TrendsRx® Report

2007

CVS CAREMARK | CAREMARK®

TrendsRx® Report 2007

Controlling Cost, Delivering Value, Transforming Care

In this, the 2007 TrendsRx® Report, we address you as part of a new organization—**CVS Caremark Corporation**. Our recent merger brings exciting possibilities and new opportunities to impact pharmacy services and improve the value we provide to you, our pharmacy benefit management (PBM) clients. In an environment ever more conscious of the importance of the pharmacy benefit to health and healthcare cost management, our new company is uniquely positioned to serve our PBM customers. As part of CVS Caremark Corporation, Caremark will strive to deliver **more cost-effective management** for payors; **provide greater access**, **information and choice** to consumers; and improve the quality and safety of **total healthcare**. We'll share more about this new vision with you in the pages that follow.

Herein, we also provide an in-depth look at the factors that drove pharmacy trend in 2006 and preview factors that will affect trend in 2007. Notably, in 2006 we marked our **fourth straight year of single-digit Book of Business (BOB) pharmacy benefit gross trend**. At 5.2 percent per member per year (PMPY), our 2006 trend declined by well over 2 percent from our 2005 number.

2006 Caremark Book of Business Gross Trend:

5.2% PMPY

Our clients made good use of Caremark programs that promoted last year's **blockbuster generic launches**. The BOB generic dispensing rate increased throughout the year. Overall, generics reduced our BOB spend by more than 33 percent in 2006. This year's report includes detailed reporting on generics and the strategies that will help you take advantