52.5% of PMPY Spend**

---

### Key Drug Information

#### Top Drugs: Market Share

<table>
<thead>
<tr>
<th>Drug</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>simvastatin</td>
<td>35.2%</td>
</tr>
<tr>
<td>Crestor® (rosuvastatin)</td>
<td>14.2%</td>
</tr>
<tr>
<td>Lipitor® (atorvastatin)</td>
<td>13.7%</td>
</tr>
<tr>
<td>pravastatin</td>
<td>8.6%</td>
</tr>
<tr>
<td>fenofibrate</td>
<td>6.0%</td>
</tr>
</tbody>
</table>

---

### New Drugs Approved in 2011

1. **10.07 Juvisync™ (sitagliptin and simvastatin)**
2. **11.30 atorvastatin (generic Lipitor®)**

---

### BY THE #S

- **$78.38** Cost PMPY
- **1.3** #Rx PMPY
- **12.2%** Prevalence
- **$58.84** Average Cost/Rx
- **9.41** #Rx/User/Year
High Blood Pressure/Heart Disease

Trend falls with increased generic use

YEAR IN REVIEW

- Several subclasses of medications are included in the high blood pressure/heart disease class. Among them are angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta blockers and calcium channel blockers (CCBs).

- Overall trend in the class was affected heavily by the first generic ARB. Cozaar® (losartan) and Hyzaar® (losartan and hydrochlorothiazide) lost patent protection in April 2010. During 2011, utilization for losartan increased 83%, while its price decreased nearly 68%.

- For treating high blood pressure, a new ARB, Edarbi™ (azilsartan), was approved early in 2011 and a combination product, Edarbyclor™ (azilsartan and chlorothalidone), followed in December. However, these medications will make little impact in a maturing market that will see three more ARBs go generic in 2012.

- New generics introduced in 2011 include ones to another ARB, Teveten® (eprosartan); a CCB, Sular® (nisoldipine 8.5mg, 17mg, 25.5mg and 34mg tablets); and an ACE and CCB combination, Lotrel® (amlodipine and benazepril 5/40mg and 10/40mg).

- The ALTITUDE Study investigated the use of Tekturna® (aliskiren), a direct renin inhibitor, with an ACE inhibitor or an ARB for high-risk diabetes patients with kidney impairment. The study was terminated in late 2011 after interim results showed no positive benefit from adding Tekturna but a higher rate of adverse events.

A CLOSER LOOK

- Approximately one-third of American adults – 76.4 million individuals – have high blood pressure. Many of these people have not been diagnosed, and more than half of those with a high blood pressure diagnosis are not controlling it adequately.

- Utilization programs can help plan sponsors maintain high use of low-cost generics in the face of newer brand entrants.

WHAT’S AHEAD


- In the ARB subclass, Avapro® (irbesartan) is expected to lose patent protection in late March 2012, Diovan® (valsartan) in September and Atacand® (candesartan) in December.
### INTRODUCTION

### Trend Overview

### Therapy Class Review

<table>
<thead>
<tr>
<th>Market Influences on Trend</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>-0.5%</td>
</tr>
<tr>
<td>Cost/Unit</td>
<td>1.6%</td>
</tr>
<tr>
<td>Units/Rx</td>
<td>0.2%</td>
</tr>
<tr>
<td>Patent Expirations</td>
<td>-2.7%</td>
</tr>
<tr>
<td>New Drugs</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Behavioral Influences on Trend</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Mix</td>
<td>-8.0%</td>
</tr>
</tbody>
</table>

**Total Trend**

-9.5%

### Pharmacy-Related Waste

- 31% of patients are NONADHERENT to medication therapy.

### Top Drugs: Market Share

<table>
<thead>
<tr>
<th>Drug Information</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>lisinopril</td>
<td>16.5%</td>
</tr>
<tr>
<td>metoprolol tartrate</td>
<td>14.3%</td>
</tr>
<tr>
<td>amlodipine</td>
<td>10.1%</td>
</tr>
<tr>
<td>Diovan HCT®</td>
<td>7.3%</td>
</tr>
<tr>
<td>lisinopril and hydrochlorothiazide</td>
<td>6.7%</td>
</tr>
</tbody>
</table>

### New Drugs Approved in 2011

- **01.03** amlodipine and benazepril 5/40mg and 10/40mg (generic Lotrel®)
- **01.17** Amturnide™ (aliskiren, amlodipine and HCTZ)
- **01.28** nisoldipine (generic Solar®)
- **02.28** Edarbi™ (azilsartan)
- **12.20** Edarbyclor™ (azilsartan and chlorthalidone)

### BY THE #S

- **$62.84** Cost PMPY
- **2.2** #Rx PMPY
- **16.1%** Prevalence
- **$28.18** Average Cost/Rx
- **11.95** #Rx/User/Year

### High Blood Pressure/Heart Disease

**Pharmacy-Related Waste**

- **32.7% of PMPY spend**
- **$10.98** Channel
- **$9.54** Mix
- **$20.52 PMPY**

**Savings Opportunity**

- **$6.38** per PMPY
- **32.7% of PMPY spend**

**Behavioral Influences on Trend**

<table>
<thead>
<tr>
<th>Channel</th>
<th>Mix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel</td>
<td>$10.98</td>
</tr>
<tr>
<td>Mix</td>
<td>$9.54</td>
</tr>
</tbody>
</table>

**Total Trend**

-9.5%
Depression

FACT

With utilization flat, use of generics drives trend down

YEAR IN REVIEW

- Overall cost trend fell 3% after the cost of generic Effexor XR® (venlafaxine extended release) decreased when multiple generics became available in June 2011.

- The cost of other generic antidepressants, such as citalopram, continues to decrease (by 9.3% in 2011), but the cost of branded products, such as Cymbalta® (duloxetine), continues to increase by double digits (10.1%).

- Drugs for depression are one of the few classes, and certainly one of the largest PMPY classes, that experienced increases in overall 2011 utilization (2.1%).

- In August 2011, the Food and Drug Administration (FDA) reduced the maximum recommended dose for citalopram (and its brand, Celexa®) to 40mg because higher doses may increase risk for abnormal heart rhythms.

A CLOSER LOOK

- A recent report from the U.S. Centers for Disease Control and Prevention (CDC) found that use of antidepressants in the U.S. rose 400 percent between 1988 and 2008. The CDC report noted further than among the approximately 11% of American adults who were taking an antidepressant, about 14% had been on drug therapy for 10 years or longer.¹

- By focusing on utilization programs that improve overall compliance while promoting generic utilization, plan sponsors can mitigate brand inflation as the price gap between some brands and generics increases.

WHAT’S AHEAD

- Generic selective serotonin reuptake inhibitors (SSRIs) will continue to be the most commonly used antidepressants. Generics to Lexapro® (escitalopram), the last of the high-selling brand-name SSRIs, became available in March 2012.

- A generic to the selective serotonin and norepinephrine reuptake inhibitor (SSNRI) Cymbalta is not expected until December 2013.

- Levomilnacipran, a new SSNRI, could be submitted to the FDA for approval in 2012.

- Among novel antidepressants in development, TC-5214 is a broad-spectrum neuronal nicotinic receptor (NNR) antagonist for use as augmentation therapy for patients who do not respond adequately to other medications alone. The first in a new subclass, TC-5214 could reach the market in 2013.
INTRODUCTION

TREND OVERVIEW

THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID

Top Drugs:

Market Share

- sertraline: 16.4%
- citalopram: 14.8%
- bupropion xl: 13.3%
- Lexapro® (escitalopram): 11.1%
- fluoxetine: 10.3%

Prevalence 1.8%
Cost/Unit 3.0%
Units/Rx 0.5%
Patent Expirations -4.1%
New Drugs 0.2%

Behavioral Influences on Trend

- Intensity 0.3%
- Mix -4.6%

Total Trend

-3.0%

DEPRESSION

42% of patients are NONADHERENT to medication therapy

SAVINGS OPPORTUNITY

| Channel | $10.44 |
| Mix     | $6.99  |

$17.43 PMPY = 32.4% OF PMPY SPEND

Top Drugs: Market Share

New Drugs Approved in 2011

- 01.24 Viibryd® (vilazodone)
- 10.14 fluoxetine (generic Prozac® 60mg tablets)
- 11.11 CPI-300 (bupropion 450mg)

BY THE #S

$53.83 Cost PMPY
1.0 #Rx PMPY
10.4% Prevalence
$56.37 Average Cost/Rx
7.88 #Rx/User/Year

DEPRESSION
Asthma

FACT

More than half of asthma patients are nonadherent to therapy

YEAR IN REVIEW

- Overall trend in the asthma class was 3.8%, driven by an increased cost trend of 7.6%.
- Although utilization of Singulair® (montelukast) decreased 5.6%, a 14.2% increase in its cost affected trend significantly.
- The largest market-share increase was 1.4% for ProAir® HFA (albuterol), despite its price increase of 2.3% from 2010.
- Although market share of Advair® Diskus (fluticasone propionate and salmeterol) decreased the most (by 0.7%), a price increase of 8% keeps it the most costly PMPY asthma drug.
- The inhaler market has reverted essentially to brand-only products following the phaseout of chlorofluorocarbon (CFC) propellants due to concerns about their effects on the atmosphere’s ozone layer. Generics to newer inhalers using hydrofluoroalkane (HFA) have yet to be approved by the Food and Drug Administration (FDA).

WHAT’S AHEAD

- Express Scripts management programs decrease utilization of Singulair for allergic rhinitis and other off-label uses but allow asthma patients immediate access to the medication.
- Although patents for many inhaled asthma drugs have expired, A-rated generics to them will be delayed by complex inhaler devices, new patents on devices and delivery forms, and additional testing requirements to ensure bioequivalence.
- The largest impact on asthma trend in 2012 will come in August, when multiple manufacturers are expected to launch generics to Singulair, an oral tablet. An immediate price drop should result.
- Following a settlement agreement, the first generic to nebulized Xopenex® (levalbuterol inhalation solution) should be on the market in August 2012.
- Competitors to the inhaled, long-acting muscarinic antagonist (LAMA), Spiriva® (tiotropium), are in development for treating chronic obstructive pulmonary disease (COPD). The first, Ekira® (aclidinium), is being reviewed by the FDA for action at the end of April. The new drug application (NDA) for a similar drug, NVA237, is expected to be filed with the FDA later in 2012. Both drugs also are being developed with other products as combination inhalers for COPD.
- Combination products in the pipeline for asthma include a once-daily formulation of mometasone and indacaterol as well as Relovair™ (vilanterol and fluticasone), a follow-on to Advair® (salmeterol and fluticasone).
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TREND OVERVIEW

THERAPY CLASS REVIEW

FORECAST

MEDICARE / MEDICAID

Top Drugs: Market Share

<table>
<thead>
<tr>
<th>Drug Information</th>
<th>Prevalence</th>
<th>Cost/Unit</th>
<th>Units/Rx</th>
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<th>New Drugs</th>
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<td>-0.1%</td>
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<td>Market Influences on Trend</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence</td>
<td>-0.2%</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Cost/Unit</td>
<td>9.4%</td>
<td></td>
<td></td>
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<tr>
<td>Units/Rx</td>
<td>0.1%</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Patent Expirations</td>
<td>-0.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Drugs</td>
<td>0.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioral Influences on Trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensity</td>
<td>-3.4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mix</td>
<td>-2.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Trend</td>
<td>3.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Behavioral Influences on Trend

Intensity: -3.4%
Mix: -2.0%
Total Trend: 3.8%

Nonadherence to inhaled corticosteroids is estimated to account for up to 60% of asthma hospitalizations.

New Drugs Approved in 2011

- 03.01 Daliresp® (roflumilast)
- 07.06 Arcapta™ (indacaterol) NeoHaler™
- 10.14 Combivent® Respimat® (albuterol and ipratropium)

BY THE #S

$50.55
Cost PMPY

0.4
#Rx PMPY

8.4%
Prevalence

$113.71
Average Cost/Rx

4.59
#Rx/User/Year

ASTHMA
Ulcer Disease

Trend driven down by movement to OTC and generics

YEAR IN REVIEW

- Since generics to the first proton pump inhibitor (PPI), Prilosec® (omeprazole), became available in December 2002, spend in the ulcer disease category has been decreasing, causing it to fall from the number-one spot by PMPY spend in 2002.
- Overall trend for the class was negative by 10.1%, heavily influenced by a -9.8% cost trend.
- The launch of multiple generics to Protonix® (pantoprazole) in January 2011 was the single event that most affected 2011 trend in this category.

A CLOSER LOOK

- Gastroesophageal reflux disease (GERD) is responsible for more than 18 million doctor’s office visits a year, with about 1.5 million more due to peptic ulcer disease. One result is annual prescriptions exceeding 5 million.19
- Although some PPIs have been approved for over-the-counter (OTC) use, most plan sponsors nonetheless continue to provide coverage for prescription-strength PPIs. Continued coverage reflects the need to cover certain clinical indications, to support longer durations of use, to minimize overall pill burden and to limit patient out-of-pocket expenses.
- GERD has a substantial negative impact on employee productivity, with reported productivity losses primarily due to reduced productivity while at work (i.e., presenteeism)11 The impact of GERD on productivity may be mitigated by the use of appropriate acid-suppressive therapy.

WHAT’S AHEAD

- Spend for ulcer drugs is expected to continue decreasing as more generic options become available.
- Although many ulcer products now are available over the counter, not every drug in the class convert to complete OTC status, however, because a health professional must manage treatment for some ulcer-related conditions.
- No novel drug subclasses are emerging from the pipeline to challenge the PPIs for treating acid-related stomach conditions.
- The next generic PPIs are scheduled in 2013, for AcipHex® (rabeprazole), and in 2014, for Nexium® (esomeprazole). Both products also are likely to become OTC around the times their patents expire.
## Market Influences on Trend

- **Prevalence**: 0.7%
- **Cost/Unit**: -3.3%
- **Units/Rx**: 0.1%
- **Patent Expirations**: -1.1%
- **New Drugs**: 0.0%

**Total Trend**: -3.6%

## Behavioral Influences on Trend

- **Intensity**: -1.0%
- **Mix**: -5.5%

**Total Trend**: -6.5%

**Total Trend**: -10.1%

---

### Top Drugs: Market Share

- **omeprazole**: 43.6%
- **Nexium® (esomeprazole)**: 18.5%
- **pantoprazole**: 13.6%
- **lansoprazole**: 9.7%
- **ranitidine**: 6.8%

---

### New Drugs Approved in 2011

- 01.19 **pantoprazole** (additional generic Protonix®)

---

### BY THE #S

- **$38.93** Cost PMPY
- **0.6** #Rx PMPY
- **8.4%** Prevalence
- **$60.23** Average Cost/Rx
- **6.64** #Rx/User/Year

---

### PHARMACY-RELATED WASTE

Patients adherent to proton pump inhibitor (PPI) therapy saved $855 per year in total healthcare costs compared to nonadherent patients.12

### Savings Opportunity

- **Channel**: $9.75
- **Mix**: $9.13

**$18.88 PMPY = 48.5% of PMPY Spend**

---

### ULCER DISEASE

- **omeprazole**
- **Nexium® (esomeprazole)**
- **pantoprazole**
- **lansoprazole**
- **ranitidine**
## Attention Disorders

### YEAR IN REVIEW
- Consisting primarily of drugs to treat attention disorders, this class also includes some other drugs, such as stimulants to treat narcolepsy.
- Driven by increases in both cost (10.3%) and utilization (9.0%), overall trend continued to rise, growing 20.3% in 2011.
- Non-stimulant products such as once-daily Vyvanse® (methylphenidate extended release) had double-digit price increases, pushing class cost upward.
- The shortage of ADHD drugs that persisted throughout 2011 is expected to continue into 2012 because increasing demand exceeds the supply of active ingredients.
- Generics to Ritalin LA® (methylphenidate extended release), launched in December 2011, will impact 2012 trend contingent on adequate supply.
- For a second year, utilization trend for Strattera® (atomoxetine) was negative due to safety concerns and additional competition from two newer non-stimulants, Intuniv® (guanfacine) and Kapvay™ (clonidine).
- Utilization of Provigil® (modafinil), a stimulant originally used to treat narcolepsy, decreased in favor of its follow-on, Nuvigil® (armodafinil). At 34.6%, the cost increase for Provigil, which faces generic competition in April, far outpaced that for Nuvigil (patent protected until December 2023).

### A CLOSER LOOK
- Among the estimated 5.4 million U.S. children age 4 to 17 who have been diagnosed with attention deficit hyperactivity disorder (ADHD), about 66.3% take medication to control the condition. Although ADHD traditionally has been considered a childhood disorder, its symptoms may be lifelong. Increased utilization therefore is partly due to continuing expansion of ADHD medications for adults.
- Step therapy and prior authorization programs offered by Express Scripts help plan sponsors counteract supply chain strategies such as the shift from Provigil to Nuvigil. A number of our solutions also help to ensure appropriate use of stimulant drugs by adults with attention disorders. Plan sponsors enrolled in these offerings saw sizable decreases in waste from unnecessary use in the class.

### WHAT’S AHEAD
- Following settlement agreements, the first generics to Provigil are due on April 6, 2012.
- True A-rated generics to both XR® (amphetamine and dextroamphetamine mixed salts, extended release) and Concerta® (methylphenidate) have been delayed by Citizen’s Petitions, lack of final Food and Drug Administration (FDA) approval or both. If the FDA approves it, a true generic to Concerta will be allowed to launch in July 2012 after a settlement.
Long-term studies have shown that at least 50% of youths are nonadherent to ADHD drug therapy over a one-year period.\textsuperscript{14}

$\text{SAVINGS OPPORTUNITY}$

$\begin{array}{|c|c|}
\hline
\text{CHANNEL} & -0.16 \\
\text{MIX} & 2.30 \\
\hline
\end{array}$

\$2.13 \text{ PMPY} \Rightarrow \text{6.0\% of PMPY SPEND}$
Infections

Another mild cold and flu season responsible for lower trend

YEAR IN REVIEW

- In 2011, overall trend in the anti-infectives category decreased 7.7%, driven by an 8.4% decrease in cost.
- Multiple generics are available across all of the major subgroups of anti-infectives.
- Levofloxacin, generic for Levaquin®, became available in June 2011. Simultaneous launches from multiple generic manufacturers resulted in rapid cost decreases for both the brand and generics.
- A concurrent decrease in cost also was observed for many of the other generically available antibiotics, including azithromycin, ciprofloxacin, and amoxicillin and potassium clavulanate.
- In 2011, generics were released for certain strengths of two antibiotics primarily used for treating acne — Doryx® (doxycycline) and Solodyn® (minocycline extended release). The generics did not impact costs, because brand manufacturers also introduced new strengths or formulations that are brand only.
- A new drug, Dificid™ (fidaxomicin), was approved in mid-2011 for treating infections with Clostridium difficile (C. difficile), often acquired in hospitals. Dificid is expected to impact spend in 2012 as it competes with Vancocin® (vancomycin).
- The use of Xifaxan® (rifaximin), approved in 2004 for treating traveler’s diarrhea, has been increasing over the past couple of years as physicians become more comfortable with prescribing it. The drug’s cost has increased as well.

A CLOSER LOOK

- Although anti-infectives are not indicated for viral illnesses, their use still is influenced by the severity of flu season. Use is seasonal as well, peaking in the winter months.
- Brand market share remains high for some anti-infectives, particularly acne treatments. Express Scripts offers multiple options that effectively manage both oral and topical products that mainly are used to treat acne. Plan sponsors can quickly take advantage of the savings delivered by our management strategies.

WHAT’S AHEAD

- Although the patents on Vancocin have expired, generics for it have been delayed due to ongoing litigation and a Citizen’s Petition.
- Generics to a cephalosporin, Cedax® (ceftibuten), and a quinolone, Avelox® (moxifloxacin), are expected in early 2014. However, neither has high utilization and each has multiple therapeutic equivalents, so the impact on trend should not be significant.
- The pipeline for anti-infective drugs is sparse, with very few new agents in late stages of development despite growing concerns over antibiotic resistance. Notable products include Taksta™ (tusidic acid) and dalbavancin, both of which are being developed to treat infections that are resistant to other drugs.
### Market Influences on Trend

- **Prevalence**: 0.9%
- **Cost/Unit**: 3.9%
- **Units/Rx**: 0.2%
- **Patent Expirations**: -6.8%
- **New Drugs**: 0.1%

Total Trend: -1.8%

### Behavioral Influences on Trend

- **Intensity**: -0.2%
- **Mix**: -5.7%

Total Trend: -5.9%

### Total Trend

Total Trend: -7.7%

---

### New Drugs Approved in 2011

- **02.01** doxycycline 75mg and 100mg enteric-coated tablets (generic Doryx®)
- **02.15** voriconazole (generic Vfend® tablets)
- **05.23** nitrofurantoin (generic Furadantin® oral suspension)
- **05.31** Dificid™ (fidaxomicin)
- **06.21** levofoxacin (generic Levaquin®)
- **11.28** minocycline (generic Solodyn® 45mg, 90mg and 135mg tablets)

---

### INFECTIONS

Noncompliance to antibiotic regimens, which is as high as 38%, is associated with negative consequences such as personal or population-level bacterial resistance.\(^{15}\)

### PHARMACY-RELATED WASTE

- **Savings Opportunity**: $12.78 PMPY = 38.9% of PMPY spend

---

### BY THE #S

- **$32.83** Cost PMPY
- **1.0** #Rx PMPY
- **38.5%** Prevalence
- **$33.85** Average Cost/Rx
- **2.17** #Rx/User/Year
Mental/Neurological Disorders

FACT

Increased use of generics plays a big part in mitigating trend

YEAR IN REVIEW

- In 2011, overall class trend increased 3.5%, compared to an increase of 11.7% in 2010.
- Increased spend primarily is due to atypical antipsychotic agents, which frequently are used to treat other conditions, such as bipolar disorder and depression.
- The full impact from generics to the atypical antipsychotic, Zyprexa® (olanzapine), was not yet felt, because the sole generic version currently on the U.S. market has exclusivity until April 2012.
- Despite the availability of olanzapine, utilization of brand atypical antipsychotics continues to increase, mostly driven by side-effect profiles of the various drugs and the need for therapeutic options to treat schizophrenia.
- Abilify® (aripiprazole) is a major trend driver in this category, with a 5.8% increase in utilization and a 9.9% increase in cost trend for 2011.
- The three most recently approved atypical antipsychotics, Fanapt® (iloperidone), Latuda® (lurasidone) and Saphris® (asenapine), all saw increased utilization in 2011.
- The first generic to Aricept® (donepezil) became available in November 2010. After its six months of generic exclusivity, multiple generics launched, decreasing cost substantially.

WHAT’S AHEAD

- After the expiration of the six-month generic exclusivity period, generics to Aricept offered substantial savings for plan sponsors using Express Scripts trend programs for patients with Alzheimer’s disease. Taking advantage of these programs for other types of drugs in the class offers exceptional savings while still delivering clinically appropriate options for treatment.
- In 2012, two blockbuster atypical antipsychotics, Seroquel® (quetiapine) and Geodon® (ziprasidone), will lose patent protection. Combined with multiple generics for Zyprexa, the introductions of generics to Seroquel and Geodon will decrease cost trend in this category.
- A new antipsychotic, cariprazine, which is a dopamine receptor antagonist, could reach the market in 2013. Like other antipsychotic drugs in development, cariprazine may offer the advantage of not increasing weight, blood glucose and blood lipids as much as older members of the class do.
- The next potential new drug for treating Alzheimer’s disease is BMS-708163, an oral gamma secretase inhibitor currently in Phase 2 clinical trials. Drugs in this new class target beta amyloid, which is believed to build up into plaques, ultimately leading to nerve degeneration and dementia.

A CLOSER LOOK

- Each year, approximately one-quarter of American adults have an existing or newly diagnosed mental condition, and 6% of adults have mental conditions considered to be serious.16

- After the expiration of the six-month generic exclusivity period, generics to Aricept offered substantial savings for plan sponsors using Express Scripts trend programs for patients with Alzheimer’s disease. Taking advantage of these programs for other types of drugs in the class offers exceptional savings while still delivering clinically appropriate options for treatment.
**Top Drugs: Market Share**

- **Seroquel®** (quetiapine) 18.7%
- **Abilify®** (aripiprazole) 15.2%
- **Aricept®** (donepezil) 13.2%
- **risperidone** 11.1%
- **Namenda®** (memantine) 9.3%

**New Drugs Approved in 2011**

- 01.20 Nuedexta® (dextromethorphan and quinidine)
- 04.08 Horizant™ (gabapentin enacarbil)
- 08.30 Gralise™ (gabapentin extended release)
- 10.24 olanzapine (generic Zyprexa®)
- 10.28 Latuda® (lurasidone)

**BY THE #S**

- **$31.37** Cost PMPY
- **0.1** #Rx PMPY
- **1.7%** Prevalence
- **$224.35** Average Cost/Rx
- **7.28** #Rx/User/Year

---

**Market Influences on Trend**

- Prevalence: -1.6%
- Cost/Unit: 12.9%
- Units/Rx: -1.1%
- Patent Expirations: -4.6%
- New Drugs: 0.4%

**Behavioral Influences on Trend**

- Intensity: 0.9%
- Mix: -3.3%

**Total Trend**

3.5%

---

**Pharmacy-Related Waste**

44% of patients are nonadherent to medication therapy.

**Savings Opportunity**

- **$6.61** Channel
- **$3.37** Mix

$9.98 PMPY = 31.8% of PMPY spend

---

**Key Drug Information**

**Mental/Neurological Disorders**

- 65

---

**Introduction**

**Trend Overview**

**Therapy Class Review**

**Forecast**

**Medicare/Medicaid**

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**BY THE #S**

- **$31.37** Cost PMPY
- **0.1** #Rx PMPY
- **1.7%** Prevalence
- **$224.35** Average Cost/Rx
- **7.28** #Rx/User/Year

---

**MENTAL/NEUROLOGICAL DISORDERS**

- 65
Facts

**FDA moves to promote safer, more clinically appropriate use of opioids**

**YEAR IN REVIEW**

- Overall trend for pain medications was -1.9% due to decreases in both cost (-0.7%) and utilization (-1.2%).
- In April 2011, the Food and Drug Administration (FDA) announced mandatory risk evaluation and mitigation strategies (REMS) for long-acting opioid medications. Taking effect in 2012, REMS focus on physician training and patient counseling. They include strategies to promote safer use of opioids.
- In November 2010, products containing propoxyphene (Darvon® and Darvocet®) were withdrawn after an FDA review found this agent put patients at risk for heart rhythm abnormalities.
- In January 2011, the FDA gave manufacturers three years to limit the amounts of acetaminophen (to 325mg in each tablet or capsule) in combination prescription pain medications that contain it. High doses of acetaminophen may cause liver damage.

**WHAT’S AHEAD**

- Designed to prevent abuse, tamper-resistant (TR) versions of OxyContin® (oxycodone extended release) and Opana® ER (oxymorphone extended release) were approved in April 2010 and December 2011, respectively. Legal settlements will allow generics to the original formulations in the first half of 2013. However, after receiving approval for their new versions, manufacturers removed the older formulations from sale. As a result, any new generics will not be interchangeable with the new TR brands, new prescriptions will have to be written specifically for generics and cost relief will be limited.
- The new drug application (NDA) for MoxDuo® IR (morphine and oxycodone immediate release) has an action date of May 11, 2012.
- Generics to Subutex® (buprenorphine) launched in October 2009. The FDA still is considering approval, however, for the combination product, Suboxone® (buprenorphine and naltrexone), even though patent protection has expired.

**A CLOSER LOOK**

- Although the U.S. population represents only 5% of the world’s total population, a 2008 report found that Americans used approximately 80% of all opioid drugs.17
- The Comprehensive Drug Abuse Prevention and Control Act of 1970 classified certain drugs into five schedules (CI through CIV) based on their safety, medical uses, potential for dependence and possibility of abuse. The lower the schedule number for these “controlled substances,” the higher the risks. Drugs in schedule I are illegal in the U.S.
- Guided by pain management protocols, Express Scripts’ Fraud, Waste and Abuse solutions ensure clinically appropriate use of controlled drugs.
A recent study demonstrated the correlation between pain intensity and adherence to analgesics in pain clinics.18

**Top Drugs: Market Share**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrocodone and acetaminophen</td>
<td>44.0%</td>
</tr>
<tr>
<td>oxycodone and acetaminophen</td>
<td>13.1%</td>
</tr>
<tr>
<td>tramadol</td>
<td>11.5%</td>
</tr>
<tr>
<td>amitriptyline</td>
<td>5.9%</td>
</tr>
<tr>
<td>oxycodone</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

**New Drugs Approved in 2011**

- 01.14 Abstral® (fentanyl sublingual tablets)
- 01.17 Butrans® (buprenorphine patches)
- 06.21 Oxecta® (oxycodone)
- 07.01 Lazanda® (fentanyl nasal spray)
- 07.15 oxymorphone extended-release 5mg and 15mg tablets (generic Opana® ER)
- 08.26 Nucynta® ER (tapentadol extended release)
- 11.11 morphine extended-release capsules (generic Kadian®)
- 12.09 Opana® ER (oxymorphone extended-release, tamper-resistant tablets)

**Savings Opportunity**

- **Channel:** $0.83
- **Mix:** $16.79

Total Savings: $17.61 PMPY = 58.2% of PMPY Spend

**Key Drug Information**

<table>
<thead>
<tr>
<th>Cost PMPY</th>
<th>#Rx PMPY</th>
<th>Prevalence</th>
<th>Average Cost/Rx</th>
<th>#Rx/User/Year</th>
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</thead>
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<tr>
<td>$30.27</td>
<td>0.8</td>
<td>18.0%</td>
<td>$40.31</td>
<td>3.60</td>
</tr>
</tbody>
</table>

**Market Influences on Trend**

- Prevalence: -1.3%
- Cost/Unit: -2.2%
- Units/Rx: 0.3%
- Patent Expirations: 0.1%
- New Drugs: 0.0%

**Behavioral Influences on Trend**

- Intensity: 0.1%
- Mix: 1.1%

**Total Trend:** -1.9%
Specialty medications are used to treat patients with chronic, serious health conditions. Complex and costly, specialty drugs usually need special storage and handling. Therapies may require frequent dosing adjustments and intensive clinical monitoring.

After several years of increase, specialty trend eased slightly in 2011, to 17.1% (down from 19.6%), although the increase still represented a substantial year-on-year cost growth for plan sponsors. Again this year, drugs used to treat inflammatory conditions, multiple sclerosis and cancer top the list, representing 57.6% of the total.

Although prevalence of specialty medication utilization is relatively low at the population level, with only about 1% of members requiring these medications, costs are high – averaging $1,766.79 per prescription. The top three specialty therapy classes (e.g., inflammatory conditions, multiple sclerosis and cancer) each had trend increases of more than 15%. Hepatitis C, which had the greatest increase in trend of 194.8%, was influenced by the release of two new oral drugs — Incivek™ (telaprevir) and Victrelis™ (boceprevir).

It is also important to note that approximately 47% of specialty medication costs are covered by medical rather than the pharmacy benefit and are not reflected in our analysis.
## Therapy Class Review: Specialty Medications

### Exhibit 17
2011 Key Metrics for Top 10 Specialty Therapy Classes, PBM-Adjudicated Claims Only, Ranked by PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Specialty Spend</th>
<th>Prevalence of Use</th>
<th>Cost Per Adjusted Rx</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammatory Conditions</td>
<td>$40.70</td>
<td>23.7%</td>
<td>0.23%</td>
<td>$2,066.77</td>
<td>17.7%</td>
</tr>
<tr>
<td>2</td>
<td>Multiple Sclerosis</td>
<td>$32.89</td>
<td>19.2%</td>
<td>0.10%</td>
<td>$3,115.93</td>
<td>20.3%</td>
</tr>
<tr>
<td>3</td>
<td>Cancer</td>
<td>$25.20</td>
<td>14.7%</td>
<td>0.15%</td>
<td>$3,259.34</td>
<td>15.7%</td>
</tr>
<tr>
<td>4</td>
<td>HIV</td>
<td>$18.08</td>
<td>10.5%</td>
<td>0.10%</td>
<td>$894.33</td>
<td>4.9%</td>
</tr>
<tr>
<td>5</td>
<td>Growth Deficiency</td>
<td>$6.72</td>
<td>3.9%</td>
<td>0.03%</td>
<td>$3,103.62</td>
<td>6.6%</td>
</tr>
<tr>
<td>6</td>
<td>Anticoagulants</td>
<td>$6.42</td>
<td>3.7%</td>
<td>0.31%</td>
<td>$1,013.35</td>
<td>5.1%</td>
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<td>7</td>
<td>Hepatitis C</td>
<td>$6.34</td>
<td>3.7%</td>
<td>0.02%</td>
<td>$3,370.99</td>
<td>194.8%</td>
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<tr>
<td>8</td>
<td>Transplant</td>
<td>$5.63</td>
<td>3.3%</td>
<td>0.11%</td>
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<td>9</td>
<td>Respiratory Conditions</td>
<td>$4.65</td>
<td>2.7%</td>
<td>0.02%</td>
<td>$2,800.35</td>
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<tr>
<td>10</td>
<td>Pulmonary Hypertension</td>
<td>$4.23</td>
<td>2.5%</td>
<td>0.01%</td>
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<td>2.6%</td>
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<tr>
<td></td>
<td>Others</td>
<td>$20.65</td>
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<td>0.22%</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>$171.51</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1.22%</strong></td>
<td></td>
<td><strong>$1,766.79</strong></td>
<td><strong>17.1%</strong></td>
</tr>
</tbody>
</table>
**YEAR IN REVIEW**

- In 2011, utilization growth for drugs in the inflammatory conditions class slowed, possibly because expanded use for broader indications has stabilized.

- Benlysta® (belimumab), the first new drug to treat systemic lupus erythematosus (SLE) in more than 50 years, was approved in March 2011. A novel, biologic drug that inhibits B-lymphocyte stimulator, Benlysta is given as a once-monthly infusion for patients with SLE.

- A new subcutaneous (SQ) formulation of Orencia® (abatacept) was approved in August 2011 for rheumatoid arthritis (RA). As its use increases, claims will shift to the pharmacy benefit from the medical benefit because Orencia previously was available only in intravenous (IV) form.

- Use of Cimzia® (certolizumab) increased just over 43% last year as uptake of the self-administered SQ formulation (approved in May 2009 for RA and Crohn’s disease) continued to rise.

- The nearly 51% utilization growth for Stelara® (ustekinumab) in 2011 significantly impacted trend in this category. Stelara is a novel, SQ biologic drug that was approved in September 2009 for psoriasis.

**A CLOSER LOOK**

- About 1% of U.S. adults (roughly 1.3 million people) have RA. About another 7.5 million Americans have psoriasis, the most common autoimmune disease.

- The increase in overall trend in the inflammatory conditions class can be attributed both to recent increases in the number of product options within the class and to the use of class members for broader indications. Nonetheless, the potential for increasing competition within the class offers plan sponsors new opportunities for clinically responsible, cost-effective utilization management.

**WHAT’S AHEAD**

- Tofacitinib, an oral Janus-Associated kinase (JAK) inhibitor, is expected to be approved for RA in August 2012. It will compete with injectable tumor necrosis factor (TNF) inhibitors, including Humira® (adalimumab) and Enbrel® (etanercept).

- Another oral drug, apremilast, an inhibitor of phosphodiesterase type-4, may be approved in early 2013 for treating psoriasis. Clinical data suggest that apremilast is more effective than methotrexate but less effective than TNF inhibitors.

- Arcalyst® (rilonacept) and Ilaris® (canakinumab) may receive expanded indications to treat gout in the near future. Currently, they are approved only to treat cryopyrin-associated periodic syndromes, rare inherited autoinflammatory conditions caused by a deficiency of interleukin-1-receptor antagonist.
Market Influences on Trend
- Prevalence: 8.5%
- Cost/Unit: 9.2%
- Units/Rx: -0.3%
- Patent Expirations: 0.0%
- New Drugs: 0.0%

Behavioral Influences on Trend
- Intensity: -1.3%
- Mix: 1.6%

Total Trend: 17.4%

Key Drug Information
- Enbrel® (etanercept): 45.3%
- Humira® (adalimumab): 45.0%
- Cimzia® (certolizumab): 3.1%
- Simponi® (golimumab): 3.0%
- Stelara® (ustekinumab): 1.3%

Top Drugs: Market Share

New Drugs Approved in 2011
- 03.09 Benlysta® (belimumab)
- 08.04 Orencia® SQ (abatacept)

Spend in Medical Benefit
- 31.8% of patients are NONADHERENT to medication therapy

PHARMACY-RELATED WASTE
- 49% of patients are NONADHERENT to medication therapy

INFLAMMATORY CONDITIONS
Double-digit drug price inflation continues

YEAR IN REVIEW

- Although overall trend and cost trend growth for multiple sclerosis (MS) drugs both have slowed, each still is increasing at double-digit rates. Cost is the primary driver of trend for the therapy class.
- At 4.8%, utilization growth was lower than the 6.0% increase seen in 2010.
- Trend was affected significantly by two oral MS drugs approved in 2010. Ampyra® (dalfampridine) helps to improve walking ability in patients with MS. Gilenya® (fingolimod) was the first oral, disease-modifying MS medication to reach the market.

A CLOSER LOOK

- Approximately 2.5 million individuals worldwide have MS, a condition that affects twice as many women as men. For the estimated 350,000 Americans who are affected, annual treatment costs exceed $10 billion.²³
- With additional oral MS products in the pipeline, plan sponsors will be challenged to manage the therapy offered by these more convenient but much more costly drugs. Express Scripts offers a number of clinical tools to manage current and future medications for the class. Plan sponsors who have instituted these programs saw favorable results in trend compared to those without management strategies.

WHAT’S AHEAD

- Several more oral, disease-modifying medications are expected to be approved in the near future for relapsing-remitting MS. Taken two times or three times daily, dimethyl fumarate (BG-12) is expected to be the market leader with high efficacy rates and moderate safety concerns, such as gastrointestinal intolerance and flushing, that subside with use. Although Laquinimod appears to have lower efficacy rates than BG-12, it is taken once daily and its side effects seem minimal. Teriflunomide has efficacy comparable to that of injectable MS therapies currently on the market; however, it cannot be used by women of child-bearing age, who represent a large portion of MS patients.
- Injectable, biologic drugs that currently are approved for other conditions may receive additional indications, allowing them to expand into the MS market. They include Lemtrada™ (alemtuzumab), which is currently marketed as Campath® to treat chronic lymphocytic leukemia. Additionally, a new SQ formulation of Zenapax® (daclizumab), a transplant medication, may gain Food and Drug Administration (FDA) approval to treat MS.
**Top Drugs: Market Share**

<table>
<thead>
<tr>
<th>Key Drug Information</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Copaxone® (glatiramer)</strong></td>
<td>35.4%</td>
</tr>
<tr>
<td><strong>Avonex® (interferon beta-1a)</strong></td>
<td>20.5%</td>
</tr>
<tr>
<td><strong>Rebif® (interferon beta-1a)</strong></td>
<td>17.2%</td>
</tr>
<tr>
<td><strong>Betaseron® (interferon beta-1b)</strong></td>
<td>11.0%</td>
</tr>
<tr>
<td><strong>Ampyra® (dalfampridine)</strong></td>
<td>7.7%</td>
</tr>
</tbody>
</table>

**Key Drug Information**

<table>
<thead>
<tr>
<th>BY THE #S</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>$32.89</strong></td>
<td>Cost PMPY</td>
</tr>
<tr>
<td><strong>0.01</strong></td>
<td>#Rx PMPY</td>
</tr>
<tr>
<td><strong>0.10%</strong></td>
<td>Prevalence</td>
</tr>
<tr>
<td><strong>$3,115.93</strong></td>
<td>Average Cost/Rx</td>
</tr>
<tr>
<td><strong>9.14</strong></td>
<td>#Rx/User/Year</td>
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</tbody>
</table>

**New Drugs Approved in 2011**

No new drugs were approved in 2011.
YEAR IN REVIEW

- Trend growth for cancer medications slowed to 15.7% compared to 23.7% growth in 2010. The 12.7% increase in PMPY cost was the major trend component.
- Revlimid® (lenalidomide) gained first-line use for patients with multiple myeloma.
- In 2011, nine new cancer medications were approved, including three – Yervoy™ (ipilimumab), Sylatron™ (peginterferon alfa-2b) and Zelboraf® (vemurafenib) – to treat melanoma, a rare, but deadly, skin cancer.
- Zelboraf and another new drug, Xalkori® (crizotinib), which treats non-small-cell lung cancer, have corresponding pharmacogenetic tests that identify appropriate patients.
- Jakafi™ (ruxolitinib) is the first medication approved to treat myelofibrosis, a rare form of blood cancer. An oral medication, it is the first in a new class, Janus-Associated kinase inhibitors.
- Two oral cancer drugs, Afinitor® (everolimus) and Sutent® (sunitinib), received additional indications to treat pancreatic cancer.
- Although the Food and Drug Administration (FDA) revoked approval of Avastin® (bevacizumab) for breast cancer, it remains on the market for certain colon, lung, kidney and brain cancers.

A CLOSER LOOK

- In late 1992, the FDA began an accelerated process for certain drugs to treat serious conditions. By mid-2010, 35 new cancer drugs had received accelerated approvals; 26 of them were converted to regular approvals after their clinical benefits were proven.24

WHAT’S AHEAD

- Inlyta® (axitinib), an oral, targeted therapy, was approved in January 2012 for advanced kidney cancer. Also in January, Erivedge™ (vismodegib) was approved to treat certain patients with basal cell carcinoma.
- Tivozanib, another oral, targeted therapy, may be approved in 2012 for advanced kidney cancer.
- Additional oral cancer drugs that may be approved within the next 12 months are cabozantinib (for thyroid cancer), regorafenib (for colorectal cancer) and ridaforolimus (for bone and soft-tissue sarcomas).
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MEDICARE / MEDICAID

37% of patients are NONADHERENT to medication therapy (oral oncology agents only)

Spend in Medical Benefit

New Drugs Approved in 2011

03.25 Yervoy™ (ipilimumab)
03.29 Sylatron™ (peginterferon alfa-2b)
04.06 Caprelsa® (vandetanib)
04.28 Ztyga® (abiraterone)
08.17 Zelboraf® (vemurafenib)
08.19 Adcetris™ (brentuximab)
08.26 Xalkori® (crizotinib)
11.16 Jakafi™ (ruxolitinib)
11.18 Erwinaze™ (asparaginase Erwinia chrysanthemi)

BY THE #S

$25.20 Cost PMPY  0.01 #Rx PMPY  0.15% Prevalence  $3,259.34 Average Cost/Rx  4.50 #Rx/User/Year

Market Influences on Trend
Prevalence -5.4%
Cost/Unit 9.0%
Units/Rx -0.2%
Patent Expirations 0.2%
New Drugs 3.4%

Behavioral Influences on Trend
Intensity 5.0%
Mix 3.7%

Total Trend
15.7%

Top Drugs: Market Share

methotrexate 21.6%
Xeloda® (capecitabine) 12.5%
Gleevec® (imatinib) 11.7%
Revlimid® (lenalidomide) 9.4%
Lupron Depot® (leuprolide) 7.6%

PHARMACY-RELATED WASTE

77.6%

Key Drug Information

337x396

+ 339x337

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Lupron Depot® (leuprolide) 7.6%

PHARMACY-RELATED WASTE

77.6%
FACT
Decrease in use offsets rising per-unit cost

YEAR IN REVIEW

- In mid-2011, oral medications for human immunodeficiency virus (HIV) joined injectable HIV medications on our specialty drug list. Previously, injectable HIV drugs had been grouped with immune deficiency drugs, which ranked 19 for 2010.
- Increased cost pushed drug trend for the expanded class up 4.9%.
- Use of the market leader, Atripla® (efavirenz, emtricitabine and tenofovir), grew as patients adopted more-convenient therapies. Current treatment guidelines recommend Atripla as preferred when starting HIV therapy.
- Utilization for Truvada® (emtricitabine and tenofovir) also is growing. Clinical guidelines recommend Truvada with a boosted protease inhibitor (PI) as preferred initial therapy in patients with HIV. Boosting combines low doses of an older PI, Norvir® (ritonavir), with another PI – either Reyataz® (atazanavir) or Prezista® (darunavir). Both PIs attach to the same enzymes, but Norvir attaches more quickly, allowing higher blood levels of the other PI.
- The twice-daily combination of Kaletra® (lopinavir and ritonavir) plus a boosted PI lost market share to once-daily PIs, which have better safety profiles.
- Approved in May, Edurant® (rilpivirine), a once-daily non-nucleoside reverse transcriptase inhibitor (NNRTI), is used with other antiretroviral medications for treatment-naive HIV patients.
- Complera™, a once-daily pill approved in August, is a three-drug combination of Edurant with Truvada.

A CLOSER LOOK

- Great advances have been made in the treatment of HIV since it was recognized in the 1980s. Still, it has caused almost 600,000 deaths in the U.S. Alarmingly, about 20% of the estimated 1.2 million Americans currently living with HIV are not aware that they have it.
- HIV treatment is highly individualized, limiting utilization management options. Although combination drugs offer convenience and increase adherence, they also may reduce treatment flexibility.

WHAT’S AHEAD

- Approval is pending for once-daily Truvada for pre-exposure prophylaxis to reduce the risk of HIV infection in uninfected adults.
- The Quad pill – a four-in-one tablet taken once daily to treat HIV – contains cobicistat, a novel booster; elvitegravir, a novel integrase inhibitor; and Truvada. Its approval is expected by August 28, 2012.
- As single agents, elvitegravir and cobicistat should be approved by the Food and Drug Administration (FDA) in 2012 and 2013, respectively.
- A single-tablet combination of Reyataz and cobicistat that is in late-phase development may be marketed in 2013.
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---

**Pharmacy-Related Waste**

24% of patients are **NONADHERENT** to medication therapy.

**Spend in Medical Benefit**

0.1%

---

**Top Drugs: Market Share**

- **Atripla®** (efavirenz, emtricitabine and tenofovir) 17.7%
- **Truvada®** (emtricitabine and tenofovir) 14.3%
- **Norvir®** (ritonavir) 11.4%
- **Viread®** (tenofovir) 7.1%
- **Isentress®** (raltegravir) 0.8%

---

**New Drugs Approved in 2011**

- 05.20 **Edurant®** (rilpivirine)
- 08.10 **Complera™** (emtricitabine, rilpivirine and tenofovir)

---

**By the #s**

- $18.08 Cost PMPY
- 0.02 #Rx PMPY
- 0.10% Prevalence
- $894.33 Average Cost/Rx
- 16.73 #Rx/User/Year

---

**HIV**
Growth Deficiency

FACT

Utilization 3 times higher among boys than girls, despite equal diagnosis

YEAR IN REVIEW

• Despite a decrease in the use of growth hormone medications in 2011, drug trend for the class still was up 6.6%, due to increased cost.
• Double-digit growth was seen in the cost of several older brands of growth hormones.
• Large utilization increases for the newer somatropin formulations, Nutropin AQ® NuSpin™ (approved in 2009) and Norditropin® FlexPro™ (approved in 2010), contributed to higher utilization trend in 2011.
• Cost for Norditropin FlexPro actually dropped considerably, however, and cost for Nutropin AQ NuSpin rose only moderately.
• Cost trends for two biosimilar growth hormones, Omnitrope® and Tev-Tropin®, were down significantly (by 21.6% and 13.8%, respectively). Utilization of each, however, increased more than 100% in 2011.

A CLOSER LOOK

• Genetic mutations are believed to cause some congenital growth hormone deficiencies, which affect one in 3,500 to 10,000 newborns. In adults, although most cases cannot be attributed to a single cause, pituitary injuries and conditions such as chronic kidney disease are common causes. For children, replacing deficient natural growth hormone generally increases adult height and also improves strength, bone mass and motor skills.

• Although growth hormone medications are primarily prescribed for children, the Food and Drug Administration (FDA) has also indicated this class for adults with chronic kidney insufficiency, HIV wasting or short-bowel syndrome. For adults, growth hormones help to control anemia, severe weight loss and muscle wasting associated with other conditions.
• All growth hormone replacements available in the U.S. are very similar recombinant human growth hormone products known as somatropins. What differentiates them are the ways they are injected. A more user-friendly delivery system is important for keeping children adherent with injectable therapy. Express Scripts offers proven solutions to improve formulary compliance and better manage cost for products in the class.

WHAT’S AHEAD

• The growth hormone class is stable, with no late-phase medications in the pipeline. No new medications will reach the market in the near term.
• One new, long-acting human growth hormone formulation that is expected to be approved in 2015 will be administered as a once-weekly or twice-monthly subcutaneous injection.
## Introduction

### Trend Overview

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Cost/Unit</th>
<th>Units/Rx</th>
<th>Patent Expirations</th>
<th>New Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8%</td>
<td>8.6%</td>
<td>-0.8%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

### Therapy Class Review

- **Top Drugs: Market Share**
  - **Genotropin®** (somatropin): 25.4%
  - **Humatrope®** (somatropin): 15.6%
  - **Nutropin AQ®** (somatropin): 15.2%
  - **Norditropin® FlexPro®** (somatropin): 12.9%
  - **Nutropin AQ® NuSpin™** (somatropin): 9.8%

### Forecast

- **Medicare/Medicaid Growth Deficiency**
  - **56%** of patients are **NONADHERENT** to medication therapy
  - **2.8%** Spend in Medical Benefit

### Key Drug Information

- **New Drugs Approved in 2011**
  - No new drugs were approved in 2011.

### By the #s

- **$6.72** Cost PMPY
- **0.002** #Rx PMPY
- **0.03%** Prevalence
- **$3,103.62** Average Cost/Rx
- **7.24** #Rx/User/Year

### Market Influences on Trend

<table>
<thead>
<tr>
<th>Prevalence</th>
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<th>Units/Rx</th>
<th>Patent Expirations</th>
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<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

### Behavioral Influences on Trend

- **Intensity**: -1.1%
- **Mix**: -1.9%

### Total Trend

- **6.6%**
Anticoagulants

YEAR IN REVIEW

- After a 16.6% increase in 2010, drug trend for anticoagulants declined to 5.1% in 2011, primarily due to a market-share shift from branded Lovenox® (enoxaparin) to its less-expensive generic alternative, which was introduced in July 2010. A second generic to Lovenox that was approved in September did not come to market until January 2012. It is considered an at-risk launch due to ongoing litigation.

- Utilization growth in the class has decelerated as well, partially due to patients shifting from specialty anticoagulants to oral anticoagulants, which typically are included on the traditional side of the pharmacy benefit. One example is Xarelto® (rivaroxaban), a novel oral anticoagulant that was approved in July to prevent blood clots for patients undergoing knee or hip replacement surgery. In November, Xarelto received a second indication to reduce the risk of stroke and systemic blood clots in patients with atrial fibrillation.

- The first A-rated generic to Arixtra® (fondaparinux) was approved in July. Its impact on class trend was minimal, though, since its market share is very small.

- Utilization of Innohep® (tinzaparin) remains at nearly zero due to a December 2008 warning of its association with a higher death rate among elderly patients with kidney conditions.

FACT

Patent expirations minimize trend

A CLOSER LOOK

- According to information from the U.S. Centers for Disease Control and Prevention (CDC), every year an estimated 30,000 to 180,000 Americans die within one month of being diagnosed as having a deep vein thrombosis or a pulmonary embolism.28

WHAT’S AHEAD

- Trend growth for specialty anticoagulants may continue to slow over the next several years as more oral anticoagulants join Xarelto and Pradaxa® (dabigatran) on the traditional-drug side of the market.

- The next new, oral anticoagulant, Eliquis® (apixaban), a potential market leader, is expected to be approved in March 2012. Already approved in Europe, apixaban is a direct factor Xa inhibitor, similar to Xarelto.

- Also in 2012, Mulsevo® (semuloparin), a next-generation Lovenox, may be approved to prevent blood clots in cancer patients starting chemotherapy. Administered as a subcutaneous injection, it is in further development to prevent blood clots for other at-risk patients.
### INTRODUCTION

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#### Medicare / Medicaid

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### Key Drug Information

#### Top Drugs: Market Share

- enoxaparin: 74.9%
- Lovenox® (enoxaparin): 13.6%
- Arixtra® (fondaparinux): 5.8%
- Fragmin® (dalteparin): 1.5%
- fondaparinux: 1.6%

### New Drugs Approved in 2011

- 07.13 fondaparinux (generic Arixtra®)

---

### Pharmacy-Related Waste

A 10% increase in warfarin nonadherence has been associated with a 14% increase in the odds of blood clots.29

---

### Market Influences on Trend

- Prevalence: 2.6%
- Cost/Unit: -0.7%
- Units/Rx: 16.4%
- Patent Expirations: -19.1%
- New Drugs: 0.8%

### Behavioral Influences on Trend

- Intensity: 3.8%
- Mix: 1.3%

### Total Trend

5.1%

---

### BY THE #S

- $6.42 Cost PMPY
- 0.01 #Rx PMPY
- 0.31% Prevalence
- $1,013.35 Average Cost/Rx
- 1.76 #Rx/User/Year

---

**ANTICOAGULANTS**
Hepatitis C

FACT
New treatments drive trend to nearly 200%

YEAR IN REVIEW

- Drug trend for hepatitis C medications increased almost 195% in 2011, primarily driven by the market entry of two new, oral protease inhibitors (PIs), Incivek™ (telaprevir) and Victrelis™ (boceprevir). After both were approved in May 2011 to treat patients with genotype 1 hepatitis C, Incivek quickly claimed 12.3% of market share in the class.

- Incivek is already in the top five drugs by market share for this class. PIs inhibit an enzyme that allows the hepatitis C virus to replicate. Viral cure rates are significantly improved when Victrelis or Incivek is added to the standard of care (ribavirin and pegylated interferon). For many patients, adding an oral PI also may shorten treatment to 24 weeks versus the standard 48 weeks.

A CLOSER LOOK

- More than three million patients in the U.S. have chronic hepatitis C, with genotype 1 accounting for approximately 75% of all cases.30

- As it has with cancer treatment, pharmacogenomics is playing a crucial role in determining the type and length of treatment for patients with hepatitis C. Victrelis and Incivek are indicated for patients with genotype 1 hepatitis C, but pharmacogenomic testing can help determine appropriate treatment options for patients with other genotypes of the disease as well. Express Scripts offers utilization programs that incorporate prior authorization to ensure that patients with hepatitis C are receiving the most clinically appropriate treatment.

WHAT’S AHEAD

- Many other kinds of oral, direct-acting antiviral medications are in development for treating hepatitis C. The next wave is expected to begin entering the market in 2014.

- Next-generation protease inhibitors may have better dosing regimens, as well as being effective in treating patients with other genotypes of the condition.

- Oral polymerase inhibitors, a new group of direct-acting antiviral medications, are in the pipeline for hepatitis C. They help to minimize viral resistance when added to therapy.

- Even though the treatment paradigm may shift to an interferon-free regimen in the future, several new interferons are in the hepatitis C pipeline. PEG-Interferon lambda is a novel formulation that may be better tolerated than currently available interferons. Locteron® (controlled-release interferon alpha-2b) is a longer-acting interferon that is dosed once every two weeks. Food and Drug Administration (FDA) approval of both PEG-Interferon lambda and Locteron is expected in 2013.
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Hepatitis C

Top Drugs: Market Share

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New Drugs Approved in 2011

BY THE #S

$6.34 Cost PMPY

0.002 #Rx PMPY

0.02% Prevalence

$3,370.99 Average Cost/Rx

8.51 #Rx/User/Year

83
Transplants

**YEAR IN REVIEW**

- In mid-2011, oral transplant medications were moved to the Express Scripts specialty drug list.

- Total trend for transplant medications declined 1.7% in 2011, still being affected by generics to Prograf® (tacrolimus) that had been launched in August 2009. Continued uptake of lower-cost generic tacrolimus and another generic, mycophenolate, the market leader, contributed to the negative trend.

- Nulojix® (belatacept) is a unique biologic drug that was approved in June 2011. It is used in combination with other transplant medications to prevent organ rejection for adult kidney transplant patients. After the initial induction phase in which it is given more frequently, Nulojix is administered once monthly as an IV infusion. Nulojix competes with oral immunosuppressants such as cyclosporine and tacrolimus that are taken twice daily.

**A CLOSER LOOK**

- The U.S. accounts for significant percentages of worldwide transplants. In 2005, the World Health Organization (WHO) estimated that 25% of the world’s kidney transplants, 31% of total liver transplants and 35% of total heart transplants were performed in the U.S. The U.S. Census Bureau reported that more than 28,600 Americans received one or more transplanted organs in 2010.

**WHAT’S AHEAD**

- Transplant is now the treatment of choice for end-stage organ failure. The kidney is the most commonly transplanted organ in the U.S.—more than 16,000 kidney transplants were performed in 2010—followed by the liver, with more than 6,000 transplants in 2010. Other commonly transplanted organs are the heart, lungs, pancreas and intestines.

- Thymoglobulin® (anti-thymocyte [rabbit]), which is currently approved to treat acute rejection following a kidney transplant, is expected to gain additional indications to prevent and treat rejection episodes following heart or liver transplantation. It also may be approved for induction therapy following a lung transplant.

- An infused immunomodulator, Diannexin, is in late-phase development to prevent delayed graft function in kidney transplant patients.
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Top Drugs: Market Share

Key Drug Information

BY THE #S

$5.63 Cost PMPY

0.02 #Rx PMPY

0.11% Prevalence

$334.68 Average Cost/Rx

12.77 #Rx/User/Year

PHARMACY-RELATED WASTE

36% of patients are NONADHERENT to medication therapy

Spend in Medical Benefit

3.9%

New Drugs Approved in 2011

06.15 Nulojix® (belatacept)
Respiratory Conditions

FACT

Treatments for allergic asthma lead therapy class

YEAR IN REVIEW

- The respiratory conditions class includes specialty drugs to treat cystic fibrosis (CF), allergic asthma and alpha-1 antitrypsin (AAT) deficiency.
- Utilization of the class leader, Xolair® (omalizumab), a drug to treat allergic asthma, increased 7% in 2011.
- Utilization of Prolastin®-C for AAT deficiency increased almost 58%. Approved in late 2009, it competes with other human alpha 1-proteinase inhibitors, including Aralast NP, Glassia™ and Zemaira®.
- Cayston® (aztreonam lysinate for inhalation), approved in 2010 to treat CF lung infections, continues to capture market share from a similar drug, TOBI® (tobramycin inhalation solution). Both are antibiotics that are inhaled through nebulizers, but Cayston needs a specialized device. TOBI is inhaled only twice a day (versus three times a day for Cayston), but each TOBI treatment takes 15 minutes (compared to three minutes for Cayston).

A CLOSER LOOK

- Around 1,000 patients are diagnosed with CF every year in the U.S. CF used to be called “the killer of young adults” because few children who had it survived much past adolescence. Today, however, about 45% of Americans with CF are older than 18. More than 30,000 Americans live with CF, many of whom are over 40 years old.
- AAT deficiency, which is rare, proportionally affects more Caucasians than Asians or other ethnic groups. The National Institutes of Health (NIH) estimates that one person in every 1,500 to 3,500 individuals of European descent is AAT deficient.
- Even though several alpha 1-proteinase inhibitors have been approved in the last few years to treat AAT deficiency, many of them continue to experience double-digit increases in cost per unit. However, because some alpha 1-proteinase inhibitors have comparable counterparts, Express Scripts solutions help mitigate price inflation, improve overall formulary compliance and still provide quality therapy options for AAT-deficient patients.

WHAT’S AHEAD

- Kalydeco™ (ivacaftor) is an oral medication that targets a defective protein, G551D, which is responsible for approximately 4% of CF cases. It was approved in January 2012 as the first drug to target the cause of CF, not just its symptoms.
- Ataluren is another oral CF drug in development. It treats the underlying disease for patients with CF due to nonsense mutations, defects in DNA that stop making a protein before it is finished. Nonsense mutations play a role in inherited diseases such as CF. A pharmacogenomic test will be used to identify appropriate candidates for treatment with ataluren, expected to be approved in 2012.
- Aeroquin™, an inhaled formulation of the anti-infective, levofloxacin, decreases pseudomonas lung infections in patients with CF. It may be approved in 2012 to compete with TOBI and Cayston.
- Among oral drugs in late-phase development for the treatment of idiopathic pulmonary fibrosis (IPF) are pifithrine and Vargatef™ (BIBF 1120). IPF is a condition characterized by scarring of lung tissue. Although IPF affects about 250,000 Americans, no treatment options for the condition have been approved by the Food and Drug Administration (FDA).
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**Top Drugs: Market Share**

- **Xolair® (omalizumab)**: 55.4%
- **Pulmozyme® (dornase alfa)**: 29.2%
- **TOBI® (tobramycin inhalation solution)**: 4.0%
- **Cayston® (aztreonam lysinate for inhalation)**: 3.1%
- **Prolastin®-C (alpha1-proteinase inhibitor)**: 3.3%

---

**New Drugs Approved in 2011**

No new drugs were approved in 2011.

---

**BY THE #S**

- **$4.65** Cost PMPY
- **0.002** #Rx PMPY
- **0.02%** Prevalence
- **$2,800.35** Average Cost/Rx
- **6.91** #Rx/User/Year

---

**PHARMACY-RELATED WASTE**

The risk of hospitalization is reduced by 60% for patients diagnosed with cystic fibrosis with high utilization of tobramycin inhalation solution (>= 4 cycles per year) compared to patients taking two or fewer cycles per year.36

**Spend in Medical Benefit**

**32.6%**
Pulmonary Hypertension

YEAR IN REVIEW

- Drug trend for pulmonary hypertension medications grew 2.6% in 2011, with increased utilization the primary driver. Factors impacting greater trend in this class include increased combination use of pulmonary hypertension medications and increased use of oral dosage forms that are billed under the pharmacy benefit instead of injectables that often are billed under medical benefits.

- Increased use of Tyvaso®, an inhaled formulation of the prostaglandin treprostinil, continues to outpace growth of Ventavis® (iloprost), an inhaled prostaglandin that must be used more frequently than Tyvaso.

- Increased use of newer, oral drugs also drove up trend in this class. A greater use of the phosphodiesterase type-5 (PDE5) inhibitor Adcirca® (tadalafil, the same drug as Cialis®) was observed compared to its counterpart Revatio® (sildenafil, the same drug as Viagra®). Use of the oral endothelin-receptor blocker Tracleer® (bosentan) was down compared to its competitor, Letairis® (ambrisentan).

A CLOSER LOOK

- Diagnosing the condition is difficult, with an average of 2.8 years between the appearance of symptoms and a definitive diagnosis.

- The high cost of drugs for pulmonary hypertension, together with continuing increases in the simultaneous use of multiple pulmonary hypertension medications, make utilization management of the class essential. The Express Scripts Pulmonary Hypertension solution gives plan sponsors clinically appropriate measures to control cost while providing patients with the drugs necessary to manage their complex disease.

- The health costs for patients with pulmonary arterial hypertension (PAH) are, on average, $1,525 per month higher than the costs for similar patients without PAH. For patients with PAH, inpatient services account for 45% of total healthcare costs and outpatient services account for 38%.

WHAT’S AHEAD

- An oral tablet formulation of treprostinil may be approved toward the end of 2012, even though a late-phase combination trial failed to reach its primary endpoint.

- Also in 2012, Gleevec® (imatinib), an oral cancer medication, may receive an expanded indication to treat pulmonary hypertension.

- Other oral pulmonary hypertension medications, including macitentan (an endothelin receptor antagonist) and riociguat (a soluble guanylate cyclase stimulator), may enter the market within the next few years as well.
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PULMONARY HYPERTENSION

Top Drugs: Market Share

Key Drug Information

BY THE #S

$4.23
Cost PMPY

0.001
#Rx PMPY

0.01%
Prevalence

$3,507.42
Average Cost/Rx

9.69
#Rx/User/Year

SPEND IN MEDICAL BENEFIT

3.3%
Prevalence

26.0%
Cost/Unit

12.9%
Units/Rx

10.2%
Patent Expirations

1.8%
New Drugs

26.8%

Spend in Medical Benefit

of patients are NONADHERENT to medication therapy

New Drugs Approved in 2011

No new drugs were approved in 2011.

Market Influences on Trend

Prevalence 3.3%
Cost/Unit 0.0%
Units/Rx -0.2%
Patent Expirations 0.0%
New Drugs 0.0%

3.1%

Behavioral Influences on Trend

Intensity 1.8%
Mix -2.3%

-0.5%

Total Trend

2.6%

Pharmacy-Related Waste

26%

Behavioral Influences on Trend

Intensity 1.8%
Mix -2.3%

Total Trend

2.6%

Revatio® (sildenafil)
47.8%

Tracleer® (bosentan)
39.0%

Adcirca® (tadalafil)
12.9%

Letairis® (ambrisentan)
10.2%

Tyvaso® (treprostinil)
5.1%

Top Drugs: Market Share

New Drugs Approved in 2011

No new drugs were approved in 2011.
In 2011, the trend for traditional drugs was flat (0.1%), with the average per-member-per-year (PMPY) spend at $804.27. We anticipate that the traditional trend will remain relatively stable over the next three-year period (Exhibit 18). In fact, we believe that the trend for traditional medications may show negative trend in 2012, for the first time since Express Scripts has been publishing the annual Drug Trend Report. Looking ahead, we expect trend to rise only modestly in 2013 and 2014, fueled primarily by increases in overall drug utilization.

Over the past 10 years, the trend for traditional drugs has been mitigated by a large number of patent expirations for blockbuster brand-name drugs. The precipice of this historic “patent cliff” will be reached in 2012 when generics to Plavix® (clopidogrel), Seroquel® (quetiapine), Singulair® (montelukast) and Lexapro® (escitalopram), among others, will enter the marketplace. As a result, cost per unit is expected to decline in 2012 and 2013 – due not only to the availability of more generic medications, but also to continued reductions in the cost per fill for generics. By 2014, we anticipate that the cost per unit for traditional drugs will increase slightly because of brand inflation, which will offset the continued downward pressure from generics.

In 2011, the utilization trend for traditional drugs was slightly negative (-0.81%) – in our opinion, a direct consequence of the national economic woes. Going forward, utilization will be relatively flat in 2012, but it is likely to grow between 2.0% and 2.2% in both 2013 and 2014 as the economy slowly rebounds. Utilization for traditional drugs will be driven by rises in both prevalence and intensity. Prevalence, the proportion of patients taking a medication, has suffered during the recent economic downturn as some patients have reacted to financial stress by foregoing their medications or taking them less frequently than prescribed to save money. We anticipate that intensity will increase as the economy improves.

For the first time, diabetes led PMPY spend categories in 2011. High blood cholesterol, which held the top PMPY spend position for the previous eight years, dropped to second place. Within the high blood cholesterol class, the main event was that Lipitor® (atorvastatin), the top revenue-generating pharmaceutical in the world, lost its patent in November 2011. We anticipate that additional generic manufacturers will enter the atorvastatin market in mid-2012, decreasing overall costs to plan sponsors and patients. Looking ahead to 2014, we believe that diabetes and high blood cholesterol will remain the top two classes for PMPY spend. Fueled by increased utilization, primarily by adults, seventh-ranking attention disorders will jump to the number-three spot in 2014, followed by high blood pressure/heart disease, depression and asthma.

Many plan sponsors using Express Scripts to manage pharmacy benefits already take advantage of our innovative clinical offerings. In addition, we constantly turn our ongoing insights into new solutions for our plan sponsors and their members. Together with major new generic opportunities, our unique interventions can help even the most successful plans continue to provide quality care while cutting unnecessary expense. Plan sponsors who take action with Express Scripts will realize the full benefits of the new generic drugs.
2012 to 2014 Forecast for the Top 10 Traditional Therapy Classes

### Watermark

#### INTRODUCTION

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#### 2012 to 2014 Forecast for the Top 10 Traditional Therapy Classes

**#1 DIABETES**

<table>
<thead>
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<th>2014</th>
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</thead>
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<td>TRENDS</td>
<td>7.1%</td>
<td>7.1%</td>
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</tr>
<tr>
<td>PMPY</td>
<td>$86.85</td>
<td>$93.01</td>
<td>$102.51</td>
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</tbody>
</table>

**COMMENTS**

Utilization will grow as the prevalence of type 2 diabetes increases. Cost increases also will continue as more patients use brand-name agents in new subclasses, such as the DPP-4 inhibitors and GLP-1 mimetics. However, “me-too” products in the pipeline should lead to greater competition among the newer drugs. Beginning in the second half of 2012, insulin degludec, a new, long-acting insulin, is expected to compete with Lantus® (insulin glargine) and Levemir® (insulin detemir) in the market. The next significant generic opportunity is for Actos® (pioglitazone), which is expected to become available generically as early as July 2012.

**#2 HIGH BLOOD CHOLESTEROL**

<table>
<thead>
<tr>
<th>TREND</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRENDS</td>
<td>-6.1%</td>
<td>-2.2%</td>
<td>2.0%</td>
</tr>
<tr>
<td>PMPY</td>
<td>$73.62</td>
<td>$72.04</td>
<td>$73.45</td>
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</tbody>
</table>

**COMMENTS**

Atorvastatin, generic Lipitor®, was launched in late 2011. Significant cost savings should emerge through 2013 as more generics to Lipitor are marketed. Management strategies have been successful in moving users of brand statins to clinically appropriate generics. Recent clinical trials call into question the value of lowering triglycerides with fenofibrates and increasing high-density lipoprotein (HDL) cholesterol with niacin. The release of new guidelines in late 2012 or early 2013 is expected to increase the utilization of statin drugs. In 2013, generics to Niaspan® (niacin extended release) should result in cost savings to clients although competition will be limited. CETP inhibitors, a new subgroup of cholesterol therapies that raise HDL, should emerge in 2014, but their early adoption is expected to be limited.
**DEPRESSION TRENDS**

2012: $52.11 PMPY
2013: $48.78 PMPY
2014: $45.07 PMPY

**TREND**

-3.2%  -6.4%  -7.6%

**COMMENTS**

Multisource generics to Effexor XR® (venlafaxine extended release) launched in mid-2011, decreasing the class cost for the year. An authorized generic to the largest-selling, brand-only SSRI, Lexapro® (escitalopram), reached the market in early 2012, continuing the decrease in cost. In late 2013, several manufacturers may launch generics to Cymbalta® (duloxetine), extending cost savings into 2014. New products in development may become available for patients who do not respond to current therapies. Uptake of the new therapies beyond nonresponding patients, however, will be limited by the availability of generics in several classes of antidepressants.

**HIGH BLOOD PRESSURE/HEART DISEASE TRENDS**

2012: $59.70 PMPY
2013: $54.26 PMPY
2014: $52.07 PMPY

**TREND**

-5.0%  -9.1%  -4.1%

**COMMENTS**

The class of high blood pressure/heart disease medications is dominated by generic products. Increased utilization is expected to continue, fueled by the aging population and the anticipated introduction of updated guidelines in 2013. However, as the ARB class continues to mature, generics to Atacand® (candesartan), Avapro® (irbesartan) and Diovan® (valsartan), which all will become available in 2012, will continue lowering class trend through 2014.

2012 to 2014 Forecast for the Top 10 Traditional Therapy Classes
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### Therapy Class Review

### Forecast

#### Medicare / Medicaid

#### 2012 to 2014 Forecast for the Top 10 Traditional Therapy Classes

### Comments

In contrast to other classes, the generic fill rate for asthma medications dropped dramatically over the last three years. Starting in 2008, generic, ozone-depleting chlorofluorocarbon (CFC) inhalers were replaced with environmentally friendly, brand-name hydrofluoroalkane (HFA) inhalers, moving the class back to mainly brand products. The next large generic opportunity in this class is the availability of generics to Singulair® (montelukast) in August 2012. Generics for this blockbuster oral asthma and allergy medication not only will decrease in cost in 2012 and 2013, they also will increase the generic fill rate in the class. Additional brand competitors to Spiriva® (tiotropium) will become available in 2012. In addition, Relovair™ (vilanterol and fluticasone), the follow-on to Advair® (fluticasone and salmeterol), is expected in 2013. These and other new brand products will increase the cost trends for the class in 2014 and beyond.

Generic introductions and over-the-counter (OTC) availability continue to affect the ulcer disease category heavily. Because additional manufacturers released pantoprazole (generic Protonix®) in early 2011, the cost trend for the class was negative. Generics to AcipHex® (rabeprazole) at the end of 2013 and Nexium® (esomeprazole) in mid-2014 will escalate negative trend. Additionally, brand manufacturers are expected to market their products in the OTC market as patents expire.
**ATTENTION DISORDERS**

<table>
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<tr>
<th>Year</th>
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<tr>
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<td>10.0%</td>
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<td>17.6%</td>
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<tr>
<td>2014</td>
<td>18.8%</td>
<td>$54.33</td>
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</table>

**COMMENTS**

Utilization of drugs for attention disorders is expected to continue increasing as more adolescents and adults are treated. Cost/Rx also will continue rising following the introduction of new nonstimulant medications. True generic competition within the category is limited as well. Despite the availability of some generics to Adderall XR® (amphetamine and dextroamphetamine extended release), true A-rated generics for it have not yet entered the market. Additionally, a settlement agreement allowed an authorized generic for Concerta® (methylphenidate) to launch in May 2011, but other generics for Concerta continue to be delayed.

**INFECTIONS**

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<th>Year</th>
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<tr>
<td>2013</td>
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<tr>
<td>2014</td>
<td>-1.0%</td>
<td>$29.63</td>
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</table>

**COMMENTS**

The infections class is greatly impacted by seasonality, often mirroring the severity and duration of the annual influenza season. Multiple manufacturers launched levofloxacin (generics to Levaquin®) in mid-2011. These generics will again decrease cost trends for the class in 2012.
2012 to 2014 Forecast for the Top 10 Traditional Therapy Classes

**MENTAL/NEUROLOGICAL DISORDERS**

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<td>8.2%</td>
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**PAIN**

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</tr>
<tr>
<td>2014</td>
<td>1.0%</td>
<td>$30.57</td>
</tr>
</tbody>
</table>

**COMMENTS**

Mental/Neurological Disorders:
This class is heavily influenced by the atypical antipsychotic medications, which are maturing. Two, Risperdal® (risperidone) and Zyprexa® (olanzapine), went generic in 2008 and 2011, respectively. Generics to two others, Seroquel® (quetiapine) and Geodon® (ziprasidone), should be launched in 2012. Cost/Rx for the class continues to increase, however, as use transitions to newer agents, including Fanapt®, Latuda® and Saphris®, that have fewer metabolic side effects.

Pain:
The pain category is highly generic. However, the introduction of newer abuse-resistant, long-acting opioids, such as Embeda®, Opana ER® and OxyContin® (reformulated), may allow manufacturers to rebrand. Already, several older opioid formulations have been discontinued by their manufacturers after new formulations were approved, protecting the new products from near-term generic competition. Even though generics to the “older” formulations of OxyContin and Opana ER could become available in 2013, they will not be A-rated generics to the current formulations.
Specialty Forecast

According to an Express Scripts analysis of 2010 data from the Thomson Reuters MarketScan® Commercial Database, approximately 47% of all specialty drug spend was covered under medical benefits. Inasmuch as the Express Scripts Drug Trend Report focuses primarily on medications that are covered by pharmacy benefits, about 53% of specialty drugs are addressed in our analysis. Historically, Express Scripts has reported that only about 45% of specialty drug spend was covered under the pharmacy benefit. Last year’s relatively large swing in specialty drug spend to the pharmacy benefit (as a percentage of total spend) can be attributed to three key factors:

- The first-time inclusion under the specialty category of HIV and transplant medications, which are almost exclusively covered by pharmacy benefits
- Physician transitioning away from “buy-and-bill” reimbursement arrangements, causing many products to move from medical benefits to pharmacy benefits
- Perhaps most important, the large number of recent drug approvals for oral solid and self-administered injectable dosage forms that are most commonly processed under pharmacy benefits; not only innovative therapies, many of these new medications allow patients more convenient access to life-saving or life-sustaining treatments

In contrast to the traditional forecast, which predicts relatively flat trend between 2012 and 2014, the specialty drug forecast anticipates approximately 20% growth, year over year (Exhibit 19). Both of the major trend components — cost per unit and utilization — will contribute to positive trend; cost per unit will be the main factor, accounting for roughly two-thirds of the total growth.

In 2011, specialty medications accounted for $171.51 in PMPY spend, or roughly 17.6% of the total pharmacy-benefit spend of $975.78. Based on our expected growth figures for traditional drugs and specialty drugs, specialty medications will represent an increasingly larger component of plan sponsors’ overall drug-related expenditures. By 2014, specialty medications will account for more than 25% of the total PMPY pharmacy spend.

Over the next three years, cost per unit will be the primary trend driver. Brand inflation and the introduction of novel, more-expensive therapies will lead to annual increases in the range of 12% to 14%. Looking ahead, we believe that the introduction of biosimilars in key therapy classes may play a significant role in decelerating cost-per-unit increases. Unlike traditional generics, which are approved via a well-defined pathway, biosimilars will follow a different pathway. When approved, they will not be substitutable automatically with the innovator brand. Additionally, biosimilars will be only modestly less expensive than their traditional counterparts, with expected price reductions of 20% to 30%. Plan sponsors who implement formulary and utilization management will reap the most substantial savings from these lower-cost alternatives.

Utilization of specialty drugs will continue to grow in the 5% to 7% range, year over year, between 2012 and 2014. Utilization will be strong in the top specialty classes due to new approvals, new FDA-approved indications and more oral and self-administered therapies. Looking ahead, we believe many of the high-cost specialty conditions —
including pulmonary hypertension, multiple sclerosis (MS) and cancer – increasingly will be managed by multiple therapies. The resulting tailored, complex regimens will drive higher utilization. In addition, we anticipate that new, direct-acting antiviral medications will expand the hepatitis C market significantly and that novel agents to manage idiopathic pulmonary fibrosis (IPF) will increase utilization greatly in the respiratory conditions drug class.

For many years, the top three specialty classes – inflammatory conditions, MS and cancer – have accounted for approximately two-thirds of the specialty-related spend captured within the pharmacy benefit. Through 2014, these three classes will remain the top three PMPY spend categories, and in their current order. HIV (new to specialty in 2011) is expected to hold its fourth-ranking position for the next few years. By 2013, hepatitis C is forecast to move up to fifth position in the specialty drug ranking based on PMPY spend.

Taken together, the top five classes will make up more than 75% of PMPY spend by 2014. No other specialty class holds more than a small percentage of specialty drug spend. As with nearly all specialty medications, therapies in the smaller classes are targeted for relatively small patient populations. They therefore are highly susceptible to significant swings in trend caused by new drug approvals, price increases, new indications, the number and cost of orphan medications, production problems and numerous other factors.
Three new oral MS drugs may be approved in late 2012 or early 2013, including BG-12, an oral disease-modifying drug. These new drugs are expected to increase utilization in the class because they will create more options for patients who avoid injectable therapies. Use of Ampyra® (dalfampridine), approved in 2010 to treat MS symptoms, in combination with disease-modifying medications will keep contributing to increased utilization in this therapy class. Continued price hikes across the class are anticipated for the next several years.

Sustained growth is expected in the inflammatory conditions therapy class as novel therapies increase utilization. However, increased competition may help to mitigate rising cost. Oral drugs for inflammatory conditions are expected to begin affecting the market in mid-2012. Tofacitinib, an oral targeted therapy expected to be approved in late 2012 for rheumatoid arthritis (RA), is an example of an oral therapy that will affect drug trend in this class.
### Cancer

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<thead>
<tr>
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<th>2014 PMPY</th>
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<td>2012</td>
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<td>2013</td>
<td>23.0%</td>
<td>$37.41 PMPY</td>
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<tr>
<td>2014</td>
<td>21.9%</td>
<td>$45.61 PMPY</td>
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</tr>
</tbody>
</table>

#### Comments

Trend for cancer therapies is forecast to grow more than 20% annually for the next few years. Several new, oral cancer drugs contribute to increased utilization by shifting cost from medical benefits to pharmacy benefits. Double-digit increases in the costs of cancer drugs are likely to continue as well.

### HIV

<table>
<thead>
<tr>
<th>Year</th>
<th>Trend</th>
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<th>2013 PMPY</th>
<th>2014 PMPY</th>
</tr>
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<td>6.1%</td>
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<td>8.1%</td>
<td>$20.73 PMPY</td>
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<td>2014</td>
<td>7.1%</td>
<td>$22.20 PMPY</td>
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</table>

#### Comments

Utilization of HIV medications is expected to increase due not only to expanded screening and increased diagnosis, but also to extended therapy as patients live longer. Usage shifts continue to newer, more-convenient regimens with less pill burden. Trend growth also is anticipated from price increases for HIV medications.
#5 GROWTH DEFICIENCY

**TREND**

<table>
<thead>
<tr>
<th>Year</th>
<th>Trend 2012</th>
<th>Trend 2013</th>
<th>Trend 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>12.4%</td>
<td>13.4%</td>
<td>12.4%</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PMPY**

<table>
<thead>
<tr>
<th>Year</th>
<th>PMPY 2012</th>
<th>PMPY 2013</th>
<th>PMPY 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>$7.55</td>
<td>$8.56</td>
<td>$9.62</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS**

Moderate growth is expected in the class due to increases in both cost and utilization. Newer growth hormone formulations will keep driving up trend as their use increases.

#6 ANTICOAGULANTS

**TREND**

<table>
<thead>
<tr>
<th>Year</th>
<th>Trend 2012</th>
<th>Trend 2013</th>
<th>Trend 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>6.1%</td>
<td>-2.0%</td>
<td>-2.0%</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PMPY**

<table>
<thead>
<tr>
<th>Year</th>
<th>PMPY 2012</th>
<th>PMPY 2013</th>
<th>PMPY 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>$6.81</td>
<td>$6.67</td>
<td>$6.54</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS**

Increasing use of enoxaparin (generic to Lovenox®) is driving down the cost in the anticoagulants therapy class. The first generic to Lovenox was released in mid-2010, with a second launched “at risk” in early 2012. Approval of new oral anticoagulants, offered under the traditional prescription-drug benefit, will pull prescriptions away from the specialty market.
## 2012 to 2014 Forecast for the Top 10 Specialty Therapy Classes

### #7 Hepatitis C

**Trend**

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trend</td>
<td>68.8%</td>
<td>32.3%</td>
<td>56.3%</td>
</tr>
<tr>
<td>PMPY</td>
<td>$10.69</td>
<td>$14.14</td>
<td>$22.10</td>
</tr>
</tbody>
</table>

**Comments**

Launched in mid-2011, two new, oral protease inhibitors, Incivek® and Victrelis®, will continue to increase trend dramatically for the hepatitis C therapy class. Expect trend to grow significantly in 2012, driven equally by increased cost and utilization. Overall trend is expected to slow slightly in 2013 while patients wait for the next generation of oral, direct-acting antiviral medications to start hitting the hepatitis C market in 2014.

### #8 Transplant

**Trend**

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trend</td>
<td>-0.1%</td>
<td>0.9%</td>
<td>2.0%</td>
</tr>
<tr>
<td>PMPY</td>
<td>$5.62</td>
<td>$5.67</td>
<td>$5.79</td>
</tr>
</tbody>
</table>

**Comments**

The trend for transplant medications should be essentially flat for the next few years. Increased use of generics in this class contributes to negative costs, which are countered by low, single-digit increases in utilization. Nulojix®, an infused transplant drug that was approved in mid-2012, may shift some utilization from the pharmacy benefit to the medical benefit.
2012 to 2014 Forecast for the Top 10 Specialty Therapy Classes

**#9 RESPIRATORY CONDITIONS**

<table>
<thead>
<tr>
<th>TREND</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>TREND</td>
<td>16.6%</td>
<td>18.8%</td>
<td>23.2%</td>
</tr>
<tr>
<td>PMPY</td>
<td>$5.42</td>
<td>$6.44</td>
<td>$7.93</td>
</tr>
</tbody>
</table>

**COMMENTS**

Several medications that are expected to be approved within the next few years for cystic fibrosis (CF) will increase trend for the class. *Kalydeco™*, approved in January 2012 to treat the underlying CF disease in a subset of patients, will contribute to increased cost and utilization. Two new medications, Vargatef™ and Esbriet®, are expected to be the first drugs approved in the U.S. to treat the devastating lung condition, idiopathic pulmonary fibrosis (IPF). If approved, they will impact drug trend significantly in 2013 and 2014.

**#10 PULMONARY HYPERTENSION**

<table>
<thead>
<tr>
<th>TREND</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>TREND</td>
<td>8.0%</td>
<td>-3.2%</td>
<td>15.5%</td>
</tr>
<tr>
<td>PMPY</td>
<td>$4.57</td>
<td>$4.42</td>
<td>$5.11</td>
</tr>
</tbody>
</table>

**COMMENTS**

New oral drugs for pulmonary hypertension that are expected to enter the market in 2012 and 2013 will increase utilization in the class. Sildenafil, a generic version of Revatio®, is expected to be approved in September 2012. Lower costs due to this generic should drive down trend in 2013. Historical growth rates are expected to return in 2014 after the main impact from generic Revatio has been realized.
Overview

For the past 25 years, Express Scripts has played an important role in managing pharmacy benefits for employers and managed care plans that provide drug benefits to retirees. Since the early days of the Medicare Drug Discount card, Express Scripts has given clients insights into the prescription-drug cost and utilization trends of their Medicare members. Our commitment to making drugs safer and more affordable for the Medicare population is as critical now as it was in the late 1980s.

Until 2003, Medicare recipients either paid for prescription medications out of pocket, had retiree drug coverage through their employers, enrolled in a supplemental coverage plan or enrolled in managed care plans that offered prescription-drug coverage. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) provided, among other changes, a comprehensive, voluntary drug benefit: Medicare Part D.

Despite the initial concerns of the Centers for Medicare & Medicaid Services (CMS) that managed care plans would not be interested in covering Part D benefits, the response by managed care plans offering Medicare Advantage Prescription Drug Plans (MAPDs) and those interested in offering standalone Prescription Drug Plans (PDPs) surpassed the federal agency’s expectations. Early provisions of the MMA also included a Retiree Drug Subsidy (RDS) Program, which provided incentives to employers who retained existing retiree drug coverage. The resulting Employer Group Waiver Plans (EGWPs) helped prevent a dramatic drop in the drug coverage for commercial retirees and allowed a phased approach to Part D plan enrollment, starting with Medicare members who lacked “creditable coverage,” drug benefit coverage equivalent to the basic Part D benefit.

Today, an estimated 60% of all Medicare beneficiaries are enrolled in a Part D plan through an option for prescription-drug coverage available under MAPD, PDP, EGWP or another creditable coverage plan.1

Continued Challenges

Costs for the Medicare Part D program have been lower than those projected in 2004.2 Nonetheless, economic conditions require that all participants, beneficiaries and providers be held accountable for both prescription-drug costs and medical costs today and in the future. This philosophy is reflected in recent enhancements to the Part D benefit that are designed to improve health and reduce total healthcare costs by encouraging beneficiaries to adhere to drug therapy. An example is the coverage gap discount program, added in 2011, which reduces beneficiary costs for brands and generic medications throughout the coverage gap (i.e., the “donut hole”). Research suggests a relationship between cost of medications and poor adherence.3 Nonadherence can be attributed to many factors, including medication costs.4 These enhancements are consistent with evidence demonstrating the importance of adherence to control medical costs such as hospitalizations.5,6

Another significant change to the Part D benefit is the focus that CMS has placed on the measurement of outcomes. The Part D benefit now is governed by the CMS Five-Star Quality (star) rating program, which is similar to the quality ratings that exist in managed care. MAPD and PDP plans are subject to a variety of quality measures intended to improve their offerings and service and to provide beneficiaries with meaningful information that can help them select a plan.

Financial incentives tied to star ratings make them even more important to Part D plans. CMS now has ratings for the use of high-risk medications in the elderly and for appropriate treatment of high blood pressure in beneficiaries with diabetes. Additionally, CMS has established medication adherence measures for the three most prevalent diseases of Medicare recipients – diabetes, high blood pressure and high blood cholesterol.
Solutions

Therapy Adherence

The Express Scripts programs that promote adherence support our mission to help optimize therapy outcomes. Regardless of whether it is intentional, nonadherence can result in disease progression that leads to unnecessary hospital admissions, avoidable emergency room visits, additional physician visits, extra laboratory tests, additional therapy and other drivers of healthcare costs. Factors that influence adherence include a member’s perception of the need for a medication, the perceived side effects, the out-of-pocket cost, and forgetfulness and procrastination around prescription refills and renewals.

Exhibit 20 compares the medication adherence rate for members of our Medicare plan sponsors with the adherence rate for members of all PDP and MAPD plans reporting to CMS in 2011. Among Express Scripts clients, the average adherence rates for diabetes, high blood pressure and high cholesterol were 75.9%, 76.8% and 71.5%, respectively.

Compared to the CMS 2011 Plan Ratings, Express Scripts clients had a higher percentage of patients taking medications as prescribed in all three classes.

CMS adherence measurements currently are limited to three prevalent conditions. However, measurement likely will be expanded to other conditions for which medication adherence is especially critical to health outcomes and overall costs. CMS is focused on helping members increase adherence to their medication regimens in plans that serve Medicare beneficiaries.

As Express Scripts continues to develop innovative ways to assist our clients with the design of prescription-drug benefits, we recognize more than ever that educating members on medication adherence and helping them increase their adherence is just as important as educating members on safe and affordable medication choices. The results of a national survey of Medicare enrollees that we conducted in 2011 offer strong support for this view. Almost half (49%) of survey respondents had missed medication doses due to simple behavioral issues such as forgetfulness or procrastination in obtaining refills. Surprisingly, cost was not a significant factor for these respondents: only 2.8% cited cost as a prohibiting factor in filling their prescription medications.

We understand that Medicare beneficiaries have individual comorbidities, economic situations, geographic locations and physician availability – along with dozens of other factors that influence medication adherence. But through years of careful study, we have found that the main barrier to adherence lies in simple behaviors like forgetfulness. The programs that Express Scripts offers address these behaviors while recognizing the uniqueness of the population within Medicare plans.
Generic Utilization

The use of generic medications and lower-cost brands is important in ensuring a financially sustainable Medicare drug benefit. Express Scripts estimates that for every 1% increase in the generic fill rate (GFR), savings increase 1.5% to 2.0%. In 2011, the GFR for Express Scripts clients was 79.2% for traditional medications, higher than the 75% reported by the Department of Health and Human Services (HHS) in 2009, the most recent year for which data was available. Unmistakably, our Medicare clients are taking advantage of the cost savings associated with generic medications.

In the top 10 Medicare traditional therapy classes, medications for pain, ulcer disease and high blood pressure/heart disease have the highest GFRs (Exhibit 21). For Express Scripts Medicare clients, the average annual cost per prescription for generics was $117.57 less than that for brands.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>GFR</th>
<th>Generic</th>
<th>Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pain</td>
<td>97.1%</td>
<td>$23.74</td>
<td>$346.64</td>
</tr>
<tr>
<td>2</td>
<td>Ulcer Disease</td>
<td>91.6%</td>
<td>$22.89</td>
<td>$164.32</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Pressure/Heart Disease</td>
<td>91.2%</td>
<td>$14.76</td>
<td>$99.93</td>
</tr>
<tr>
<td>4</td>
<td>Seizures</td>
<td>90.5%</td>
<td>$29.83</td>
<td>$182.60</td>
</tr>
<tr>
<td>5</td>
<td>Depression</td>
<td>87.5%</td>
<td>$20.50</td>
<td>$144.58</td>
</tr>
<tr>
<td>6</td>
<td>High Blood Cholesterol</td>
<td>76.0%</td>
<td>$14.68</td>
<td>$128.19</td>
</tr>
<tr>
<td>7</td>
<td>Mental/Neurological Disorders</td>
<td>56.0%</td>
<td>$58.63</td>
<td>$325.68</td>
</tr>
<tr>
<td>8</td>
<td>Diabetes</td>
<td>46.5%</td>
<td>$12.89</td>
<td>$108.54</td>
</tr>
<tr>
<td>9</td>
<td>Blood Modifying</td>
<td>18.6%</td>
<td>$25.36</td>
<td>$184.91</td>
</tr>
<tr>
<td>10</td>
<td>Asthma</td>
<td>14.3%</td>
<td>$44.05</td>
<td>$137.90</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL</strong></td>
<td>79.2%</td>
<td><strong>$17.47</strong></td>
<td><strong>$135.04</strong></td>
</tr>
</tbody>
</table>
Exhibit 22 provides a closer look at GFRs for the major types of Medicare plan sponsors—MAPDs, PDPs, and EGWPs. At 79.9%, MAPD plan sponsors had the highest GFR, followed by EGWPs, at 76.1%; and then PDPs, at 71.9%.

**Medicare Trend**

Medicare trend, based on spend per member per year (PMPY), rose 3.0%, to a PMPY of $2,436.22 in 2011. Increased trend resulted from two primary factors pulling in opposite directions: PMPY utilization increased 3.6%, to 50.99; by contrast, ingredient cost per prescription decreased 2.6%, to $47.78. The increase in overall GFR, which rose from 76.7% to 78.9%, contributed to the reduction in the cost per prescription.

**Medicare Traditional Therapy Class Review**

Despite overall rising costs for the federal Medicare program, traditional drug spend among our Medicare plans remained relatively flat between 2010 and 2011. Plans using Express Scripts saw a very modest decrease of 0.9%, to an average PMPY cost of $2,129.35. This nearly flat trend reflects increased utilization (3.6%; average 50.77 prescriptions PMPY) and decreased cost per prescription (-2.6%; average $41.94 per prescription).

Shown in Exhibit 23, the top 10 traditional therapy classes represented 71% of Medicare traditional spending in 2011. As in 2010, medications used to treat diabetes, high blood pressure/heart disease, and high blood cholesterol accounted for approximately $1 of every $3 spent for traditional drugs and for nearly 40% of the prescriptions filled. The depression class and seizure therapy class made the top 10 this year, pushing drugs to treat viral infection and urinary disorders out of the top rankings by PMPY spend.
## Exhibit 23
Components and Drivers of Trend for the Top 10 Medicare Traditional Therapy Classes, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$319.00</td>
<td>15.0%</td>
<td>$30.77</td>
<td>5.1%</td>
<td>5.5%</td>
<td>10.7%</td>
</tr>
<tr>
<td>2</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$226.65</td>
<td>10.6%</td>
<td>-$33.70</td>
<td>2.6%</td>
<td>-15.6%</td>
<td>-12.9%</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Cholesterol</td>
<td>$205.58</td>
<td>9.7%</td>
<td>$8.24</td>
<td>4.4%</td>
<td>-0.2%</td>
<td>4.2%</td>
</tr>
<tr>
<td>4</td>
<td>Mental/Neurological Disorders</td>
<td>$201.15</td>
<td>9.4%</td>
<td>-$16.91</td>
<td>-0.3%</td>
<td>-7.4%</td>
<td>-7.8%</td>
</tr>
<tr>
<td>5</td>
<td>Asthma</td>
<td>$140.36</td>
<td>6.6%</td>
<td>$12.38</td>
<td>0.3%</td>
<td>9.4%</td>
<td>9.7%</td>
</tr>
<tr>
<td>6</td>
<td>Blood Modifying</td>
<td>$131.22</td>
<td>6.2%</td>
<td>$14.14</td>
<td>-1.8%</td>
<td>13.9%</td>
<td>12.1%</td>
</tr>
<tr>
<td>7</td>
<td>Ulcer Disease</td>
<td>$87.00</td>
<td>4.1%</td>
<td>-$18.69</td>
<td>5.9%</td>
<td>-23.6%</td>
<td>-17.7%</td>
</tr>
<tr>
<td>8</td>
<td>Depression</td>
<td>$69.89</td>
<td>3.3%</td>
<td>-$1.32</td>
<td>5.9%</td>
<td>-7.8%</td>
<td>-1.9%</td>
</tr>
<tr>
<td>9</td>
<td>Pain</td>
<td>$64.24</td>
<td>3.0%</td>
<td>$2.14</td>
<td>2.9%</td>
<td>0.5%</td>
<td>3.4%</td>
</tr>
<tr>
<td>10</td>
<td>Seizures</td>
<td>$61.57</td>
<td>2.9%</td>
<td>$5.40</td>
<td>7.6%</td>
<td>2.0%</td>
<td>9.6%</td>
</tr>
<tr>
<td></td>
<td><strong>Top 10</strong></td>
<td><strong>$1,506.66</strong></td>
<td><strong>70.8%</strong></td>
<td><strong>$2.44</strong></td>
<td><strong>3.7%</strong></td>
<td><strong>-3.6%</strong></td>
<td><strong>0.2%</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Others</strong></td>
<td><strong>$622.69</strong></td>
<td><strong>29.2%</strong></td>
<td><strong>$17.21</strong></td>
<td><strong>3.3%</strong></td>
<td><strong>-0.5%</strong></td>
<td><strong>2.8%</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>$2,129.35</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>$19.66</strong></td>
<td><strong>3.6%</strong></td>
<td><strong>-2.6%</strong></td>
<td><strong>0.9%</strong></td>
</tr>
</tbody>
</table>
Exhibit 24 displays the PMPY costs for the top 10 traditional therapy classes. Each bubble plots the 2011 PMPY spend for one therapy class against the change in spend for that class from 2010 to 2011. The size of the bubble depicts the number of PMPY prescriptions filled in that therapy class. Spend decreased for high blood pressure/heart disease, the most intensely used class on a PMPY basis. Drugs for mental/neurological disorders, depression and ulcer disease also experienced spend decreases. All of the other top 10 therapeutic categories, including the expensive and intensely utilized classes for diabetes and high blood cholesterol, saw increases in spend.
When considering the PMPY spend as shown in Exhibit 25, brand drugs dominate the top 10 with the exception of omeprazole and simvastatin. The most-expensive medication by PMPY spend was the blood-modifying agent, Plavix® (clopidogrel), with a PMPY cost of $118.75. The availability of new generic alternatives – including generics for Seroquel® (quetiapine), expected in March 2012, and Plavix, expected in May 2012 – is expected to increase over the next few years. Additionally, generic alternatives to Lipitor® (atorvastatin), which became available in late 2011, are anticipated to have a significant impact on costs in the high blood cholesterol class in 2012.

### Exhibit 25
Top 10 Medicare Traditional Therapy Drugs, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug Name</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Plavix® (clopidogrel)</td>
<td>Blood Modifying</td>
<td>$118.75</td>
<td>5.6%</td>
<td>$11.79</td>
<td>-2.5%</td>
<td>13.8%</td>
<td>11.0%</td>
</tr>
<tr>
<td>2</td>
<td>Advair diskus® (fluticasone and salmeterol)</td>
<td>Asthma</td>
<td>$54.48</td>
<td>2.6%</td>
<td>$2.03</td>
<td>-2.5%</td>
<td>6.6%</td>
<td>3.9%</td>
</tr>
<tr>
<td>3</td>
<td>Lipitor® (atorvastatin)</td>
<td>High Blood Cholesterol</td>
<td>$45.79</td>
<td>2.2%</td>
<td>-$4.41</td>
<td>-22.8%</td>
<td>18.2%</td>
<td>-8.8%</td>
</tr>
<tr>
<td>4</td>
<td>Seroquel® (quetiapine)</td>
<td>Mental/Neurological Disorders</td>
<td>$42.85</td>
<td>2.0%</td>
<td>$2.59</td>
<td>-7.1%</td>
<td>14.5%</td>
<td>6.4%</td>
</tr>
<tr>
<td>5</td>
<td>Crestor® (rosuvastatin)</td>
<td>High Blood Cholesterol</td>
<td>$42.74</td>
<td>2.0%</td>
<td>$9.24</td>
<td>14.8%</td>
<td>11.1%</td>
<td>27.6%</td>
</tr>
<tr>
<td>6</td>
<td>Actos® (pioglitazone)</td>
<td>Diabetes</td>
<td>$42.24</td>
<td>2.0%</td>
<td>$0.09</td>
<td>-9.0%</td>
<td>10.1%</td>
<td>0.2%</td>
</tr>
<tr>
<td>7</td>
<td>Spiriva® (tiotropium)</td>
<td>COPD</td>
<td>$34.84</td>
<td>1.6%</td>
<td>$6.70</td>
<td>6.0%</td>
<td>16.8%</td>
<td>23.8%</td>
</tr>
<tr>
<td>8</td>
<td>omeprazole</td>
<td>Ulcer Disease</td>
<td>$31.80</td>
<td>1.5%</td>
<td>-$1.91</td>
<td>9.6%</td>
<td>-13.9%</td>
<td>-5.7%</td>
</tr>
<tr>
<td>9</td>
<td>Januvia® (sitagliptin)</td>
<td>Diabetes</td>
<td>$30.56</td>
<td>1.4%</td>
<td>$6.83</td>
<td>18.6%</td>
<td>8.6%</td>
<td>28.8%</td>
</tr>
<tr>
<td>10</td>
<td>simvastatin</td>
<td>High Blood Cholesterol</td>
<td>$30.00</td>
<td>1.4%</td>
<td>-$0.32</td>
<td>8.4%</td>
<td>-8.8%</td>
<td>-1.1%</td>
</tr>
<tr>
<td></td>
<td><strong>Top 10</strong></td>
<td></td>
<td><strong>$474.06</strong></td>
<td><strong>22.3%</strong></td>
<td><strong>$32.64</strong></td>
<td>4.0%</td>
<td>3.3%</td>
<td>7.4%</td>
</tr>
<tr>
<td></td>
<td><strong>Others</strong></td>
<td></td>
<td><strong>$1,655.29</strong></td>
<td><strong>77.7%</strong></td>
<td><strong>-$12.98</strong></td>
<td>3.6%</td>
<td>-4.2%</td>
<td>-0.8%</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td></td>
<td><strong>$2,129.35</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>$19.66</strong></td>
<td>3.6%</td>
<td>-2.6%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>
Comparison of Medicare Trend and Commercial Trend

Exhibits 26 and 27 compare the Express Scripts Medicare trend with the trend for the Express Scripts commercial book of business. In each exhibit, key therapy classes are ranked by Medicare trend. With the exception of the pain and mental/neurological disorders classes, traditional drug class trends for both Medicare and commercial clients moved in the same direction. Several recently introduced generics for drugs that treat Alzheimer’s disease and Parkinson’s disease contributed to a substantial decrease in Medicare trend for the mental/neurological disorders class. In general, specialty drug trends for Medicare clients were also consistent with those for commercial clients. The two exceptions in specialty were osteoporosis and blood cell deficiency, which reflected population demographic differences between commercial and Medicare members.

<table>
<thead>
<tr>
<th>Traditional Therapy Class</th>
<th>Trend Medicare</th>
<th>Trend Commercial</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Modifying</td>
<td>12.1%</td>
<td>8.6%</td>
<td>3.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10.7%</td>
<td>7.0%</td>
<td>3.7</td>
</tr>
<tr>
<td>Asthma</td>
<td>9.7%</td>
<td>3.8%</td>
<td>5.9</td>
</tr>
<tr>
<td>Seizures</td>
<td>9.6%</td>
<td>5.1%</td>
<td>4.5</td>
</tr>
<tr>
<td>High Blood Cholesterol</td>
<td>4.2%</td>
<td>2.5%</td>
<td>1.7</td>
</tr>
<tr>
<td>Pain</td>
<td>3.4%</td>
<td>-1.9%</td>
<td>5.3</td>
</tr>
<tr>
<td>Depression</td>
<td>-1.9%</td>
<td>-3.0%</td>
<td>1.1</td>
</tr>
<tr>
<td>Mental/Neurological Disorders</td>
<td>-7.8%</td>
<td>3.5%</td>
<td>-11.3</td>
</tr>
<tr>
<td>High Blood Pressure/Heart Disease</td>
<td>-12.9%</td>
<td>-9.5%</td>
<td>-3.4</td>
</tr>
<tr>
<td>Ulcer Disease</td>
<td>-17.7%</td>
<td>-10.1%</td>
<td>-7.6</td>
</tr>
<tr>
<td>Other</td>
<td>2.8%</td>
<td>0.4%</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>0.9%</strong></td>
<td><strong>0.1%</strong></td>
<td><strong>0.8</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specialty Therapy Class</th>
<th>Trend Medicare</th>
<th>Trend Commercial</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C</td>
<td>190.4%</td>
<td>194.8%</td>
<td>-4.4</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>34.4%</td>
<td>20.3%</td>
<td>14.1</td>
</tr>
<tr>
<td>Cancer</td>
<td>27.2%</td>
<td>15.7%</td>
<td>11.5</td>
</tr>
<tr>
<td>Inflammatory Conditions</td>
<td>21.5%</td>
<td>17.7%</td>
<td>3.8</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>17.4%</td>
<td>2.6%</td>
<td>14.8</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>12.5%</td>
<td>-14.9%</td>
<td>27.4</td>
</tr>
<tr>
<td>HIV</td>
<td>10.3%</td>
<td>4.9%</td>
<td>5.4</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>2.1%</td>
<td>5.1%</td>
<td>-3.0</td>
</tr>
<tr>
<td>Blood Cell Deficiency</td>
<td>-0.1%</td>
<td>0.0%</td>
<td>-0.1</td>
</tr>
<tr>
<td>Transplant</td>
<td>-4.7%</td>
<td>-1.7%</td>
<td>-3.0</td>
</tr>
<tr>
<td>Other</td>
<td>28.1%</td>
<td>21.8%</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20.0%</strong></td>
<td><strong>17.1%</strong></td>
<td><strong>2.9</strong></td>
</tr>
</tbody>
</table>
Trends by Medicare Plan Type

We further examined Medicare trend for 2011 by Medicare plan type: MAPD, PDP and EGWP. Although the number of MAPD and PDP plans decreased between 2010 and 2011, the number of firms offering the Part D plans remained relatively constant. Benefit coverage of MAPD and PDP plans (offered to Medicare beneficiaries at-large) and EGWP plans (offered to qualified retired employees) typically have a tiered cost-sharing structure designed to encourage the use of lower-cost drugs and mitigate the use of more costly drugs.

- As noted in Exhibit 28, 2011 trend for our MAPDs decreased 0.8%, stemming from a 2.9% decrease in cost per prescription, which was offset by a 3.7% increase in PMPY utilization.
- Medicare drug spend increased 2.7% for our PDP plans, to $2,471.55, largely driven by a 2.0% increase in PMPY utilization.
- EGWPs, which comprise plan sponsors who continue to offer benefits to their retirees, tend to have broader formularies, lower copayments and fewer member restrictions. In 2011, our EGWP plans had the highest 2011 PMPY cost but also the highest cost decrease – a 7.1% drop, to $2,754.51.
Top Medicare Traditional Therapy Classes

Diabetes

According to CMS, diabetes is the fourth most prevalent chronic condition among Medicare beneficiaries.\(^1\) Accounting for about 95% of diabetes cases, type 2 diabetes is caused by decreased insulin production, insulin resistance (the inability to use insulin that is produced) or both. Although type 2 diabetes can occur at any age, prevalence rates increase with age, and 25% of Americans 65 and older have been diagnosed with the condition.\(^4\)

Between 2010 and 2011, the utilization of prescription diabetes medications increased 5.1% in Medicare. As shown in Exhibit 29, the PMPY cost of antidiabetic medications increased 10.7%, to $319.00, and cost per prescription increased 5.5%, to $64.06. The generic fill rate (GFR) remained nearly constant, at 46.5%, in both 2010 and 2011. As in 2010, metformin remained the top-used diabetic drug in 2011, with 22.7% of the market share. Despite small market shares, the top two drugs by cost, Actos\(^\circledR\) (pioglitazone) and Januvia\(^\circledR\) (sitagliptin), accounted for 20.7% of overall diabetes spend.

Exhibit 29 | Top Five Medicare Diabetes Drugs and Devices by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>metformin</td>
<td>22.8%</td>
<td>22.7%</td>
<td>$11.88</td>
</tr>
<tr>
<td>glipizide</td>
<td>6.5%</td>
<td>6.1%</td>
<td>$13.32</td>
</tr>
<tr>
<td>glimepiride</td>
<td>4.6%</td>
<td>4.7%</td>
<td>$12.20</td>
</tr>
<tr>
<td>OneTouch Ultra(^\circledR) Test Strips</td>
<td>5.2%</td>
<td>4.6%</td>
<td>$82.71</td>
</tr>
<tr>
<td>glyburide</td>
<td>4.6%</td>
<td>4.1%</td>
<td>$18.77</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cost PMPY</th>
<th>#Rx PMPY</th>
<th>GFR</th>
<th>Average Cost/Rx</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>$319.00</td>
<td>4.98</td>
<td>46.5%</td>
<td>$64.06</td>
<td>10.7%</td>
</tr>
</tbody>
</table>
High Blood Pressure/Heart Disease

The overall Medicare trend for high blood pressure/heart disease fell 12.9% in 2011 (Exhibit 30), fueled by a 15.6% decrease in the average cost per prescription, which more than offset a PMPY utilization increase of 2.6%. The 4.3% increase in the generic fill rate (GFR), which reached 91.2%, contributed greatly to reduced cost. For the second year, Diovan® (valsartan) and Diovan HCT® (valsartan and hydrochlorothiazide) were the two most-expensive drugs in the class, accounting for 11.9% and 7.9% of overall high blood pressure/heart disease spend, respectively. Diovan, scheduled to face generic competition in the third quarter of 2012, had a 16.6% decrease in trend in 2011, resulting from a 26.3% decrease in utilization and a 13.2% increase in cost per prescription. Although Diovan and Diovan HCT are the most-expensive drugs in the class, the top five drugs by market share are all generics.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>lisinopril</td>
<td>15.1%</td>
<td>15.1%</td>
<td>$ 8.90</td>
</tr>
<tr>
<td>amlodipine</td>
<td>12.5%</td>
<td>13.1%</td>
<td>$15.57</td>
</tr>
<tr>
<td>atenolol</td>
<td>9.8%</td>
<td>9.0%</td>
<td>$ 8.04</td>
</tr>
<tr>
<td>metoprolol tartrate</td>
<td>8.8%</td>
<td>8.5%</td>
<td>$ 8.66</td>
</tr>
<tr>
<td>enalapril</td>
<td>5.6%</td>
<td>5.3%</td>
<td>$13.83</td>
</tr>
</tbody>
</table>

| Exhhibit 30 | Top Five Medicare High Blood Pressure/Heart Disease Drugs by Market Share, 2010 and 2011 |

Cost PMPY: $226.65
#Rx PMPY: 10.18
GFR: 91.2%
Average Cost/Rx: $22.25
TREND: -12.9%
**High Blood Cholesterol**

By far the most common drugs prescribed for high cholesterol are HMG-CoA reductase inhibitors – commonly called “statins.” Three generic statin medications and two brand statins accounted for all of the top five Medicare drugs for high cholesterol in 2011, as ranked by market share (Exhibit 31).

The overall Medicare trend for high blood cholesterol was 4.2% in 2011. A 4.4% increase in utilization was tempered by a 0.2% decrease in cost per prescription. The generic fill rate (GFR) increased 4.9%, to 76.0%. Even though Lipitor® (atorvastatin) accounted for almost one-quarter of overall class spend in 2011, its impact on PMPY spend will decrease greatly because it lost brand patent protection in December 2011.

---

**Exhibit 31**

Top Five Medicare High Blood Cholesterol Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>2010 Market Share</th>
<th>2011 Market Share</th>
<th>2010 Cost/Rx ($)</th>
<th>2011 Cost/Rx ($)</th>
<th>Cost/Rx Trend (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>simvastatin</td>
<td>50.4%</td>
<td>52.4%</td>
<td>$12.79</td>
<td>$11.67</td>
<td>-8.8%</td>
</tr>
<tr>
<td>lovastatin</td>
<td>10.2%</td>
<td>9.0%</td>
<td>$15.02</td>
<td>$13.33</td>
<td>-11.2%</td>
</tr>
<tr>
<td>pravastatin</td>
<td>6.5%</td>
<td>7.9%</td>
<td>$13.07</td>
<td>$11.57</td>
<td>-11.5%</td>
</tr>
<tr>
<td>Lipitor® (atorvastatin)</td>
<td>9.6%</td>
<td>7.1%</td>
<td>$111.34</td>
<td>$131.59</td>
<td>18.2%</td>
</tr>
<tr>
<td>Crestor® (rosuvastatin)</td>
<td>6.0%</td>
<td>6.7%</td>
<td>$117.87</td>
<td>$130.97</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

- **Total Medicare Spending (PMPY)**: $205.58
- **#Rx PMPY**: 4,912,900
- **GFR**: 76.0%
- **Average Cost/Rx**: $41.90
- **Trend**: 4.2%
**Mental/Neurological Disorders**

Several recently introduced generics for drugs that treat Alzheimer’s disease and Parkinson’s disease contributed to a substantial decrease (-7.8%) in Medicare trend for the class (Exhibit 32). Driven primarily by a 7.4% decrease in the cost per prescription, the trend also reflects a 61.1% increase in the generic fill rate (GFR), up to 56.0%.

**Exhibit 32**
Top Five Medicare Mental/Neurological Disorders Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>donepezil</td>
<td>1.2%</td>
<td>21.8%</td>
<td>$180.74</td>
</tr>
<tr>
<td>Namenda® (memantine)</td>
<td>13.1%</td>
<td>13.5%</td>
<td>$160.68</td>
</tr>
<tr>
<td>Seroquel® (quetiapine)</td>
<td>13.8%</td>
<td>12.9%</td>
<td>$254.59</td>
</tr>
<tr>
<td>risperidone</td>
<td>9.9%</td>
<td>10.6%</td>
<td>$35.81</td>
</tr>
<tr>
<td>Abilify® (aripiprazole)</td>
<td>4.4%</td>
<td>4.5%</td>
<td>$504.93</td>
</tr>
</tbody>
</table>

| $201.15 Cost PMPY | 1.14 #Rx PMPY | 56.0% GFR | $176.05 Average Cost/Rx | -7.8% TREND |
Asthma

Anti-asthma drugs fall into two primary subclasses – long-term controller medications, taken on a regular basis to prevent attacks, and quick-relief medications, used to stop or alleviate acute asthma symptoms. Successfully treating asthma generally requires both kinds of medications.

Overall Medicare trend for asthma in 2011 was 9.7% (Exhibit 33), mostly due to a 9.4% increase in cost per prescription. The generic fill rate (GFR) increased only 2.7% to reach 14.3%. Considering that the asthma market has reverted to mostly brand products, however, any increase in GFR is impressive. Two brands, Advair Diskus® (fluticasone and salmeterol) and Singulair® (montelukast), accounted for 58.2% of overall asthma spend. As an inhaler with a recent patent, Advair Diskus will not face generic competition for many years, but Singulair, an oral tablet, will lose patent protection in August 2012.

Exhibit 33  Top Five Medicare Asthma Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>2010</th>
<th>2011</th>
<th>Cost/Rx</th>
<th>2010</th>
<th>2011</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advair Diskus® (fluticasone and salmeterol)</td>
<td>21.7%</td>
<td>21.1%</td>
<td></td>
<td>$214.80</td>
<td>$228.91</td>
<td>6.6%</td>
<td></td>
</tr>
<tr>
<td>Singulair® (montelukast)</td>
<td>18.2%</td>
<td>17.1%</td>
<td></td>
<td>$122.84</td>
<td>$141.04</td>
<td>14.8%</td>
<td></td>
</tr>
<tr>
<td>Proair® HFA (albuterol)</td>
<td>13.7%</td>
<td>13.0%</td>
<td></td>
<td>$ 41.84</td>
<td>$ 42.45</td>
<td>1.5%</td>
<td></td>
</tr>
<tr>
<td>Ventolin® HFA (albuterol aerosol)</td>
<td>8.3%</td>
<td>10.2%</td>
<td></td>
<td>$ 34.27</td>
<td>$ 37.92</td>
<td>10.7%</td>
<td></td>
</tr>
<tr>
<td>albuterol</td>
<td>6.7%</td>
<td>6.8%</td>
<td></td>
<td>$ 24.98</td>
<td>$ 27.17</td>
<td>8.8%</td>
<td></td>
</tr>
</tbody>
</table>

$140.36  Cost PMPY  1.13  #Rx PMPY  14.3%  GFR  $124.50  Average Cost/Rx  9.7%  TREND
Blood-Modifying Agents

Many of the blood-modifying agents belong to a class of drugs called platelet-aggregation inhibitors (antiplatelet medications). They are used mainly to prevent blood clots that could cause strokes and heart attacks in at-risk patients.

The overall Medicare trend for the class was 12.1% in 2011 (Exhibit 34). A 13.9% increase in cost per prescription resulted, in part, from a relatively flat generic fill rate (GFR) of 18.6%. Plavix® (clopidogrel), which accounted for 76.2% of market share and 90.5% of pharmaceutical spend within the class, had a 13.8% increase in cost per prescription between 2010 and 2011. Trend should decrease and GFR should increase after generics for Plavix are introduced in May 2012. The number of PMPY prescriptions in the class decreased 1.8%.

Exhibit 34  Top Five Medicare Blood-Modifying Agents by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>Plavix® (clopidogrel)</td>
<td>76.8%</td>
<td>76.2%</td>
<td>$162.05</td>
</tr>
<tr>
<td>cilostazol</td>
<td>7.2%</td>
<td>6.9%</td>
<td>$20.55</td>
</tr>
<tr>
<td>dipyridamole</td>
<td>6.5%</td>
<td>5.9%</td>
<td>$20.89</td>
</tr>
<tr>
<td>pentoxifylline</td>
<td>3.9%</td>
<td>5.1%</td>
<td>$21.14</td>
</tr>
<tr>
<td>Aggrenox® (aspirin and extended-release dipyridamole)</td>
<td>4.2%</td>
<td>4.1%</td>
<td>$161.97</td>
</tr>
</tbody>
</table>

$131.22  Cost PMPY
0.85  #Rx PMPY
18.6%  GFR
$155.25  Average Cost/Rx
12.1%  TREND
Ulcer Disease

Ulcer disease medications center on the treatment of peptic ulcer disease and gastroesophageal reflux disease (GERD). Proton pump inhibitors (PPIs) are the most-used prescription medication in this class, filling all five top spots by market share. Several PPIs along with another type of anti-ulcer drug, histamine-2 blockers, are available over the counter.

In 2011, the PMPY cost for ulcer drugs decreased 17.7% (Exhibit 35), reflecting a 23.6% decrease in cost per prescription. Since the introduction of generics to the first PPI, Prilosec® (omeprazole), in December 2002, the PMPY cost for the ulcer disease category has been decreasing. Omeprazole, which held 51.3% of 2011 market share, decreased 13.9% in cost per prescription between 2010 and 2011.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>omeprazole</td>
<td>50.0%</td>
<td>51.3%</td>
<td>$28.78</td>
<td>$24.78</td>
<td>-13.9%</td>
</tr>
<tr>
<td>ranitidine</td>
<td>19.2%</td>
<td>19.0%</td>
<td>$11.97</td>
<td>$9.27</td>
<td>-22.6%</td>
</tr>
<tr>
<td>pantoprazole</td>
<td>10.6%</td>
<td>9.6%</td>
<td>$91.30</td>
<td>$24.36</td>
<td>-73.3%</td>
</tr>
<tr>
<td>famotidine</td>
<td>4.9%</td>
<td>5.5%</td>
<td>$12.48</td>
<td>$11.63</td>
<td>-6.8%</td>
</tr>
<tr>
<td>Nexium® (esomeprazole)</td>
<td>5.5%</td>
<td>5.2%</td>
<td>$178.89</td>
<td>$188.73</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

Exhibit 35: Top Five Medicare Ulcer Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Cost PMPY</th>
<th>#Rx PMPY</th>
<th>GFR</th>
<th>Average Cost/Rx</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>$87.00</td>
<td>2.50</td>
<td>91.6%</td>
<td>$34.79</td>
<td>-17.7%</td>
</tr>
</tbody>
</table>
Depression

Antidepressant medications are not only used to treat depression but also have been approved for chronic pain conditions. When used to treat depression, they enhance the activity of one or more neurotransmitters — chemicals that facilitate electrical signals along nerve cells. Three principal neurotransmitters involved in depression are dopamine, norepinephrine and serotonin. Newer antidepressants called selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) have fewer side effects than older tricyclics and monoamine oxidase inhibitors (MAOIs).

The overall Medicare trend for depression medications decreased 1.9% (Exhibit 36), even though utilization increased 5.9% between 2010 and 2011. Decreased spend was fueled by a 7.8% decrease in cost per prescription and a 3.2% increase in the generic fill rate (GFR), to 87.5%. All of the top five market-share drugs are generics.

Exhibit 36  Top Five Medicare Depression Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>citalopram</td>
<td>16.5%</td>
<td>17.9%</td>
<td>$12.85</td>
<td>$11.29</td>
<td>-12.2%</td>
</tr>
<tr>
<td>sertraline</td>
<td>16.9%</td>
<td>16.8%</td>
<td>$17.22</td>
<td>$15.90</td>
<td>-7.6%</td>
</tr>
<tr>
<td>trazodone</td>
<td>11.3%</td>
<td>11.3%</td>
<td>$10.69</td>
<td>$10.53</td>
<td>-1.4%</td>
</tr>
<tr>
<td>fluoxetine</td>
<td>12.0%</td>
<td>11.1%</td>
<td>$16.58</td>
<td>$14.06</td>
<td>-15.2%</td>
</tr>
<tr>
<td>bupropion sustained release</td>
<td>11.1%</td>
<td>10.4%</td>
<td>$20.72</td>
<td>$17.66</td>
<td>-14.7%</td>
</tr>
</tbody>
</table>

Total:

- Cost PMPY: $69.89
- #Rx PMPY: 1.94
- GFR: 87.5%
- Average Cost/Rx: $35.98
- Trend: -1.9%
Pain

Approximately 20% of Americans age 65 and older report having chronic pain, defined by the International Association for the Study of Pain as “pain that persists beyond normal healing time, which is about 3 months.” Pain can result from several sources, including skeletal-muscular causes and arthritis. In addition, neuropathic pain associated with diabetes is an issue for this age group.

Among Medicare plans, overall trend for the pain class increased 3.4% (Exhibit 37), fueled by a 2.9% increase in the number of PMPY prescriptions. This class, comprised mainly of generic medications, maintained a constant 97.1% generic fill rate (GFR). Between 2010 and 2011, the average cost per prescription for the market-share leader, generic hydrocodone and acetaminophen, was flat.

Exhibit 37  Top Five Medicare Pain Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrocodone and acetaminophen</td>
<td>25.9%</td>
<td>25.8%</td>
<td>$14.28</td>
<td>$14.25</td>
<td>-0.2%</td>
</tr>
<tr>
<td>tramadol</td>
<td>12.4%</td>
<td>14.6%</td>
<td>$24.17</td>
<td>$22.59</td>
<td>-6.6%</td>
</tr>
<tr>
<td>oxycodone and acetaminophen</td>
<td>7.9%</td>
<td>7.9%</td>
<td>$16.47</td>
<td>$15.88</td>
<td>-3.6%</td>
</tr>
<tr>
<td>amitriptyline</td>
<td>7.8%</td>
<td>7.5%</td>
<td>$ 6.72</td>
<td>$ 6.39</td>
<td>-5.0%</td>
</tr>
<tr>
<td>tramadol and acetaminophen</td>
<td>6.5%</td>
<td>7.3%</td>
<td>$25.82</td>
<td>$23.58</td>
<td>-8.7%</td>
</tr>
</tbody>
</table>

$64.24  Cost PMPY  1.93  #Rx PMPY  97.1%  GFR  $33.24  Average Cost/Rx  3.4%  TRENDS
Seizures

In 2011, anticonvulsant (seizure) medications rounded out the top 10 Medicare traditional therapy classes, replacing the urinary disorders class. Although epilepsy is the most common cause, seizures also can result from several other medical conditions, including stroke and infection. Many drugs in the class are also used for treating non-seizure conditions such as pain and mental illnesses.

The overall Medicare trend for the seizure class in 2011 was 9.6% (Exhibit 38), including a 7.6% increase in the number of prescriptions filled PMPY and a 2.0% increase in cost per prescription. Overall, the class was heavily dominated by generic medications, with gabapentin, the generic form of Neurontin®, continuing to have the largest market share at 47.2%. The already very high 89.4% generic fill rate (GFR) increased another 1.1% from 2010 to 2011. Lyrica® (pregabalin), the only brand in the top five medications by market share, is approved by the Food and Drug Administration (FDA) for treating epilepsy in combination with other drugs. However, Lyrica is used much more for other indications, including fibromyalgia, postherpetic neuralgia and pain caused by diabetic nerve damage. In 2011, the average cost for a Lyrica prescription increased double digits.

Exhibit 38  Top Five Medicare Seizure Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>gabapentin</td>
<td>44.1%</td>
<td>47.2%</td>
<td>$27.32</td>
</tr>
<tr>
<td>clonazepam</td>
<td>15.1%</td>
<td>14.1%</td>
<td>$20.51</td>
</tr>
<tr>
<td>Lyrica® (pregabalin)</td>
<td>6.2%</td>
<td>5.9%</td>
<td>$149.67</td>
</tr>
<tr>
<td>levetiracetam</td>
<td>4.0%</td>
<td>4.3%</td>
<td>$64.64</td>
</tr>
<tr>
<td>divalproex sodium</td>
<td>4.7%</td>
<td>4.3%</td>
<td>$42.49</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>$61.57</th>
<th>1.39</th>
<th>90.5%</th>
<th>$44.38</th>
<th>9.6%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost PMPY</td>
<td>#Rx PMPY</td>
<td>GFR</td>
<td>Average Cost/Rx</td>
<td>TREND</td>
<td></td>
</tr>
</tbody>
</table>
Medicare Specialty Therapy Class Review

Exhibit 39 | Components and Drivers of Trend for the Top 10 Medicare Specialty Therapy Classes, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Specialty Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cancer</td>
<td>$78.53</td>
<td>25.6%</td>
<td>$16.82</td>
<td>12.5%</td>
<td>14.7%</td>
<td>27.2%</td>
</tr>
<tr>
<td>2</td>
<td>HIV</td>
<td>$69.30</td>
<td>22.6%</td>
<td>$6.45</td>
<td>4.3%</td>
<td>6.0%</td>
<td>10.3%</td>
</tr>
<tr>
<td>3</td>
<td>Inflammatory Conditions</td>
<td>$38.52</td>
<td>12.6%</td>
<td>$6.81</td>
<td>13.2%</td>
<td>8.3%</td>
<td>21.5%</td>
</tr>
<tr>
<td>4</td>
<td>Multiple Sclerosis</td>
<td>$32.10</td>
<td>10.5%</td>
<td>$8.22</td>
<td>20.3%</td>
<td>14.1%</td>
<td>34.4%</td>
</tr>
<tr>
<td>5</td>
<td>Pulmonary Hypertension</td>
<td>$17.04</td>
<td>5.6%</td>
<td>$2.53</td>
<td>19.8%</td>
<td>-2.4%</td>
<td>17.4%</td>
</tr>
<tr>
<td>6</td>
<td>Blood Cell Deficiency</td>
<td>$13.76</td>
<td>4.5%</td>
<td>-0.01</td>
<td>-12.0%</td>
<td>11.9%</td>
<td>-0.1%</td>
</tr>
<tr>
<td>7</td>
<td>Anticoagulants</td>
<td>$13.59</td>
<td>4.4%</td>
<td>$0.28</td>
<td>6.0%</td>
<td>-3.9%</td>
<td>2.1%</td>
</tr>
<tr>
<td>8</td>
<td>Transplant</td>
<td>$8.41</td>
<td>2.7%</td>
<td>-0.42</td>
<td>9.5%</td>
<td>-14.2%</td>
<td>-4.7%</td>
</tr>
<tr>
<td>9</td>
<td>Hepatitis C</td>
<td>$7.78</td>
<td>2.5%</td>
<td>$5.10</td>
<td>106.7%</td>
<td>83.7%</td>
<td>190.4%</td>
</tr>
<tr>
<td>10</td>
<td>Osteoporosis</td>
<td>$6.63</td>
<td>2.2%</td>
<td>$0.74</td>
<td>5.6%</td>
<td>6.9%</td>
<td>12.5%</td>
</tr>
<tr>
<td></td>
<td><strong>Top 10</strong></td>
<td><strong>$285.66</strong></td>
<td><strong>93.1%</strong></td>
<td><strong>$46.51</strong></td>
<td><strong>8.0%</strong></td>
<td><strong>11.4%</strong></td>
<td><strong>19.4%</strong></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td><strong>$21.21</strong></td>
<td><strong>6.9%</strong></td>
<td><strong>$4.66</strong></td>
<td><strong>18.9%</strong></td>
<td><strong>9.3%</strong></td>
<td><strong>28.1%</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>$306.87</strong></td>
<td><strong>100.00%</strong></td>
<td><strong>$51.16</strong></td>
<td><strong>8.4%</strong></td>
<td><strong>11.6%</strong></td>
<td><strong>20.0%</strong></td>
</tr>
</tbody>
</table>
Although specialty medications represent only a fraction of total Medicare drug spend, their contribution to trend continues to increase. Specialty drugs increased 20.0% in total 2011 per-member-per-year (PMPY) cost compared to a 12.7% increase in 2010. In contrast to the traditional market, in which new, lower-cost generic entrants have slowed year-over-year growth in spend, the specialty market will see continued year-over-year growth in spend, driven by the anticipated 27% annual expansion of the proportion of specialty trend covered under pharmacy benefits over the next three years. And generics will not offer relief in the specialty market as they will in the traditional market; even though most states require generic alternatives to be substituted for brand products when appropriate, few generic alternatives for specialty medications are available.

The top 10 specialty therapy classes for our Medicare plans are detailed in Exhibit 39. Seven had trend increases exceeding 10%. Medications to treat hepatitis C saw the largest increase, at 190.4%, followed by multiple sclerosis (MS), which grew 34.4%. More than 71% of the specialty pharmaceutical cost for Medicare recipients in 2011 was attributable to the top four specialty drug classes: cancer, HIV, inflammatory conditions and MS (Exhibit 40). For Medicare, the total PMPY specialty ingredient cost was $306.87 (Exhibit 39).

Reorganization of the HIV class in 2011 moved it to the top 10 for the first time. HIV medication regimens are costly and complex, requiring intensive clinical monitoring. CuraScript®, a subsidiary of Express Scripts, offers an HIV specialty drug program to assist patients.
The top 10 specialty medications accounted for more than 40% of the overall specialty spend in 2011. Medications used to treat cancer appeared most frequently on the top 10 Medicare specialty drug list. As shown in Exhibit 41, the PMPY spend for one cancer drug, Revlimid® (lenalidomide), represented 6.1% of total specialty spend. The only generic in the top 10 specialty medications for 2011 was enoxaparin; launched in July 2010, this medication saw its trend nearly triple (292.5% increase) in 2011.

### Exhibit 41
Top 10 Medicare Specialty Drugs, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Medication</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Specialty Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Revlimid® (lenalidomide)</td>
<td>Cancer</td>
<td>$18.79</td>
<td>6.1%</td>
<td>$2.65</td>
<td>10.8%</td>
<td>5.1%</td>
<td>16.4%</td>
</tr>
<tr>
<td>2</td>
<td>Enbrel® (etanercept)</td>
<td>Inflammatory Conditions</td>
<td>$17.85</td>
<td>5.8%</td>
<td>$2.76</td>
<td>9.1%</td>
<td>8.4%</td>
<td>18.3%</td>
</tr>
<tr>
<td>3</td>
<td>Humira® (adalimumab)</td>
<td>Inflammatory Conditions</td>
<td>$14.64</td>
<td>4.8%</td>
<td>$2.75</td>
<td>12.7%</td>
<td>9.2%</td>
<td>23.1%</td>
</tr>
<tr>
<td>4</td>
<td>Copaxone® (glatiramer)</td>
<td>Multiple Sclerosis</td>
<td>$13.50</td>
<td>4.4%</td>
<td>$3.14</td>
<td>9.5%</td>
<td>19.0%</td>
<td>30.3%</td>
</tr>
<tr>
<td>5</td>
<td>Gleevec® (imatinib)</td>
<td>Cancer</td>
<td>$12.97</td>
<td>4.2%</td>
<td>$2.45</td>
<td>4.3%</td>
<td>18.2%</td>
<td>23.3%</td>
</tr>
<tr>
<td>6</td>
<td>Truvada® (emtricitabine and tenofovir)</td>
<td>HIV</td>
<td>$12.26</td>
<td>4.0%</td>
<td>$1.85</td>
<td>8.3%</td>
<td>8.7%</td>
<td>17.7%</td>
</tr>
<tr>
<td>7</td>
<td>enoxaparin</td>
<td>Anticoagulants</td>
<td>$9.62</td>
<td>3.1%</td>
<td>$7.17</td>
<td>279.3%</td>
<td>3.5%</td>
<td>292.5%</td>
</tr>
<tr>
<td>8</td>
<td>Atripla® (efavirenz, emtricitabine and tenofovir)</td>
<td>HIV</td>
<td>$9.33</td>
<td>3.0%</td>
<td>$1.24</td>
<td>9.5%</td>
<td>5.4%</td>
<td>15.4%</td>
</tr>
<tr>
<td>9</td>
<td>Avonex® (interferon beta-1a)</td>
<td>Multiple Sclerosis</td>
<td>$7.45</td>
<td>2.4%</td>
<td>$2.32</td>
<td>28.4%</td>
<td>13.2%</td>
<td>45.3%</td>
</tr>
<tr>
<td>10</td>
<td>Tarceva® (erlotinib)</td>
<td>Cancer</td>
<td>$6.94</td>
<td>2.3%</td>
<td>$1.13</td>
<td>7.9%</td>
<td>10.6%</td>
<td>19.4%</td>
</tr>
<tr>
<td>Top 10</td>
<td></td>
<td></td>
<td>$123.37</td>
<td>40.2%</td>
<td>$27.46</td>
<td>36.6%</td>
<td>-5.8%</td>
<td>28.6%</td>
</tr>
</tbody>
</table>

Others $183.50 59.8% $23.70 -0.9% 15.9% 14.8%

Total $306.87 100.0% $51.16 8.4% 11.6% 20.0%
Top Medicare Specialty Therapy Classes

Cancer

Although cancer is the second-leading cause of death in the U.S., the number of cancer survivors has continued to increase since 1975, thanks in large part to new cancer medications that have come to market. But these new drugs have put additional stress on Medicare budgets. The cost of treating cancer is projected to be $173 billion in 2020, a 39% increase over the 2010 treatment cost.

For the second year, cancer drugs had a double-digit trend increase. Medicare trend for cancer drugs in 2011 was 27.2% (Exhibit 42), reflecting a 12.5% increase in utilization and a 14.7% increase in cost per prescription. The generic fill rate (GFR) increased 4.4% to reach 24.0%. The top two drugs by cost, Gleevec® (imatinib) and Revlimid® (lenalidomide), together accounted for 33.9% of overall cancer spend.

Exhibit 42 | Top Five Medicare Cancer Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>methotrexate</td>
<td>16.6%</td>
<td>15.2%</td>
<td>$11.81</td>
</tr>
<tr>
<td>Lupron Depot® (leuprolide)</td>
<td>16.2%</td>
<td>13.8%</td>
<td>$1,412.42</td>
</tr>
<tr>
<td>Xeloda® (capecitabine)</td>
<td>11.1%</td>
<td>11.3%</td>
<td>$1,641.28</td>
</tr>
<tr>
<td>Gleevec® (imatinib)</td>
<td>10.6%</td>
<td>9.9%</td>
<td>$4,202.91</td>
</tr>
<tr>
<td>Revlimid® (lenalidomide)</td>
<td>9.1%</td>
<td>9.1%</td>
<td>$7,492.04</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total $78.53</th>
<th>Cost PMPY</th>
<th>0.03</th>
<th>$Rx PMPY</th>
<th>24.0%</th>
<th>GFR</th>
<th>$2,985.16</th>
<th>Average Cost/Rx</th>
<th>27.2%</th>
<th>TREND</th>
</tr>
</thead>
</table>

178.53

Cost PMPY

0.03

$Rx PMPY

24.0%

GFR

2,985.16

Average Cost/Rx

27.2%

TREND
HIV

The Centers for Disease Control and Prevention (CDC) estimates that 1.2 million Americans are living with HIV and AIDS,24 many of them covered under Medicare disability. Although the average age of members with HIV/AIDS in the Express Scripts Medicare population is only 57, better treatments for HIV/AIDS are prolonging life well into later years.25

The 2011 Medicare cost for the class of drugs used to treat HIV was $69.30 per member per year (PMPY), an increase of 10.3% over 2010 PMPY cost (Exhibit 43). The average cost per prescription for these medications was $824.96, up 6.0% from $778.41 in 2010. Two products, Truvada® (emtricitabine and tenofovir) and Atripla® (efavirenz, emtricitabine and tenofovir), accounted for 31.2% of pharmaceutical spend in the class.

Exhibit 43 | Top Five Medicare HIV Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Norvir® (ritonavir)</td>
<td>13.9%</td>
<td>14.4%</td>
<td>$ 359.46</td>
<td>$ 353.60</td>
<td>-1.6%</td>
</tr>
<tr>
<td>Truvada® (emtricitabine and tenofovir)</td>
<td>13.0%</td>
<td>13.5%</td>
<td>$ 995.39</td>
<td>$1,082.42</td>
<td>8.7%</td>
</tr>
<tr>
<td>Reyataz® (atazanavir)</td>
<td>8.0%</td>
<td>8.1%</td>
<td>$ 932.78</td>
<td>$ 945.26</td>
<td>1.3%</td>
</tr>
<tr>
<td>Isentress® (raltegravir)</td>
<td>5.7%</td>
<td>7.2%</td>
<td>$ 941.54</td>
<td>$ 993.88</td>
<td>5.6%</td>
</tr>
<tr>
<td>Atripla® (efavirenz, emtricitabine and tenofovir)</td>
<td>6.4%</td>
<td>6.7%</td>
<td>$1,571.77</td>
<td>$1,656.40</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

$69.30
Cost PMPY

0.08
#Rx PMPY

2.6%
GFR

$824.96
Average Cost/Rx

10.3%
TREND
Inflammatory Conditions

Inflammatory conditions include rheumatoid arthritis (RA), Crohn’s disease, psoriasis, lupus and gout. In 2011, the overall Medicare trend for inflammatory conditions was 21.5% (Exhibit 44), combining an 8.3% increase in the cost per prescription and a 13.2% increase in the number of per-member-per-year (PMPY) prescriptions. Almost 88% of the utilization within the class was for the top two drugs, Enbrel® (etanercept) and Humira® (adalimumab). No generic medications are available within this class.

Exhibit 44  Top Five Medicare Inflammatory Conditions Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>Enbrel® (etanercept)</td>
<td>50.7%</td>
<td>49.3%</td>
<td>$1,727.84</td>
</tr>
<tr>
<td>Humira® (adalimumab)</td>
<td>38.2%</td>
<td>38.4%</td>
<td>$1,803.36</td>
</tr>
<tr>
<td>Remicade® (infliximab)</td>
<td>4.9%</td>
<td>4.3%</td>
<td>$3,049.69</td>
</tr>
<tr>
<td>Simponi® (golimumab)</td>
<td>2.3%</td>
<td>2.9%</td>
<td>$1,778.35</td>
</tr>
<tr>
<td>Cimzia® (certolizumab)</td>
<td>2.1%</td>
<td>2.6%</td>
<td>$1,903.88</td>
</tr>
</tbody>
</table>

$38.52  Cost PMPY  0.02  #Rx PMPY  0.0%  GFR  $1,991.19  Average Cost/Rx  21.5%  TREND
Multiple Sclerosis

The 2011 Medicare trend for multiple sclerosis (MS) was 34.4% (Exhibit 45), coupling a 20.3% increase in per-member-per-year (PMPY) utilization with a 14.1% increase in cost per prescription. Similar to the situation for the inflammatory conditions class, almost 92.0% of MS drug utilization was for the top five drugs, all of which except Ampyra® (dalfampridine) had a double-digit increase in cost per prescription between 2010 and 2011. No generics are available for the treatment of MS.

Exhibit 45
Top Five Medicare Multiple Sclerosis Drugs by Market Share, 2010 and 2011

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Copaxone® (glatiramer)</td>
<td>38.6%</td>
<td>35.9%</td>
<td>$3,061.39</td>
<td>$3,642.53</td>
<td>19.0%</td>
</tr>
<tr>
<td>Avonex® (interferon beta-1a)</td>
<td>21.2%</td>
<td>23.1%</td>
<td>$2,765.56</td>
<td>$3,130.25</td>
<td>13.2%</td>
</tr>
<tr>
<td>Rebif® (interferon beta-1a)</td>
<td>14.4%</td>
<td>13.2%</td>
<td>$2,527.64</td>
<td>$2,909.36</td>
<td>15.1%</td>
</tr>
<tr>
<td>Ampyra® (dalfampridine)</td>
<td>6.9%</td>
<td>10.2%</td>
<td>$1,083.65</td>
<td>$1,169.60</td>
<td>7.9%</td>
</tr>
<tr>
<td>Betaseron® (interferon beta-1b)</td>
<td>12.4%</td>
<td>9.6%</td>
<td>$2,701.94</td>
<td>$3,132.94</td>
<td>16.0%</td>
</tr>
</tbody>
</table>

$32.10 Cost PMPY
0.01 #Rx PMPY
0.0% GFR
$3,111.11 Average Cost/Rx
34.4% TREND
Pulmonary Hypertension

Drugs to treat pulmonary arterial hypertension (PAH) represent a relatively new class, with the majority of agents approved in the last few years. Utilization is high in this predominantly brand class because combination treatment with more than one drug is common.

The overall Medicare trend for pulmonary hypertension drugs in 2011 was 17.4% (Exhibit 46), resulting from a 19.8% increase in the per-member-per year (PMPY) prescriptions and a 2.4% decrease in the cost per prescription. Together, Revatio® (sildenafil) and Tracleer® (bosentan) accounted for 54.7% of 2011 pharmaceutical spend in the class.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Revatio® (sildenafil)</td>
<td>44.4%</td>
<td>38.5%</td>
<td>$ 1,560.48</td>
<td>$ 1,535.31</td>
<td>-1.6%</td>
</tr>
<tr>
<td>Tracleer® (bosentan)</td>
<td>30.0%</td>
<td>26.6%</td>
<td>$ 5,975.64</td>
<td>$ 5,990.37</td>
<td>0.3%</td>
</tr>
<tr>
<td>Adcirca® (tadalafil)</td>
<td>7.8%</td>
<td>15.9%</td>
<td>$ 1,080.33</td>
<td>$ 1,197.93</td>
<td>10.9%</td>
</tr>
<tr>
<td>Letairis® (ambrisentan)</td>
<td>11.7%</td>
<td>13.9%</td>
<td>$ 5,742.75</td>
<td>$ 5,912.77</td>
<td>3.0%</td>
</tr>
<tr>
<td>Remodulin® (treprostinil)</td>
<td>3.8%</td>
<td>2.4%</td>
<td>$15,602.72</td>
<td>$20,768.42</td>
<td>33.1%</td>
</tr>
</tbody>
</table>

- **Cost PMPY:** $17.04
- **Rx PMPY:** 0.004
- **GFR:** 0.0%
- **Average Cost/Rx:** $4,000.43
- **TREND:** 17.4%
Looking Ahead

When the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) was passed, the Centers for Medicare and Medicaid Services (CMS) was not sure that enough Part D plans would be available to give Medicare beneficiaries adequate choice. Most regions, however, currently offer 30 or more plans.

Now, CMS clearly is focused on improving the quality of care for Medicare beneficiaries, as reflected by the star ratings that are tied to MAPD and PDP plan beneficiary outcomes. Star ratings provide significant financial incentives for plans to work hard to ensure that their Medicare members receive the highest-quality care. The incentive program will force some plans out of the market and raise the bar for those remaining. Managing trend for Medicare beneficiaries will continue to be important, forcing plans to be efficient while still providing quality care.

The Express Scripts suite of clinical products gives plan sponsors effective solutions for achieving continual improvement in CMS five-star quality ratings. Our clinical programs leverage our predictive analytics, build on our pharmacy data and tap into our unique understanding of member behavior to focus on CMS outcome measures. The results are improved care for members and enhanced efficiency for the plans with whom we partner.

Medicaid

Overview

The program commonly known as Medicaid (Medical Assistance Programs), the largest source of health-related services for Americans with limited incomes, was established in 1965 through Title XIX of the Social Security Act. Medicaid is jointly funded by the federal government and by state governments, and is managed by the individual states for their beneficiaries.

According to the Centers for Medicare & Medicaid Services (CMS) – the federal agency that oversees the program – Medicaid now provides health insurance to 60 million individuals in the U.S., including children, parents, seniors, pregnant women and those with disabilities.¹

As with most large-scale programs, the federal Medicaid program has experienced significant changes over time, including:²

- **1990s**: Throughout the 1990s, states utilized waivers to test and evaluate new coverage approaches that were different from the traditional fee-for-service Medicaid model. During the decade, the particular focus was on managed care.

- **1991**: The Medicaid Drug Rebate Program was put in place. Designed to help control the costs of prescription drugs, this program requires drug manufacturers to rebate part of Medicaid drug spending to the federal government in exchange for coverage under state Medicaid programs. The program allows states to pursue supplemental
rebates from drug manufacturers over and above the federal rates, but there is no requirement that they do so.

- **1996**: The Aid to Families with Dependent Children (AFDC) entitlement program was replaced with Temporary Aid for Needy Families/Aid to Blind and Disabled (TANF/ABD) block grants. As a result of this change in eligibility rules, Medicaid beneficiaries gained the ability to work without losing their medical benefits.

- **1997**: A provision of the Balanced Budget Act created the Children's Health Insurance Program (CHIP), which extended benefits to low-income children who do not qualify for traditional Medicaid. All states now have some form of this program. In addition, Freedom of Choice Waivers were created, allowing states to:
  - Enroll beneficiaries arbitrarily in managed care plans via a state plan amendment
  - Create “carve-outs” for specialty care
  - Offer localized programs
  - Provide beneficiaries with enhanced service packages funded by the savings from managed care products

- **2001**: The Health Insurance Flexibility and Accountability Initiative (HIFA) simplified the process of requesting waivers from Medicaid and CHIP rules. By encouraging states to administer their Medicaid programs with some individuality, HIFA allows for the use of federal funds to provide adequate medical care while increasing savings.

- **2003**: The Medicare Prescription Drug, Improvement, and Modernization Act (MMA) assigned individuals who are eligible for both Medicaid and Medicare to a Medicare Part D prescription plan. These dual-eligible (DE) beneficiaries now receive most of their prescription drug coverage through Medicare.

- **2008**: The recession drove up Medicaid enrollment. The Kaiser Commission on Medicaid and the Uninsured determined that for every 1% rise in the unemployment rate, one million lives are added to Medicaid and an additional 1.1 million people remain uninsured.¹

- **2009**: The American Recovery and Reinvestment Act (ARRA) approved additional federal funding for state Medicaid programs for the period 2008 through 2010. Later, ARRA funding was extended at lower levels until June 2011.

- **2010**: The Patient Protection and Affordable Care Act (PPACA) increased the amount of federal rebates from drug manufacturers and allowed states to collect federal Medicaid rebates on drugs reimbursed under capitation arrangements with Medicaid managed care organizations (MCOs). As a result, many states began to include pharmacy benefits in their managed care offerings.

- **June 2011**: When the additional funding that had been provided through ARRA was suspended, states had to create and manage their fiscal year 2012 budgets at the pre-2008 reimbursement level from CMS. In response to the prolonged recession, increased Medicaid membership and simultaneous decrease in tax revenues, more states began moving their fee-for-service programs to managed care.

## Medicaid Challenges

Over the past 25 years, various adaptations in Medicaid legislation, like those mentioned previously, have expanded the program’s coverage beyond its original design, directly impacting costs. The Medicaid program now provides health insurance coverage to some elderly participants and those with certain conditions (such as breast cancer, cervical cancer and a variety of genetic disorders) in addition to the covered groups mentioned previously. Other than meeting the requirement of providing benefits to all covered groups, states have considerable flexibility in their application of Medicaid benefits.

A healthcare safety net for many low-income Americans, Medicaid has become even more important during the current economic downturn. Between 2008 and 2011, the number of Medicaid enrollees increased 12.2%, rising from 50.0 million to 56.1 million.² With increases in enrollees, of course, have come increases in costs. From 2010 to 2011, state Medicaid spending increased 10.1%, accounting for 23.6% of state budgets.³
Looking ahead, changes in eligibility requirements under the PPACA are expected to further expand state Medicaid programs, which are expected to experience a 27.4% increase in enrollment between 2014 and 2019. Although the federal government will initially fully fund the costs associated with this anticipated enrollment increase, the federal funding will gradually decrease to 90% of program costs by the year 2020 and will remain at that level. States, many of which already face other financial difficulties, are likely to continue to pursue opportunities with managed care to reduce operational costs and thus lower the costs of the state-funded portions of the benefit as they increase over time.

Recognizing the difficult challenges that states have in managing Medicaid costs, the U.S. Department of Health and Human Services (HHS) has suggested several ways to reduce the cost of pharmacy coverage for Medicaid beneficiaries, including the use of generic medications and mail order, as well as technology designed to encourage appropriate prescribing and the avoidance of adverse events.

Solutions

The opportunity for significant savings is very real. A projection from the 2011 Lewin Group report estimated that state Medicaid Fee-for-Service (FFS) programs could realize potential savings in pharmacy spend of 31.7% if optimally managed. As Medicaid managed care plans position themselves to serve more Americans in 2014, states will continue to seek savings by moving from Medicaid FFS to managed care.

Express Scripts – which has more than 25 years of experience in helping clients manage pharmacy benefits in the commercial insurance arena – has been assisting Medicaid MCOs to adapt to changing environments for more than a decade.

Currently managing more than 5 million (roughly 12.8%) of Medicaid’s managed care lives, Express Scripts is an industry leader in understanding the factors that drive prescription-drug trend in Medicaid.

We help our clients manage pharmacy spend while promoting evidence-based clinical care. Our programs increase the utilization of lower-cost brands and generic medications, while ensuring clinically effective, safe treatment for patients. We leverage less-expensive delivery channels, such as home delivery for maintenance medications. And we help patients adhere to the treatment regimens that their doctors prescribe. One measure of our success is that Medicaid plans that used Express Scripts in both 2010 and 2011 to help manage their pharmacy benefits experienced only a modest 2.9% trend increase in 2011.

Generic Medications

As they face increasing budget pressures, states are looking for new and innovative ways to reduce Medicaid costs. Almost all states now encourage the use of generic medications as one way to maximize the value of Medicaid prescription-drug plans.

In the past several years, many top-selling brand medications have lost patent protection, representing significant potential savings for states. Generally, a higher generic fill rate
(GFR) translates to lower costs. It should be noted, however, that market pressures on brand manufacturers today can result in pricing concessions that significantly drop the costs of some brand products, so drug mix must be considered on a case-by-case basis to achieve the lowest net cost.

Shown in Exhibit 47, generic medications cost our Medicaid clients, on average, about $122 less per prescription than brand medications. When compared to both Medicare and commercially insured plans managed by Express Scripts, our Medicaid plans have a higher average GFR (Exhibit 48).

Channel Management

The use of mail order can offer significant cost-savings opportunity for Medicaid programs because for many therapy classes, being adherent with medications is the first step to improving overall health outcomes and offsetting major medical expenses. In general, Express Scripts members who receive their medications via home delivery have...
adherence rates averaging 8% higher than members who use retail. Additionally, the Express Scripts Pharmacy provides greater than 99.9% accuracy, compared to 98.3% accuracy for retail pharmacies. This difference equates to 1,000 errors per 1 million prescriptions filled in mail order versus 17,000 errors per 1 million prescriptions filled in retail.

**Medication Adherence**

More than one-quarter of Medicaid drug spending is on maintenance medications, whose effectiveness depends directly on medication adherence – the degree to which a patient follows the prescribed drug regimen. Nonadherence results from multiple factors that range from forgetfulness to skepticism about a drug’s effectiveness. No matter the nature and severity of the disease being treated, interruptions in drug therapy diminish medication effectiveness, increasing the chances of overall treatment failure and disease progression. In addition, in some cases the resulting diminished health may cause or exacerbate other medical conditions, leading to the need for further care. As a result, patients who fail to take medications as prescribed have higher healthcare costs.

By improving medication adherence for their member populations, plans can improve disease outcomes, enhance patients’ quality of life and decrease disability from avoidable disease-related events. Put simply, maximizing the use of Medicaid dollars demands an advanced, effective and applied understanding of medication adherence – which Express Scripts offers with impressive results.

As shown in Exhibit 49, medication adherence for Express Scripts Medicare patients (measured as the percentage of patients with a medication possession ratio of 80% or greater) is below 60% for the top traditional therapy classes. For the top specialty therapy classes, medication adherence by pulmonary hypertension patients is greatest, as shown in Exhibit 50.
Medicaid Trend

In this edition of the Express Scripts Drug Trend Report, the Medicaid section is expanded to provide additional insights into the trends for cost and utilization. This year, we included the 2010-2011 Medicaid trend based on the year-over-year percentage change in the per-member-per-year (PMPY) spend. Also, PMPY prescription trend by Medicaid plan type (i.e., Children’s Health Insurance Program (CHIP), Temporary Assistance for Needy Families/Aid to Blind and Disabled (TANF/ABD), and Dual Eligible (DE)) was examined.

Exhibit 51 Components and Drivers of Trend for the Top 10 Medicaid Traditional Therapy Classes, Ranked by PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asthma</td>
<td>$ 55.96</td>
<td>14.6%</td>
<td>$0.25</td>
<td>-6.0%</td>
<td>6.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>2</td>
<td>Diabetes</td>
<td>$ 44.45</td>
<td>11.6%</td>
<td>$1.72</td>
<td>-5.4%</td>
<td>9.4%</td>
<td>4.0%</td>
</tr>
<tr>
<td>3</td>
<td>Mental/Neurological Disorders</td>
<td>$ 32.20</td>
<td>8.4%</td>
<td>$1.47</td>
<td>-2.7%</td>
<td>7.5%</td>
<td>4.8%</td>
</tr>
<tr>
<td>4</td>
<td>Pain</td>
<td>$ 32.20</td>
<td>8.4%</td>
<td>$0.03</td>
<td>-5.0%</td>
<td>5.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>5</td>
<td>Infections</td>
<td>$ 22.91</td>
<td>6.0%</td>
<td>-$2.17</td>
<td>-4.2%</td>
<td>-4.5%</td>
<td>-8.7%</td>
</tr>
<tr>
<td>6</td>
<td>Attention Disorders</td>
<td>$ 21.35</td>
<td>5.6%</td>
<td>$3.22</td>
<td>6.4%</td>
<td>11.4%</td>
<td>17.7%</td>
</tr>
<tr>
<td>7</td>
<td>Seizures</td>
<td>$ 19.10</td>
<td>5.0%</td>
<td>$0.88</td>
<td>2.8%</td>
<td>2.0%</td>
<td>4.8%</td>
</tr>
<tr>
<td>8</td>
<td>Depression</td>
<td>$ 13.73</td>
<td>3.6%</td>
<td>-$0.16</td>
<td>2.0%</td>
<td>-3.2%</td>
<td>-1.2%</td>
</tr>
<tr>
<td>9</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$ 11.08</td>
<td>2.9%</td>
<td>-$1.97</td>
<td>-2.5%</td>
<td>-12.7%</td>
<td>-15.1%</td>
</tr>
<tr>
<td>10</td>
<td>Ulcer Disease</td>
<td>$  9.66</td>
<td>2.5%</td>
<td>-$1.63</td>
<td>-3.1%</td>
<td>-11.4%</td>
<td>-14.5%</td>
</tr>
<tr>
<td>Top 10</td>
<td></td>
<td>$262.65</td>
<td>68.5%</td>
<td>$1.63</td>
<td>-3.2%</td>
<td>3.8%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>$120.75</td>
<td>31.5%</td>
<td>$0.07</td>
<td>-2.9%</td>
<td>2.9%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>$383.40</td>
<td>100.0%</td>
<td>$1.71</td>
<td>-3.0%</td>
<td>3.5%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>
Because asthma and diabetes were again the top two ranked traditional therapy classes based on total PMPY spend to Medicaid, we took a closer look into their cost and utilization trends. Additionally, we examined mental/neurological disorders and attention disorders in greater detail.

Including both traditional and specialty drugs, overall Medicaid trend rose 2.9%, to a PMPY of $489.48. The increase resulted from opposing market forces: PMPY utilization decreased 3.0%, to 10.15, whereas cost per prescription increased 6.0%, to $48.23. GFR rose almost 1.0%, to 84.7%.

Medicaid Traditional Therapy Class Review

The annual traditional drug expenditure for Medicaid was essentially flat, increasing a modest 0.4% between 2010 and 2011 (Exhibit 51). A 3.0% decrease in utilization balanced a 3.5% increase in cost per prescription. It should be noted that nearly all of the top traditional classes include maintenance medications, which are taken on a long-term basis to treat chronic diseases.

Exhibit 52 compares the top 10 traditional therapy classes based on PMPY cost and the trend in PMPY cost. The size of each circle reflects the relative utilization (PMPY Rx) for each of the classes. As shown, the largest Medicaid spend was for drugs to treat asthma and diabetes; the smallest PMPY spend occurred in the ulcer disease and high blood pressure/heart disease classes. PMPY trend decreased the most for two of the three most intensely utilized drug classes, infections and high blood pressure/heart disease. The most intensely utilized class – pain – observed a nearly flat trend in PMPY spend. The largest increases in PMPY spend were for the attention disorders and diabetes classes.

Trends by Medicaid Plan Type

As illustrated by Exhibit 53, traditional spend increased more for TANF/ABD (6.6%) and DE (3.8%) than for CHIP (3.0%). Although pharmacy cost trend appears lower for DE than for TANF/ABD or CHIP, these data represent prescriptions captured only through the Medicaid benefit, not prescriptions paid for under Medicare.
As illustrated in Exhibit 54, 2011 PMPY ingredient costs and utilization for the traditional therapy classes vary across age groups. Members age 19 and younger had the lowest utilization and costs; those age 35 and older had the highest utilization and cost.
Children and Adolescents (Age 0 to 19)

Approximately 61% of Express Scripts Medicaid enrollees are children and adolescents age 0 to 19 years. Although prescription utilization is lowest among this Medicaid age group, PMPY utilization increased 7.6% between 2010 and 2011 (Exhibit 55), rising from 3.75 to 4.03. PMPY cost also increased for this age group, rising from $137.24 to $155.36. The medications most used by children, antibiotics for the treatment of infections, contributed to the group’s generic fill rate (GFR) of 82.7%. Asthma medications accounted for 27.0% of the total traditional spend by the Medicaid population age 0 to 19 years.

Exhibit 55: Components and Drivers of Trend for the Top 10 Medicaid Traditional Therapy Classes, Enrollees Age 0 to 19, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asthma</td>
<td>$42.01</td>
<td>27.0%</td>
<td>$3.30</td>
<td>2.1%</td>
<td>6.4%</td>
<td>8.5%</td>
</tr>
<tr>
<td>2</td>
<td>Attention Disorders</td>
<td>$27.90</td>
<td>18.0%</td>
<td>$5.12</td>
<td>10.7%</td>
<td>11.8%</td>
<td>22.5%</td>
</tr>
<tr>
<td>3</td>
<td>Infections</td>
<td>$18.40</td>
<td>11.8%</td>
<td>$0.07</td>
<td>4.6%</td>
<td>-4.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>4</td>
<td>Diabetes</td>
<td>$7.85</td>
<td>5.1%</td>
<td>$1.45</td>
<td>14.2%</td>
<td>8.5%</td>
<td>22.7%</td>
</tr>
<tr>
<td>5</td>
<td>Mental/Neurological Disorders</td>
<td>$7.60</td>
<td>4.9%</td>
<td>$1.18</td>
<td>12.0%</td>
<td>6.3%</td>
<td>18.3%</td>
</tr>
<tr>
<td>6</td>
<td>Allergies</td>
<td>$6.21</td>
<td>4.0%</td>
<td>$0.69</td>
<td>9.6%</td>
<td>3.0%</td>
<td>12.6%</td>
</tr>
<tr>
<td>7</td>
<td>Seizures</td>
<td>$4.78</td>
<td>3.1%</td>
<td>$0.37</td>
<td>12.9%</td>
<td>-4.5%</td>
<td>8.5%</td>
</tr>
<tr>
<td>8</td>
<td>Skin Infections</td>
<td>$3.53</td>
<td>2.3%</td>
<td>$0.81</td>
<td>4.1%</td>
<td>25.7%</td>
<td>29.8%</td>
</tr>
<tr>
<td>9</td>
<td>Contraceptives</td>
<td>$3.24</td>
<td>2.1%</td>
<td>$0.74</td>
<td>31.2%</td>
<td>-1.8%</td>
<td>29.4%</td>
</tr>
<tr>
<td>10</td>
<td>Skin Conditions</td>
<td>$3.04</td>
<td>2.0%</td>
<td>$0.76</td>
<td>2.1%</td>
<td>31.3%</td>
<td>33.4%</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>$30.78</td>
<td>19.8%</td>
<td>$3.63</td>
<td>9.0%</td>
<td>4.3%</td>
<td>13.4%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>$155.36</td>
<td>100.0%</td>
<td>$18.12</td>
<td>7.6%</td>
<td>5.6%</td>
<td>13.2%</td>
</tr>
</tbody>
</table>
Young Adults (Age 20 to 34)

Enrollees in their early adult years account for approximately 18% of Express Scripts Medicaid enrollees. Overall spend for this population decreased 4.4% in 2011 (Exhibit 56), due to an 9.1% decrease in utilization and a 4.8% increase in cost per prescription. GFR increased 0.7%, to 88.5%. Medications to treat mental and neurological disorders accounted for 11.5% of the total spend within this age group, influenced by PMPY cost increases for Abilify® (aripiprazole), Seroquel® (quetiapine) and Zyprexa® (olanzapine). However, a generic for Zyprexa is now available and Seroquel will lose patent protection in 2012, offering new opportunities for savings within the class. Drugs to treat chemical dependence, which had a 19.4% trend increase, are among the top 10 traditional therapy classes for this age group.

Exhibit 56

Components and Drivers of Trend for the Top 10 Medicaid Traditional Therapy Classes, Enrollees Age 20 to 34, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mental/Neurological Disorders</td>
<td>$43.36</td>
<td>11.5%</td>
<td>$0.13</td>
<td>$43.36</td>
<td>11.5%</td>
<td>$0.13</td>
<td>-8.7%</td>
<td>9.0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>2</td>
<td>Pain</td>
<td>$36.91</td>
<td>9.8%</td>
<td>-$0.40</td>
<td>$36.51</td>
<td>9.8%</td>
<td>-$0.40</td>
<td>-11.8%</td>
<td>10.7%</td>
<td>-1.1%</td>
</tr>
<tr>
<td>3</td>
<td>Asthma</td>
<td>$32.55</td>
<td>8.6%</td>
<td>-$3.39</td>
<td>$29.16</td>
<td>7.7%</td>
<td>-$3.39</td>
<td>-14.6%</td>
<td>5.2%</td>
<td>-9.4%</td>
</tr>
<tr>
<td>4</td>
<td>Diabetes</td>
<td>$31.33</td>
<td>8.3%</td>
<td>$0.92</td>
<td>$32.25</td>
<td>8.5%</td>
<td>$0.92</td>
<td>-5.7%</td>
<td>8.8%</td>
<td>3.0%</td>
</tr>
<tr>
<td>5</td>
<td>Seizures</td>
<td>$26.20</td>
<td>6.9%</td>
<td>$0.40</td>
<td>$25.80</td>
<td>6.8%</td>
<td>$0.40</td>
<td>0.7%</td>
<td>0.8%</td>
<td>1.5%</td>
</tr>
<tr>
<td>6</td>
<td>Contraceptives</td>
<td>$25.69</td>
<td>6.8%</td>
<td>-$4.30</td>
<td>$21.39</td>
<td>5.9%</td>
<td>-$4.30</td>
<td>-15.3%</td>
<td>0.9%</td>
<td>-14.3%</td>
</tr>
<tr>
<td>7</td>
<td>Infections</td>
<td>$23.76</td>
<td>6.3%</td>
<td>-$5.37</td>
<td>$18.39</td>
<td>4.8%</td>
<td>-$5.37</td>
<td>-13.7%</td>
<td>4.7%</td>
<td>-18.4%</td>
</tr>
<tr>
<td>8</td>
<td>Chemical Dependence</td>
<td>$23.18</td>
<td>6.1%</td>
<td>$3.77</td>
<td>$26.95</td>
<td>8.0%</td>
<td>$3.77</td>
<td>16.4%</td>
<td>3.1%</td>
<td>19.4%</td>
</tr>
<tr>
<td>9</td>
<td>Depression</td>
<td>$18.22</td>
<td>4.8%</td>
<td>-$1.03</td>
<td>$17.19</td>
<td>4.8%</td>
<td>-$1.03</td>
<td>-4.3%</td>
<td>1.1%</td>
<td>-5.4%</td>
</tr>
<tr>
<td>10</td>
<td>Attention Disorders</td>
<td>$12.24</td>
<td>3.2%</td>
<td>$0.93</td>
<td>$13.17</td>
<td>3.2%</td>
<td>$0.93</td>
<td>-0.3%</td>
<td>8.5%</td>
<td>8.2%</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>$104.28</td>
<td>27.6%</td>
<td>-$8.94</td>
<td>$95.34</td>
<td>25.8%</td>
<td>-$8.94</td>
<td>-7.3%</td>
<td>-0.6%</td>
<td>-7.9%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>$377.73</td>
<td>100.0%</td>
<td>-$17.26</td>
<td>$360.47</td>
<td>100.0%</td>
<td>-$17.26</td>
<td>-9.1%</td>
<td>4.8%</td>
<td>-4.4%</td>
</tr>
</tbody>
</table>
**Mid-Age Adults (Age 35 to 64)**

Enrollees who are 35 years old to 64 years old accounted for about 20% of our Medicaid members in 2011. Although individuals in the group had the highest average PMPY Medicaid cost for the year – $1,052.10 – their cost decreased 9.1%, from $1,157.18 in 2010 (Exhibit 57). Overall trend for this Medicaid age group was influenced primarily by an 11.6% decrease in utilization. Cost per prescription increased 2.5%, even as GFR increased 1.1%, to reach 84.9%. Medications used to treat pain and cardiovascular diseases dominate utilization for enrollees in this age group.

### Exhibit 57

**Components and Drivers of Trend for the Top 10 Medicaid Traditional Therapy Classes, Enrollees Age 35 to 64, Ranked by 2011 PMPY Spend**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$160.01</td>
<td>15.2%</td>
<td>-$7.28</td>
<td>-13.1%</td>
<td>8.8%</td>
<td>-4.4%</td>
</tr>
<tr>
<td>2</td>
<td>Pain</td>
<td>$121.41</td>
<td>11.5%</td>
<td>-$11.45</td>
<td>-13.3%</td>
<td>4.7%</td>
<td>-8.6%</td>
</tr>
<tr>
<td>3</td>
<td>Asthma</td>
<td>$117.92</td>
<td>11.2%</td>
<td>-$10.18</td>
<td>-15.3%</td>
<td>7.4%</td>
<td>-7.9%</td>
</tr>
<tr>
<td>4</td>
<td>Mental/Neurological Disorders</td>
<td>$94.52</td>
<td>9.0%</td>
<td>-$4.54</td>
<td>-12.0%</td>
<td>7.4%</td>
<td>-4.6%</td>
</tr>
<tr>
<td>5</td>
<td>Seizures</td>
<td>$55.76</td>
<td>5.3%</td>
<td>-$2.07</td>
<td>-6.8%</td>
<td>3.3%</td>
<td>-3.6%</td>
</tr>
<tr>
<td>6</td>
<td>Depression</td>
<td>$46.88</td>
<td>4.5%</td>
<td>-$5.49</td>
<td>-7.3%</td>
<td>3.2%</td>
<td>-10.5%</td>
</tr>
<tr>
<td>7</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$46.02</td>
<td>4.4%</td>
<td>-$12.14</td>
<td>-8.4%</td>
<td>12.5%</td>
<td>-20.9%</td>
</tr>
<tr>
<td>8</td>
<td>High Blood Cholesterol</td>
<td>$38.77</td>
<td>3.7%</td>
<td>-$8.88</td>
<td>-9.2%</td>
<td>9.5%</td>
<td>-18.6%</td>
</tr>
<tr>
<td>9</td>
<td>Infections</td>
<td>$35.87</td>
<td>3.4%</td>
<td>-$8.15</td>
<td>-14.8%</td>
<td>3.7%</td>
<td>-18.5%</td>
</tr>
<tr>
<td>10</td>
<td>Ulcer Disease</td>
<td>$30.91</td>
<td>2.9%</td>
<td>-$9.05</td>
<td>-11.0%</td>
<td>11.7%</td>
<td>-22.6%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>$304.03</td>
<td>28.9%</td>
<td>-$25.81</td>
<td>-11.9%</td>
<td>4.1%</td>
<td>-7.8%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>$1,052.10</td>
<td>100.0%</td>
<td>-$105.08</td>
<td>-11.6%</td>
<td>2.5%</td>
<td>-9.1%</td>
</tr>
</tbody>
</table>
Seniors (Age 65 and Older)

Individuals age 65 and older account for only about 1.1% of enrollees in the Medicaid plans that Express Scripts manages. Inasmuch as seniors using Medicaid tend to have multiple conditions, their Medicaid prescription-drug utilization is higher than that of other age groups.

In this Medicaid age group, the drug trend for members who are not also eligible for Medicare (dual eligible) is very similar to that for low-income subsidy (LIS) members enrolled in Medicare Part D. Between 2010 and 2011, significant decreases in both PMPY utilization (-31.5%) and cost per prescription (-4.4%) for this group contributed to a -35.9% trend (Exhibit 58). GFR increased 2.0% between 2010 and 2011, to reach 84.3%.

Exhibit 58 Components and Drivers of Trend for the Top 10 Medicaid Traditional Therapy Classes, Enrollees Age 65 and Older, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Traditional Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Total</td>
<td>$890.98</td>
<td>100.0%</td>
<td>-$499.79</td>
<td>-31.5%</td>
<td>-4.4%</td>
<td>-35.9%</td>
</tr>
<tr>
<td>1</td>
<td>Diabetes</td>
<td>$177.28</td>
<td>19.9%</td>
<td>-$ 86.03</td>
<td>-34.7%</td>
<td>2.0%</td>
<td>-32.7%</td>
</tr>
<tr>
<td>2</td>
<td>Asthma</td>
<td>$ 90.14</td>
<td>10.1%</td>
<td>-$ 57.58</td>
<td>-41.5%</td>
<td>2.5%</td>
<td>-39.0%</td>
</tr>
<tr>
<td>3</td>
<td>High Blood Pressure/Heart Disease</td>
<td>$ 83.05</td>
<td>9.3%</td>
<td>-$ 51.39</td>
<td>-30.9%</td>
<td>-7.3%</td>
<td>-38.2%</td>
</tr>
<tr>
<td>4</td>
<td>Mental/Nervological Disorders</td>
<td>$ 69.63</td>
<td>7.8%</td>
<td>-$ 30.43</td>
<td>-30.8%</td>
<td>0.3%</td>
<td>-30.4%</td>
</tr>
<tr>
<td>5</td>
<td>High Blood Cholesterol</td>
<td>$ 58.27</td>
<td>6.5%</td>
<td>-$ 38.26</td>
<td>-32.3%</td>
<td>-7.4%</td>
<td>-39.6%</td>
</tr>
<tr>
<td>6</td>
<td>Blood Modifying</td>
<td>$ 51.79</td>
<td>5.8%</td>
<td>-$ 22.14</td>
<td>-37.1%</td>
<td>7.2%</td>
<td>-29.9%</td>
</tr>
<tr>
<td>7</td>
<td>Pain</td>
<td>$ 35.35</td>
<td>4.0%</td>
<td>-$ 29.70</td>
<td>-33.3%</td>
<td>-12.3%</td>
<td>-45.7%</td>
</tr>
<tr>
<td>8</td>
<td>Ulcer Disease</td>
<td>$ 30.48</td>
<td>3.4%</td>
<td>-$ 18.59</td>
<td>-33.4%</td>
<td>-4.5%</td>
<td>-37.9%</td>
</tr>
<tr>
<td>9</td>
<td>Seizures</td>
<td>$ 24.81</td>
<td>2.8%</td>
<td>-$ 12.66</td>
<td>-31.5%</td>
<td>-2.2%</td>
<td>-33.8%</td>
</tr>
<tr>
<td>10</td>
<td>COPD</td>
<td>$ 22.57</td>
<td>2.5%</td>
<td>-$  9.30</td>
<td>-45.5%</td>
<td>16.3%</td>
<td>-29.2%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>$247.66</td>
<td>27.8%</td>
<td>-$143.44</td>
<td>-28.8%</td>
<td>-7.9%</td>
<td>-36.7%</td>
</tr>
</tbody>
</table>

TREND
### Top Medicaid Traditional Therapy Classes

#### Asthma

The Centers for Disease Control and Prevention (CDC) has reported that one of every 10 children had asthma in 2009, and more than half of all children with asthma had an acute asthma episode. Exacerbation of this inflammatory respiratory disease is largely preventable through adherence to treatment recommendations, including taking prescription asthma medications — typically inhaled corticosteroids — as directed.

Asthma is the top-ranked traditional therapy class by cost for Medicaid clients. From 2010 to 2011, PMPY costs for asthma (Exhibit 59) increased 0.4%, to $55.96. The cost per prescription increased 6.4%, to $92.82. Express Scripts data indicate that utilization for asthma medications decreased 6.0% in 2011.

With a medication adherence rate of only 35.2%, asthma is the lowest-ranked therapy class by the percentage of patients who are considered adherent (e.g., those with an medication process ratio (MPR) greater than 80%) (Exhibit 60). Adherence to asthma medications appears to be greatest for older Medicaid patients for whom medications may be used to treat conditions such as chronic obstructive pulmonary disease (COPD) in addition to asthma (Exhibit 60).

Because maintaining better asthma control can result in fewer emergency room visits and inpatient hospitalizations, we looked more closely at medication adherence to the most frequently prescribed asthma controller medications.

Both inhaled corticosteroids (ICSs) alone and inhaled combinations of an ICS and a long-acting beta-agonist (LABA) are used for the long-term control of asthma. Leukotriene modulators are oral medications that also are used as maintenance for asthma. These three drug subclasses act in different ways and therefore are prescribed differently.

#### Exhibit 59

Top 10 Medicaid Asthma Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proair HFA® (albuterol)</td>
<td>31.8%</td>
<td>$41.79</td>
<td>2.3%</td>
</tr>
<tr>
<td>albuterol sulfate</td>
<td>16.0%</td>
<td>$29.60</td>
<td>-1.6%</td>
</tr>
<tr>
<td>Singulair® (montelukast)</td>
<td>11.2%</td>
<td>$119.33</td>
<td>14.7%</td>
</tr>
<tr>
<td>Advair Diskus® (fluticasone and salmeterol)</td>
<td>10.8%</td>
<td>$209.88</td>
<td>6.8%</td>
</tr>
<tr>
<td>Ventolin® HFA (albuterol)</td>
<td>7.8%</td>
<td>$33.70</td>
<td>12.0%</td>
</tr>
<tr>
<td>Flonext® HFA (fluticasone)</td>
<td>7.6%</td>
<td>$123.92</td>
<td>10.3%</td>
</tr>
<tr>
<td>budesonide</td>
<td>2.8%</td>
<td>$239.55</td>
<td>7.1%</td>
</tr>
<tr>
<td>Proventil® HFA (albuterol)</td>
<td>2.4%</td>
<td>$45.51</td>
<td>7.0%</td>
</tr>
<tr>
<td>Combivent® (albuterol and ipratropium)</td>
<td>2.1%</td>
<td>$145.84</td>
<td>25.0%</td>
</tr>
<tr>
<td>Qvar® (beclamethasone)</td>
<td>1.7%</td>
<td>$81.72</td>
<td>36.1%</td>
</tr>
</tbody>
</table>

$55.96 Cost PMPY  
0.60 #Rx PMPY  
20.1% GFR  
$92.82 Average Cost/Rx  
0.4% TREND
According to the asthma treatment guidelines issued by the National Heart, Lung and Blood Institute, both ICSs and leukotriene modulators may be required for patients with moderate to severe asthma.

Adherence to controller medications is critical to the successful treatment of asthma. A study of CHIP enrollees living in Florida and Texas found that the average MPR was 20% for children treated with ICSs and 28% for children taking a leukotriene modulator. Adherence to asthma controller medications is poor, even for patients who are well educated about asthma.

In usual-care clinical-practice settings, commercially insured patients using oral controllers are twice as likely to be adherent to their medication as patients using inhaled asthma controller medications. An Express Scripts study found a similar, but narrower, relationship among our Medicaid patients. In our study, 47.5% of patients were adherent to their leukotriene modulators, compared with 42.7% of patients who used inhaled controller medications. But regardless of the differing adherence rates for inhaled controllers and leukotriene modulators, consistent use of both by asthma patients is important to decreasing overall medical spending for this therapy class.

### Exhibit 60 2011 Medicaid PMPY Utilization for Asthma Drugs by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2010</th>
<th>2011</th>
<th>% Change in Utilization</th>
<th>% Adherent to Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.473</td>
<td>0.483</td>
<td>2.1%</td>
<td>11.8%</td>
</tr>
<tr>
<td>20-34</td>
<td>0.467</td>
<td>0.401</td>
<td>-14.6%</td>
<td>18.9%</td>
</tr>
<tr>
<td>35-64</td>
<td>1.337</td>
<td>1.140</td>
<td>-15.3%</td>
<td>39.5%</td>
</tr>
<tr>
<td>65 +</td>
<td>1.405</td>
<td>0.831</td>
<td>-41.5%</td>
<td>40.8%</td>
</tr>
</tbody>
</table>
## Diabetes

Diabetes is a chronic disease with the potential for causing severe complications. Type 1 diabetes is an autoimmune disease that usually is diagnosed in children. All patients with Type 1 diabetes, characterized by an inability to produce natural insulin, need insulin replacement to manage their disease.

By far the more common type of diabetes, type 2 can occur at any age. Type 2 diabetes is caused by decreased insulin production, increased insulin resistance or both. Medications used for type 2 diabetes include oral agents, insulin and non-insulin injectable medications.

The overall 2011 trend for diabetic medications in our Medicaid population was 4.0% (Exhibit 61), composed of a 5.4% decrease in utilization and a 9.4% increase in cost per prescription. Among the top 10 most used diabetes drugs and devices, drugs accounted for 46.3% of the total market share and diabetic devices for 20.7%.

A closer look into the use of diabetes medications by age shows that these medications are primarily used by older adults, particularly adults 65 years of age and older (Exhibit 62). However, use increased 14.2% for Medicaid beneficiaries under 20 years of age in 2011. Adherence to diabetes medications appears to be greatest for older Medicaid patients. Because inadequately controlled diabetes can lead to severe complications, lower adherence among younger members increases the potential for complications at earlier ages. In 2011, only 44.4% of overall Medicaid patients were adherent to diabetes therapy (MPR ≥ 80%), lower than the percentage of patients who were adherent to drugs for high cholesterol and high blood pressure/heart disease, conditions also associated with adverse medical outcomes.\(^\text{22}\)

### Exhibit 61

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin</td>
<td>22.2%</td>
<td>22.8%</td>
<td>$10.39</td>
<td>$9.97</td>
<td>-4.0%</td>
</tr>
<tr>
<td>Lantus® <em>(insulin glargine)</em></td>
<td>8.2%</td>
<td>8.5%</td>
<td>$142.20</td>
<td>$154.84</td>
<td>8.9%</td>
</tr>
<tr>
<td>Accu-Chek® Aviva Test Strips</td>
<td>6.2%</td>
<td>6.3%</td>
<td>$86.60</td>
<td>$89.30</td>
<td>3.1%</td>
</tr>
<tr>
<td>insulin syringes</td>
<td>6.8%</td>
<td>6.2%</td>
<td>$19.27</td>
<td>$19.85</td>
<td>3.0%</td>
</tr>
<tr>
<td>glipizide</td>
<td>4.4%</td>
<td>4.3%</td>
<td>$10.08</td>
<td>$9.19</td>
<td>-8.8%</td>
</tr>
<tr>
<td>Novolog® <em>(insulin aspart)</em></td>
<td>3.8%</td>
<td>4.2%</td>
<td>$184.42</td>
<td>$210.18</td>
<td>14.0%</td>
</tr>
<tr>
<td>Onetouch® Ultra® Test Strips</td>
<td>3.3%</td>
<td>4.1%</td>
<td>$110.00</td>
<td>$111.95</td>
<td>1.8%</td>
</tr>
<tr>
<td>Accu-Chek® Test Strips</td>
<td>4.4%</td>
<td>4.1%</td>
<td>$14.34</td>
<td>$13.81</td>
<td>-3.7%</td>
</tr>
<tr>
<td>glyburide</td>
<td>3.9%</td>
<td>3.6%</td>
<td>$20.75</td>
<td>$20.62</td>
<td>-0.7%</td>
</tr>
<tr>
<td>Actos® <em>(pioglitazone)</em></td>
<td>3.8%</td>
<td>3.4%</td>
<td>$199.05</td>
<td>$218.69</td>
<td>9.9%</td>
</tr>
</tbody>
</table>

\(|44.45_\text{Cost PMPY}| 0.61_\text{Rx PMPY}| 37.4_\text{GFR}| 73.28_\text{Average Cost/Rx}| 4.0\%_\text{TREND}\)
## 2011 Medicaid PMPY Utilization for Diabetes Drugs by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>#Rx PMPY 2010</th>
<th>#Rx PMPY 2011</th>
<th>% Change in Utilization</th>
<th>% Adherent to Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.06</td>
<td>0.07</td>
<td>14.2%</td>
<td>25.0%</td>
</tr>
<tr>
<td>20-34</td>
<td>0.40</td>
<td>0.38</td>
<td>-5.7%</td>
<td>27.2%</td>
</tr>
<tr>
<td>35-64</td>
<td>2.63</td>
<td>2.30</td>
<td>-13.1%</td>
<td>46.5%</td>
</tr>
<tr>
<td>65 +</td>
<td>4.55</td>
<td>2.99</td>
<td>-34.7%</td>
<td>43.2%</td>
</tr>
</tbody>
</table>
Mental/Neurological Disorders

The PMPY Medicaid cost for mental and neurological disorders was $32.20 in 2011, an increase of 4.8% over the 2010 PMPY cost. In the same period, PMPY utilization decreased 2.7% and the average cost per prescription increased 7.5%, to $219.59. The generic fill rate (GFR) was 56.0%, an increase of 8.5% from 2010.

Atypical antipsychotics account for close to one-half of all medications prescribed to treat mental and neurological disorders. However, an Express Scripts study found that 35% of Medicaid patients who filled their first atypical antipsychotic prescriptions changed the dosage or discontinued the medications within 30 days. Additionally, among Medicaid patients who were prescribed an atypical antipsychotic for the first time, one-quarter of them received prescriptions from their physicians for less than a 30-day supply. The research indicates that prescribers may be limiting the days’ supply for initial atypical antipsychotics.

Exhibit 63 | Top 5 Medicaid Mental/Neurological Disorders Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>risperidone</td>
<td>17.0%</td>
<td>19.2%</td>
<td></td>
<td>$31.84</td>
<td></td>
<td>$31.25</td>
</tr>
<tr>
<td>Seroquel® (quetiapine)</td>
<td>18.4%</td>
<td>16.5%</td>
<td></td>
<td>$316.87</td>
<td></td>
<td>$360.84</td>
</tr>
<tr>
<td>Abilify® (aripiprazole)</td>
<td>13.1%</td>
<td>12.4%</td>
<td></td>
<td>$454.92</td>
<td></td>
<td>$507.76</td>
</tr>
<tr>
<td>benztropine</td>
<td>10.9%</td>
<td>11.1%</td>
<td></td>
<td>$6.92</td>
<td></td>
<td>$7.29</td>
</tr>
<tr>
<td>lithium carbonate</td>
<td>6.6%</td>
<td>6.7%</td>
<td></td>
<td>$13.96</td>
<td></td>
<td>$14.31</td>
</tr>
</tbody>
</table>

$32.20  
Cost PMPY  
0.15  
#Rx PMPY  
56.0%  
GFR  
$219.59  
Average Cost/Rx  
4.8%  
TREND
A closer look into mental/neurological medications by age (Exhibit 64) indicates that the primary use of these medications is by adults, with those in the 35-to-64 age group the highest users. Interestingly, the PMPY prescriptions filled for these medications in Medicaid decreased at least 8.7% for all but the youngest age group; PMPY prescriptions for the youngest group, although low, increased 12.0%. As Exhibit 64 shows, PMPY spending also increased the most for the youngest age group, 18.3% in 2011.

Exhibit 64  
2011 Medicaid PMPY Utilization for Mental/Neurological Disorders Drugs by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>#Rx PMPY 2010</th>
<th>#Rx PMPY 2011</th>
<th>% Change in Utilization</th>
<th>% Change in PMPY Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.04</td>
<td>0.04</td>
<td>12.0%</td>
<td>18.3%</td>
</tr>
<tr>
<td>20-34</td>
<td>0.21</td>
<td>0.19</td>
<td>-8.7%</td>
<td>0.3%</td>
</tr>
<tr>
<td>35-64</td>
<td>0.47</td>
<td>0.41</td>
<td>-12.0%</td>
<td>-4.6%</td>
</tr>
<tr>
<td>65 +</td>
<td>0.56</td>
<td>0.39</td>
<td>-30.8%</td>
<td>-30.4%</td>
</tr>
</tbody>
</table>
Pain

Pain medications, which are prescribed for both long- and short-term use, ranked fourth in PMPY Medicaid cost in 2011. PMPY utilization decreased 5.0% between 2010 and 2011, whereas PMPY cost increased a very modest 0.1% (Exhibit 65). The average cost per prescription increased 5.1% in 2011. Two generic combination products—hydrocodone and acetaminophen, and oxycodone and acetaminophen—together accounted for 47.4% of market share.

Controlled pain medications are often a focus for managed Medicaid plans because of their potential for diversion or abuse. In 2011, the Express Scripts Program Integrity unit examined the controlled-pain prescription-filling behavior of a large cross-section of Medicaid members and identified key indicators for potentially problematic member activity (e.g., a high number of claims, doctor-shopping behavior as defined by CMS, use of multiple pharmacies for filling prescriptions). Although only 2.0% of Medicaid members are exhibiting behaviors of concern, this group’s average cost—$1,173 per year—is more than 10 times greater than the $113 average cost for members not exhibiting problematic behavior. The Express Scripts Fraud, Waste and Abuse reporting service provides Medicaid clients with greater visibility to help them accurately target and then intervene with members who may be misusing their benefit.

Exhibit 65 | Top 5 Medicaid Pain Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>hydrocodone and acetaminophen</td>
<td>34.3%</td>
<td>32.7%</td>
<td>$12.38</td>
</tr>
<tr>
<td>oxycodone and acetaminophen</td>
<td>15.3%</td>
<td>14.7%</td>
<td>$15.93</td>
</tr>
<tr>
<td>tramadol</td>
<td>8.7%</td>
<td>9.6%</td>
<td>$23.26</td>
</tr>
<tr>
<td>oxycodone</td>
<td>7.2%</td>
<td>9.3%</td>
<td>$52.10</td>
</tr>
<tr>
<td>morphine sulfate</td>
<td>4.6%</td>
<td>4.8%</td>
<td>$48.39</td>
</tr>
</tbody>
</table>

$32.20
Cost PMPY
1.14
#Rx PMPY
98.4%
GFR
$28.24
Average Cost/Rx
0.1%
TREND
Infections

The overall Medicaid spend for the infection therapy class decreased 8.7% in 2011 (Exhibit 66). PMPY prescriptions and cost per prescription had similar decreases of 4.2% and 4.5%, respectively. The average cost per prescription dropped to $23.44, from $24.56 in 2010. Most drugs in the class have generic equivalents, and drugs for infections typically are taken for only short periods, contributing to low utilization.

Exhibit 66 | Top 5 Medicaid Infection Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>amoxicillin</td>
<td>25.8%</td>
<td>26.2%</td>
<td>$ 8.86</td>
</tr>
<tr>
<td>azithromycin</td>
<td>17.8%</td>
<td>18.6%</td>
<td>$22.17</td>
</tr>
<tr>
<td>cephalexin</td>
<td>9.0%</td>
<td>8.8%</td>
<td>$17.35</td>
</tr>
<tr>
<td>amoxicillin and potassium clavulanate</td>
<td>8.6%</td>
<td>8.7%</td>
<td>$41.87</td>
</tr>
<tr>
<td>sulfamethoxazole and trimethoprim</td>
<td>8.2%</td>
<td>7.8%</td>
<td>$11.01</td>
</tr>
</tbody>
</table>

\[\begin{array}{c|c|c|c|c|c}
\hline
& \text{2010} & \text{2011} & \text{2010} & \text{2011} & \text{Cost/Rx Trend} \\
\hline
\text{Medication} & & & & & \\
\hline
amoxicillin & 25.8% & 26.2% & $8.86 & $8.62 & -2.7% \\
azithromycin & 17.8% & 18.6% & $22.17 & $18.10 & -18.4% \\
cephalexin & 9.0% & 8.8% & $17.35 & $16.27 & -6.2% \\
amoxicillin and potassium clavulanate & 8.6% & 8.7% & $41.87 & $38.60 & -7.8% \\
sulfamethoxazole and trimethoprim & 8.2% & 7.8% & $11.01 & $9.51 & -13.6% \\
\hline
\end{array}\]
Attention Disorders

The 2011 PMPY Medicaid spend in the attention disorders therapy class increased 17.7%, to $21.35 (Exhibit 67). PMPY utilization for the class was up 6.4% over 2010. Central nervous system (CNS) stimulants, such as methylphenidate, prescribed for attention disorders accounted for 17.9% of all prescriptions and 14.4% of total costs in Medicaid traditional drug spend for the therapy class. Shortages of several CNS stimulants in 2011, however, resulted in large price increases as patients were switched to more-expensive, brand medications. The price differential is particularly dramatic in the case of prescription changes from generic methylphenidate to the corresponding brands Ritalin®, and Concerta®, and from mixed amphetamine salts to corresponding brand-drug Adderall®.

Exhibit 67 | Top 5 Medicaid Attention Disorders Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>methylphenidate</td>
<td>5.6%</td>
<td>17.9%</td>
<td>$14.38</td>
<td>$102.66</td>
<td>614.0%</td>
</tr>
<tr>
<td>mixed amphetamine salts</td>
<td>14.8%</td>
<td>16.4%</td>
<td>$32.32</td>
<td>$50.95</td>
<td>57.7%</td>
</tr>
<tr>
<td>dextroamphetamine and amphetamine</td>
<td>18.8%</td>
<td>15.7%</td>
<td>$164.46</td>
<td>$164.25</td>
<td>-0.1%</td>
</tr>
<tr>
<td>Vyvanse® (lisdexamfetamine)</td>
<td>9.0%</td>
<td>10.0%</td>
<td>$130.56</td>
<td>$146.17</td>
<td>12.0%</td>
</tr>
<tr>
<td>Concerta® (methylphenidate)</td>
<td>20.2%</td>
<td>9.7%</td>
<td>$152.03</td>
<td>$184.03</td>
<td>21.1%</td>
</tr>
</tbody>
</table>

| $21.35 | 0.17 | 49.5% | $128.00 | 17.7% |
| Cost PMPY | #Rx PMPY | Average Cost/Rx | TREND |
As shown in Exhibit 68, the primary use of these medications, by children, increased 10.7% in 2011. The largest increase in PMPY spending (22.5%) also occurred in the youngest age group, compared to a modest 0.6% increase in the oldest age group.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2010</th>
<th>2011</th>
<th>% Change in Utilization</th>
<th>% Change to PMPY Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.20</td>
<td>0.22</td>
<td>10.7%</td>
<td>22.5%</td>
</tr>
<tr>
<td>20-34</td>
<td>0.10</td>
<td>0.10</td>
<td>-0.3%</td>
<td>8.2%</td>
</tr>
<tr>
<td>35-64</td>
<td>0.08</td>
<td>0.08</td>
<td>3.7%</td>
<td>15.5%</td>
</tr>
<tr>
<td>65+</td>
<td>0.02</td>
<td>0.01</td>
<td>-39.3%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
Seizures

According to a study of seizure visits to U.S. emergency rooms, seizures — which strike approximately 11% of Americans at some point in life — account for about 1% (1 million) of emergency department visits annually. Although most medications in this class primarily are indicated for controlling seizures, many have additional indications for treating other conditions — such as Lyrica® (pregabalin), also used for fibromyalgia, and Topamax® (topiramate), also used for migraine headache.

For Medicaid clients, overall PMPY cost in the class increased 4.8%, to $19.10 in 2011; PMPY utilization increased 2.8%, to 0.37; and the average cost per prescription increased 2.0%, to $52.03. The generic fill rate (GFR) within this class was 94.0%, with generics occupying all positions in the top five drugs by market share. The top two drugs, gabapentin and clonazepam, had opposite cost-per-prescription trends. Gabapentin increased in both market share and cost per prescription (15.3%). Conversely, clonazepam, which lost market share, had a 3.3% decrease in the per prescription cost between 2010 and 2011.

Exhibit 69: Top 5 Medicaid Seizure Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>gabapentin</td>
<td>29.3%</td>
<td>31.5%</td>
<td>$42.46</td>
<td>$48.96</td>
<td>15.3%</td>
</tr>
<tr>
<td>clonazepam</td>
<td>23.2%</td>
<td>22.2%</td>
<td>$21.85</td>
<td>$21.13</td>
<td>-3.3%</td>
</tr>
<tr>
<td>topiramate</td>
<td>7.5%</td>
<td>8.1%</td>
<td>$40.44</td>
<td>$32.71</td>
<td>-19.1%</td>
</tr>
<tr>
<td>lamotrigine</td>
<td>6.9%</td>
<td>7.0%</td>
<td>$37.71</td>
<td>$26.15</td>
<td>-30.7%</td>
</tr>
<tr>
<td>levetiracetam</td>
<td>4.8%</td>
<td>5.3%</td>
<td>$82.67</td>
<td>$71.05</td>
<td>-14.1%</td>
</tr>
</tbody>
</table>

$19.10 Cost PMPY
0.37 #Rx PMPY
94.0% GFR
$52.03 Average Cost/Rx
4.8% TREND
Depression

In 2011, the Medicaid PMPY cost for antidepressants decreased 1.2%, to $13.73 (Exhibit 70). PMPY utilization had an increase of 2.0%, and the average cost per prescription decreased 3.2%, to $30.97. Most utilization within this class is from the generic selective serotonin reuptake inhibitors – citalopram, sertraline and fluoxetine. Market shares remained relatively constant between 2010 and 2011, but the generic fill rate (GFR) increased 2.1%, to 93.8% in 2011.

### Exhibit 70
Top 5 Medicaid Depression Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Market Share Trend</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
<td>2011</td>
</tr>
<tr>
<td>citalopram</td>
<td>21.0%</td>
<td>21.4%</td>
<td>$13.41</td>
<td>$13.98</td>
</tr>
<tr>
<td>sertraline</td>
<td>16.3%</td>
<td>16.2%</td>
<td>$18.55</td>
<td>$19.82</td>
</tr>
<tr>
<td>trazodone</td>
<td>15.6%</td>
<td>15.9%</td>
<td>$10.78</td>
<td>$11.39</td>
</tr>
<tr>
<td>fluoxetine</td>
<td>14.2%</td>
<td>13.4%</td>
<td>$14.79</td>
<td>$16.62</td>
</tr>
<tr>
<td>bupropion sustained release</td>
<td>5.8%</td>
<td>6.6%</td>
<td>$48.33</td>
<td>$46.35</td>
</tr>
</tbody>
</table>

| $13.73 | Cost PMPY |
| 0.44   | #Rx PMPY  |
| 93.8%  | GFR       |
| $30.97 | Average Cost/Rx |
| -1.2%  | TREND     |
**High Blood Pressure/Heart Disease**

The PMPY cost for high blood pressure/heart disease in 2011 was $11.08 (Exhibit 71). Each of the top three drugs, together accounting for 54.3% of market share, had decreases in the cost per prescription ranging from 14.0% to 22.2%. The generic fill rate (GFR) within this class was 96.1%, leading to a 12.7% decrease in average cost per prescription, to $15.97, in 2011.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>lisinopril</td>
<td>32.5%</td>
<td>32.1%</td>
<td>$10.73</td>
<td>$ 8.86</td>
<td>-17.5%</td>
</tr>
<tr>
<td>amlodipine</td>
<td>11.5%</td>
<td>12.4%</td>
<td>$15.56</td>
<td>$12.11</td>
<td>-22.2%</td>
</tr>
<tr>
<td>metoprolol tartrate</td>
<td>10.2%</td>
<td>9.8%</td>
<td>$ 9.93</td>
<td>$ 8.54</td>
<td>-14.0%</td>
</tr>
<tr>
<td>atenolol</td>
<td>9.3%</td>
<td>8.7%</td>
<td>$ 7.85</td>
<td>7.93</td>
<td>1.0%</td>
</tr>
<tr>
<td>lisinopril and hydrochlorothiazide</td>
<td>5.5%</td>
<td>5.8%</td>
<td>$12.34</td>
<td>$ 8.91</td>
<td>-27.8%</td>
</tr>
</tbody>
</table>

$11.08  
Cost PMPY  
0.69  
#Rx PMPY  
96.1%  
GFR  
$15.97  
Average Cost/Rx  
-15.1%  
TREND
Ulcer Disease

The significant, 14.5% decrease in overall spend within the ulcer therapy class – to $9.66 – (Exhibit 72) likely reflects the increasing use of generic medications. Most of the major drugs in the class are now generic. Omeprazole, the generic for Prilosec®, claimed almost 50% of the market share. The class generic fill rate (GFR) increased 3.7% in 2011, to 95.1%. PMPY utilization decreased 3.1%. The average Medicaid cost per prescription in the ulcer disease class decreased 11.4%, to $26.81.

Exhibit 72  Top 5 Medicaid Ulcer Disease Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>omeprazole</td>
<td>44.3%</td>
<td>49.6%</td>
<td>$24.87</td>
<td>$23.01</td>
<td>-7.5%</td>
</tr>
<tr>
<td>ranitidine</td>
<td>35.2%</td>
<td>31.6%</td>
<td>$15.43</td>
<td>$15.81</td>
<td>2.4%</td>
</tr>
<tr>
<td>famotidine</td>
<td>3.8%</td>
<td>3.9%</td>
<td>$17.33</td>
<td>$13.04</td>
<td>-24.8%</td>
</tr>
<tr>
<td>pantoprazole</td>
<td>2.8%</td>
<td>3.7%</td>
<td>$100.58</td>
<td>$25.48</td>
<td>-74.7%</td>
</tr>
<tr>
<td>lansoprazole</td>
<td>2.1%</td>
<td>3.3%</td>
<td>$95.98</td>
<td>$94.46</td>
<td>-1.6%</td>
</tr>
</tbody>
</table>

$9.66 Cost PMPY  0.36 #Rx PMPY  95.1% GFR  $26.81 Average Cost/Rx  -14.5% TREND
Medicaid Specialty Therapy Class Review

Although specialty medications represent only 0.7% of total prescriptions filled in Medicaid, they account for 21.7% of drug spend. In contrast to the traditional medications, in which lower-cost generics have slowed year-over-year growth in spend, the share of specialty trend covered under pharmacy benefits is expected to expand about 27% annually over the next three years.26

Among Express Scripts clients, almost 60% of Medicaid specialty pharmaceutical costs are in five of the top 10 specialty drug classes. Overall specialty spend increased 12.7% between 2010 and 2011 due to a 1.6% increase in utilization and a 11.0% increase in average cost per prescription (Exhibit 74). In 2011, total Medicaid PMPY cost for specialty medications was $106.08. Although most states require that generic alternatives be substituted for brand products when appropriate, generic specialty medications are not readily available in most specialty classes and many specialty drugs have few or no brand alternatives. As shown in Exhibit 73, PMPY specialty trend was greatest for Medicaid (12.7%), followed by TANF/ABD (10.0%).

Exhibit 75 details the top 10 specialty medications, which accounted for nearly 38.2% of overall Medicaid specialty spend in 2011. Medications used to treat HIV, inflammatory conditions and hepatitis C appeared most often on the top 10 Medicare specialty drug list. The top two drugs are used to treat HIV. Together, the $5.22 PMPY for Atripla® (efavirenz, emtricitabine and tenofovir) and $4.93 PMPY for Truvada® (emtricitabine and tenofovir) made up 9.6% of total specialty spend. Incivek®, a drug for hepatitis C that became available in 2011, was the sixth-most-expensive drug by PMPY cost ($3.92). Enoxaparin had the largest increase in PMPY cost among drugs available in 2010 and 2011. Available for only the latter half of 2010, enoxaparin’s 254.4% increase in utilization in 2011 accounted for most of the drug’s 256.8% increase in PMPY cost.

| PMPY Cost Trend for Specialty Therapy Classes by Medicaid Enrollee Type, 2010 and 2011 (Medicaid Prescription only) |
|---|---|---|
| CHIP | TANF/ABD | DE | Medicaid |
| $0 | $20 | $40 | $60 | $80 | $100 | $120 |
| -5.3% | 10.0% | 25.6% | 12.7% |

Exhibit 73
### Exhibit 74
Components and Drivers of Trend for the Top 10 Medicaid Specialty Therapy Classes, Ranked by 2011 PMPY Spend

<table>
<thead>
<tr>
<th>Rank</th>
<th>Therapy Class</th>
<th>PMPY Spend</th>
<th>% of Total Specialty Spend</th>
<th>PMPY $ Change from 2010</th>
<th>Utilization</th>
<th>Cost</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HIV</td>
<td>$22.62</td>
<td>21.3%</td>
<td>$1.47</td>
<td>1.6%</td>
<td>5.3%</td>
<td>7.0%</td>
</tr>
<tr>
<td>2</td>
<td>Hepatitis C</td>
<td>$11.41</td>
<td>10.8%</td>
<td>$3.40</td>
<td>-11.6%</td>
<td>54.0%</td>
<td>42.5%</td>
</tr>
<tr>
<td>3</td>
<td>Inflammatory Conditions</td>
<td>$10.94</td>
<td>10.3%</td>
<td>$1.83</td>
<td>10.9%</td>
<td>9.2%</td>
<td>20.1%</td>
</tr>
<tr>
<td>4</td>
<td>Cancer</td>
<td>$9.53</td>
<td>9.0%</td>
<td>$2.22</td>
<td>17.5%</td>
<td>12.9%</td>
<td>30.4%</td>
</tr>
<tr>
<td>5</td>
<td>Multiple Sclerosis</td>
<td>$8.81</td>
<td>8.3%</td>
<td>$1.44</td>
<td>3.6%</td>
<td>15.9%</td>
<td>19.5%</td>
</tr>
<tr>
<td>6</td>
<td>Hemophilia</td>
<td>$8.69</td>
<td>8.2%</td>
<td>$0.20</td>
<td>3.5%</td>
<td>-1.2%</td>
<td>2.3%</td>
</tr>
<tr>
<td>7</td>
<td>Pulmonary Hypertension</td>
<td>$4.92</td>
<td>4.6%</td>
<td>$0.04</td>
<td>-4.5%</td>
<td>5.4%</td>
<td>0.9%</td>
</tr>
<tr>
<td>8</td>
<td>Growth Deficiency</td>
<td>$4.70</td>
<td>4.4%</td>
<td>$0.15</td>
<td>0.3%</td>
<td>3.0%</td>
<td>3.3%</td>
</tr>
<tr>
<td>9</td>
<td>Anticoagulants</td>
<td>$4.50</td>
<td>4.2%</td>
<td>-$0.16</td>
<td>6.7%</td>
<td>-10.0%</td>
<td>-3.4%</td>
</tr>
<tr>
<td>10</td>
<td>Respiratory Syncytial Virus</td>
<td>$3.73</td>
<td>3.5%</td>
<td>-$0.22</td>
<td>-14.3%</td>
<td>8.7%</td>
<td>-5.6%</td>
</tr>
<tr>
<td></td>
<td>Prevention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Top 10</td>
<td></td>
<td>$89.85</td>
<td>84.7%</td>
<td>$10.38</td>
<td>2.2%</td>
<td>10.9%</td>
<td>13.1%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>$16.23</td>
<td>15.3%</td>
<td>$1.54</td>
<td>-0.4%</td>
<td>10.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>$106.08</td>
<td>100.0%</td>
<td>$11.91</td>
<td>1.6%</td>
<td>11.0%</td>
<td>12.7%</td>
</tr>
</tbody>
</table>
Exhibit 75: PMPY Cost for the Top 10 Medicaid Specialty Drugs, 2010 and 2011

- Atripla
- Truvada
- Humira
- Enbrel
- Pegasys
- Incivek
- Synagis
- enoxaparin
- Copaxone
- Reyataz

<table>
<thead>
<tr>
<th>Drug</th>
<th>2010 PMPY Cost</th>
<th>2011 PMPY Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atripla</td>
<td>$6.50</td>
<td>$6.00</td>
</tr>
<tr>
<td>Truvada</td>
<td>$5.90</td>
<td>$5.40</td>
</tr>
<tr>
<td>Humira</td>
<td>$4.80</td>
<td>$4.30</td>
</tr>
<tr>
<td>Enbrel</td>
<td>$4.20</td>
<td>$3.70</td>
</tr>
<tr>
<td>Pegasys</td>
<td>$3.80</td>
<td>$3.30</td>
</tr>
<tr>
<td>Incivek</td>
<td>$3.60</td>
<td>$3.10</td>
</tr>
<tr>
<td>Synagis</td>
<td>$2.90</td>
<td>$2.40</td>
</tr>
<tr>
<td>enoxaparin</td>
<td>$1.20</td>
<td>$1.70</td>
</tr>
<tr>
<td>Copaxone</td>
<td>$1.00</td>
<td>$0.50</td>
</tr>
<tr>
<td>Reyataz</td>
<td>$0.80</td>
<td>$0.30</td>
</tr>
</tbody>
</table>
**HIV**

The Centers for Disease Control and Prevention (CDC) estimates that about 1.2 million Americans are living with HIV and AIDS.\(^{27}\) Prevalence remained constant between 2006 and 2009.\(^{28}\) HIV medication regimens are both costly and complex, requiring intensive clinical monitoring. CuraScript\(^{®}\), the Express Scripts specialty pharmacy, offers an HIV specialty drug program to assist patients in obtaining, monitoring and adhering to HIV therapies.

In this report, we combine oral and injectable HIV medications into one class that is treated under specialty medications. The increased overall spend within the HIV therapy class of 7.0% in 2011 (Exhibit 76) was influenced by a 5.3% increase in cost per prescription and a 1.6% increase in utilization. Generic medications are not readily available for this class.

<table>
<thead>
<tr>
<th>Exhibit 76</th>
<th>Top 5 Medicaid HIV Drugs, Ranked by 2011 Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication</strong></td>
<td><strong>Market Share</strong></td>
</tr>
<tr>
<td>Truvada(^{®}) (emtricitabine and tenofovir)</td>
<td>16.8%</td>
</tr>
<tr>
<td>Norvir(^{®}) (ritonavir)</td>
<td>14.5%</td>
</tr>
<tr>
<td>Atripla(^{®}) (efavirenz, emtricitabine and tenofovir)</td>
<td>12.4%</td>
</tr>
<tr>
<td>Reyataz(^{®}) (atazanavir)</td>
<td>8.7%</td>
</tr>
<tr>
<td>Isentress(^{®}) (raltegravir)</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Total</strong></th>
<th><strong>Cost PMPY</strong></th>
<th><strong>Rx PMPY</strong></th>
<th><strong>GFR</strong></th>
<th><strong>Average Cost/Rx</strong></th>
<th><strong>TREND</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>$22.62</td>
<td>0.03</td>
<td>1.8%</td>
<td>$860.97</td>
<td>7.0%</td>
<td></td>
</tr>
</tbody>
</table>
Hepatitis C

Medicaid spend for the therapy class used to treat hepatitis C increased 42.5% (Exhibit 77), to $11.41 in 2011. Pegasys® (peginterferon alfa-2a), the top drug by market share, accounted for 39.2% of hepatitis C PMPY spend. Ribavirin®, Ribapak® and Ribasphere®, all forms of ribavirin, are used in combination with an interferon for the treatment of hepatitis C. Two new oral drugs, Incivek™ (telaprevir) and Victrelis™ (boceprevir), that were released in May represent a true breakthrough for patients with hepatitis C. Each of these drugs is used in combination with pegylated interferon and ribavarin, but they have different protocols: 12 weeks for Incivek; and 24, 32 or 44 weeks for Victrelis, depending on the patient’s response as therapy progresses.

Exhibit 77
Top 5 Medicaid Hepatitis C Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>Pegasys® (peginterferon alfa-2a)</td>
<td>41.2%</td>
<td>38.7%</td>
<td>$2,176.86</td>
</tr>
<tr>
<td>Ribavirin® (ribavirin)</td>
<td>33.1%</td>
<td>27.9%</td>
<td>$625.65</td>
</tr>
<tr>
<td>Ribapak® (ribavirin)</td>
<td>11.9%</td>
<td>13.6%</td>
<td>$1,089.51</td>
</tr>
<tr>
<td>Pegintron® Redipen® (peginterferon alfa-2b)</td>
<td>8.0%</td>
<td>6.4%</td>
<td>$2,189.18</td>
</tr>
<tr>
<td>Ribasphere® (ribavirin)</td>
<td>3.7%</td>
<td>5.2%</td>
<td>$644.12</td>
</tr>
</tbody>
</table>

$11.41
Cost PMPY
0.01
#Rx PMPY
46.6%
GFR
$2,336.47
Average Cost/Rx
42.5% TRENDS
**Inflammatory Conditions**

Inflammatory conditions — which include diseases such as rheumatoid arthritis (RA), psoriasis and Crohn’s disease — constituted the third-largest share of Medicaid PMPY spend among specialty classes in 2011. Spend for the class was up 20.1%, to $10.94 (Exhibit 78). Cost per prescription increased 9.2%, to $2,085.13. With no generics available in the class, the generic fill rate (GFR) was, of course, zero. Almost all utilization, which increased 10.9% in 2011, was for the top five drugs.

***Exhibit 78*** | Top 5 Medicaid Inflammatory Conditions Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Enbrel®</em> (etanercept)</td>
<td>46.7%</td>
<td>$1,808.50</td>
<td>6.3%</td>
</tr>
<tr>
<td><em>Humira®</em> (adalimumab)</td>
<td>44.4%</td>
<td>$1,855.43</td>
<td>10.7%</td>
</tr>
<tr>
<td><em>Remicade®</em> (infliximab)</td>
<td>3.1%</td>
<td>$3,396.58</td>
<td>-4.2%</td>
</tr>
<tr>
<td><em>Cimzia®</em> (certolizumab)</td>
<td>2.8%</td>
<td>$2,006.31</td>
<td>5.9%</td>
</tr>
<tr>
<td><em>Simponi®</em> (golimumab)</td>
<td>1.8%</td>
<td>$1,767.61</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

$10.94 Cost PMPY | 0.01 #Rx PMPY | 0.0% GFR | $2,085.13 Average Cost/Rx | 20.1% TREND
**Cancer**

The overall Medicaid cancer trend in 2011 was 30.4%, reflecting a 17.5% increase in utilization and an 12.9% increase in the cost per prescription (Exhibit 79). In 2011, the Government Accountability Office (GAO) reported that drug shortages, which have tripled since 2006, are particularly common for certain cancer drugs. Methotrexate, whose average cost per prescription decreased 12.8% in 2011, accounted for 16.6% of Medicaid cancer prescriptions. Gleevec® (imatinib) accounted for 16.2% of overall cancer spend and had 7.5% of the market share for Medicaid cancer drugs billed under the pharmacy benefit. The generic fill rate (GFR) for the class increased 4.3% in 2011, to 32.4%.

### Exhibit 79

Top 5 Medicaid Cancer Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>methotrexate</td>
<td>18.9%</td>
<td>16.6%</td>
<td>$12.82</td>
<td>$11.17</td>
<td>-12.8%</td>
</tr>
<tr>
<td>Lupron Depot® (leuprolide)</td>
<td>15.0%</td>
<td>11.7%</td>
<td>$968.96</td>
<td>$1,055.79</td>
<td>9.0%</td>
</tr>
<tr>
<td>Xeloda® (capecitabine)</td>
<td>9.7%</td>
<td>8.4%</td>
<td>$1,846.00</td>
<td>$2,091.73</td>
<td>13.3%</td>
</tr>
<tr>
<td>Temodar® (temozolomide)</td>
<td>10.4%</td>
<td>8.3%</td>
<td>$2,274.41</td>
<td>$2,261.81</td>
<td>-0.6%</td>
</tr>
<tr>
<td>Gleevec® (imatinib)</td>
<td>8.9%</td>
<td>7.5%</td>
<td>$4,469.61</td>
<td>$5,139.34</td>
<td>15.0%</td>
</tr>
</tbody>
</table>

| $9.53                      | 0.004             | 32.4%             | $2,376.88     | 30.4%         |
| Cost PMPY                  | #Rx PMPY          | GFR               | Average Cost/Rx | TREND         |
Multiple Sclerosis

The 2011 Medicaid PMPY trend for multiple sclerosis (MS) was 19.5%, reflecting a 15.9% increase in the cost per prescription and a 3.6% increase in PMPY utilization (Exhibit 80). Similar to the inflammatory conditions class, the MS class has no generic opportunities. The top five drugs accounted for 90.5% of MS drug utilization among Express Scripts Medicaid members in 2011. Every drug in the top five had a double-digit increase in the cost per prescription, resulting in costs ranging from about $3,000 to $3,600.

Exhibit 80  Top 5 Medicaid Multiple Sclerosis Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th>Medication</th>
<th>Market Share</th>
<th>Cost/Rx</th>
<th>Cost/Rx Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010</td>
<td>2011</td>
<td>2010</td>
</tr>
<tr>
<td>Copaxone® (glatiramer)</td>
<td>34.2%</td>
<td>32.3%</td>
<td>$2,994.71</td>
</tr>
<tr>
<td>Rebif® (interferon beta-1a)</td>
<td>24.1%</td>
<td>22.0%</td>
<td>$2,590.81</td>
</tr>
<tr>
<td>Avonex® (interferon beta-1a)</td>
<td>22.0%</td>
<td>21.2%</td>
<td>$2,686.98</td>
</tr>
<tr>
<td>Betaseron® (interferon beta-1b)</td>
<td>11.2%</td>
<td>9.4%</td>
<td>$2,673.53</td>
</tr>
<tr>
<td>Tysabri® (natalizumab)</td>
<td>4.7%</td>
<td>5.6%</td>
<td>$2,882.09</td>
</tr>
</tbody>
</table>

$8.81  Cost PMPY  0.003  #Rx PMPY  0.0%  GFR  $3,169.36  Average Cost/Rx  19.5%  TREND
Hemophilia

With annual per-patient treatment costs ranging from $60,000 to $150,000, hemophilia, a rare bleeding disorder, is one of the most expensive chronic diseases in the U.S. The overall Medicaid spend for hemophilia drugs in 2011 increased 2.3%, primarily due to a 3.5% increase in utilization (Exhibit 81). The average cost per prescription decreased 1.2%. All medications in this class are available only as brand.

Exhibit 81: Top 5 Medicaid Hemophilia Drugs, Ranked by 2011 Market Share
Pulmonary Hypertension

Although PMPY utilization for pulmonary hypertension drugs decreased 4.5% in 2011, the cost per prescription increased 5.4%, resulting in an overall 0.9% Medicaid trend for the class (Exhibit 82). The increased cost resulted largely from increases in the cost per prescription of Revatio® (sildenafil) and Adcirca® (tadalafil) of 14.4% and 12.6%, respectively. Among the top five drugs by 2011 market share, the two most-expensive drugs per prescription, Remodulin® (treprostinil) and Letairis® (ambrisentan), accounted for 27.3% and 19.9%, respectively, of overall PMPY Medicaid spend for the class.

Exhibit 82
Top 5 Medicaid Pulmonary Hypertension Drugs, Ranked by 2011 Market Share

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Revatio® (sildenafil)</td>
<td>49.5%</td>
<td>46.5%</td>
<td>$1,667.17</td>
<td>$1,907.14</td>
<td>14.4%</td>
</tr>
<tr>
<td>Adcirca® (tadalafil)</td>
<td>10.1%</td>
<td>15.1%</td>
<td>$1,045.10</td>
<td>$1,176.27</td>
<td>12.6%</td>
</tr>
<tr>
<td>Letairis® (ambrisentan)</td>
<td>12.1%</td>
<td>14.8%</td>
<td>$5,595.17</td>
<td>$5,814.86</td>
<td>3.9%</td>
</tr>
<tr>
<td>Tracleer® (bosentan)</td>
<td>15.7%</td>
<td>11.7%</td>
<td>$5,643.65</td>
<td>$5,490.23</td>
<td>-2.7%</td>
</tr>
<tr>
<td>Remodulin® (treprostinil)</td>
<td>6.4%</td>
<td>7.1%</td>
<td>$14,900.57</td>
<td>$16,559.30</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

| $4.92                      | 0.001               | 0.0%              | $4,302.56     | 0.9%          |
| Cost PMPY                  | #Rx PMPY            | GFR               | Average Cost/Rx | TREND         |
Growth Deficiency

Treatment for growth deficiency may be started when a child’s pituitary gland produces insufficient growth hormone resulting in short stature. The cause for this insufficiency is not well understood. A slight increase in utilization (0.3%) in 2011, along with a 3.0% increase in cost per prescription contributed to a Medicaid PMPY spend of $4.70 for this therapy class and a 3.3% cost trend (Exhibit 83). All medications in this class are available only as brand.
Looking Ahead

Looking ahead, the Patient Protection and Affordable Care Act (PPACA) will increase the number of Americans eligible for Medicaid. States and their Medicaid managed care organizations (MMCOs) will need to carefully evaluate how to integrate these new lives into the program as well as the impact on their overall expenditures.

Over the past 12 years, MMCOs working together with Express Scripts have provided their Medicaid members better care with less waste. Our proven, innovative approaches help Medicaid sponsors improve medication adherence, optimize drug mix and ensure safety. Through distribution channel management and continued emphasis on the use of generic medications, Express Scripts can help maximize Medicaid savings.
Appendices

Appendix 1: Methods for Calculating the Proportion of Adherence Waste

POTENTIAL SAVINGS FROM OPTIMIZING CHANNEL: We estimated the impact of moving all maintenance prescriptions currently dispensed in retail pharmacies to home delivery at the highest clinically appropriate and practical rate. The direct effect of this movement is reductions in both unit cost and dispensing fee. However, because generic fill rate (GFR) and adherence are higher in home delivery than in retail, we accounted for these effects as well. For the drug-mix component, we determined the savings associated with moving from the current GFR to the clinical maximum GFR separately for each therapy class. The savings associated with increased GFR reflect the average unit-cost savings from generic use in home delivery over branded use. For the adherence component of channel waste, we analyzed peer-reviewed scientific literature to determine nationally representative differences in adherence for diabetes, high blood pressure/heart disease and high blood cholesterol medications between home delivery and retail for members in managed pharmacy benefits.1

Based on these differences, we estimated the savings for total healthcare costs. Estimates from the literature were selected for their rigorous methodology, accounting for adjusted member-level differences from dispensing channels. The number of potential home-delivery users was estimated using 2011 (projected) U.S. census population estimates, state-level disease-prevalence estimates from the U.S. Centers for Disease Control and Prevention (CDC) and home-delivery penetration rates estimated using Express Scripts claims data. Next, the estimated savings were applied to each potential home-delivery user in the U.S. with one of the three conditions studied using the optimal home-delivery penetration rate to obtain total channel savings from better adherence in home delivery.2,3,4

POTENTIAL SAVINGS FROM OPTIMIZING DRUG MIX: For the remainder of appropriate retail prescriptions, we then estimated the impact of moving brand-name prescriptions to generic, when possible, to the maximum extent by applying the average unit savings from generic use over brand-name use to all eligible brand-name prescriptions. The mix waste associated with maximizing home delivery was not included in this calculation, thus avoiding double-counting.

POTENTIAL SAVINGS FROM OPTIMIZING ADHERENCE: To calculate the savings from improvements in adherence, we modeled an estimate using literature sources, maximum national nonadherence-related savings (using 2010 U.S. Census figures), state-level disease-prevalence numbers from the CDC and national population insurance rates. To make our estimates more conservative, we calculated overlapping savings from patients taking medications for more than one condition at the lowest savings rate. To avoid double-counting, we deducted the savings that would be obtained by maximizing the use of home delivery.

Prescription-drug use for a random sample of approximately four million members who had prescription-drug coverage in 2010 or 2011 was analyzed for the 2011 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; they used CuraScript®, the Express Scripts specialty pharmacy, for specialty drug prescriptions. To allow for varying benefit structures and adjust for differential home-delivery usage rates, prescription counts were converted to equivalent quantities that would have been dispensed through retail pharmacies. Each year (2010 and 2011) was sampled independently to ensure a representative and realistic view of the members covered each year. Therefore, the data for the two years taken together include some members who were covered in both years and some who were covered in only one of the two years.

Nonprescription medications (except diabetic supplies) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings were 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 this volume.

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

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. 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.

Generic fill rate (GFR) was determined by dividing the total number of 30-day adjusted generic prescriptions by the total number of 30-day adjusted prescriptions.

Please Note: Although up to nine decimal points were allowed in making all calculations, in most cases the results were rounded down to one or two decimals for easier reading. Therefore, dollar and percentage calculations may be slightly off due to rounding.

Prescription-drug use for a random sample of approximately 1.02 million Medicare members, 390,000 Medicare Employer Group Waiver Plan (EGWP) members, and 2.65 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 2011 was analyzed for the 2011 Drug Trend Report Medicare and Medicaid section. 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 dispensed in hospitals, long-term care facilities and other institutional settings were not included in this analysis.

Cost includes ingredient costs, dispensing fees and taxes. Rebates and administrative fees are not a component of cost. Cost was determined on a per-member-per-year (PMPY) basis and was calculated by dividing the total cost 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. Average cost per prescription was calculated by dividing the total cost by the total number of 30-day adjusted prescriptions.

Utilization was determined on a PMPY basis. It was calculated by dividing the total number of 30-day adjusted prescriptions by the total number of member-years. The average number of prescriptions per member per year is the total number of 30-day adjusted prescriptions divided by the total number of member-years.

Generic fill rate (GFR) was determined by dividing the total number of 30-day adjusted generic prescriptions by the total number of 30-day adjusted prescriptions.

Generic cost and brand cost were estimated on a PMPY basis. Generic cost was calculated by dividing the total generic cost by the total number of member-years. Similarly, brand cost was calculated by dividing the total brand cost by the total number of member-years. Generic cost per prescription was calculated by dividing the total generic cost by the total number of 30-day adjusted generic prescriptions. Brand cost per prescription was calculated by dividing the total brand cost by the total number of 30-day adjusted brand prescriptions.

Market share was estimated based on percentage of the total 30-day adjusted prescriptions for each drug divided by the total number of 30-day adjusted prescriptions of all drugs within the therapy class.

Please Note: Although up to nine decimal points were allowed in making all calculations, in most cases the results were rounded down to one or two decimals for easier reading. Therefore, dollar and percentage calculations may be slightly off due to rounding.
INTRODUCTION


3. This will apply to adults as well on January 1, 2014.


7. Express Scripts analysis of 2010 MarketScan® commercial data.

8. Express Scripts analysis.


23. Cozaar® (losartan) and Hyzaar® (losartan and hydrochlorothiazide) lost patent protection in April 2010.


33. Express Scripts analysis.
42. Participants included only members who had provided individual consent to participate in the survey and for whom pharmacy benefits were covered by plan sponsors who had provided authorization for their members to be contacted for the survey. Study respondents = 1,514.
47. Express Scripts Research, 2011.
49. Express Scripts PharmacoAnalytics.
50. Express Scripts PharmacoAnalytics.
51. Express Scripts PharmacoAnalytics.
55. Prescription count is estimated by normalizing each prescription fill to a 30-day supply.
TREND OVERVIEW
2. 2010 is the latest full year for which MarketScan data are available.

THERAPY CLASS REVIEW
2. Intensity increases as adherence increases; thus, a negative intensity trend is undesirable in classes for which adherence is important. This applies to all therapy classes.
3. Nonadherent to therapy: patients with MPR less than 80% during 2011. This applies to all therapy classes.


21. Intensity increases as adherence increases; thus, a negative intensity trend is undesirable in classes for which adherence is important. This applies to all therapy classes.

22. Nonadherent to therapy: patients with MPR less than 80% during 2011. This applies to all therapy classes.


**MEDICARE**


8. Calculated based on CMS guidance to simulate the Acumen calculation.


**MEDICAID**


APPENDICES


The authors would like to thank the many individuals throughout the Express Scripts organization who contributed time and expertise toward the 2011 Drug Trend Report.
Express Scripts is committed to following, promoting and implementing sustainable practices. We apply global sustainability principles to the way we do business and the way we fulfill the needs of clients, patients and employees. Express Scripts is committed to proactively balancing economic development with environmental stewardship and social development, and operates its business in a manner that respects the environment and conserves natural resources.

We uphold our commitment to environmental stewardship by printing this report using solvent-free inks on papers that are certified by the Forest Stewardship Council™ (FSC®). The interior of this publication was printed on stock that has 30% post-consumer waste content, and was produced by a certified Sustainable Green Printing (SGP) facility. The electricity used to produce this book has been offset 100% with Missouri wind energy credits procured from the Ameren Missouri Pure Power program.

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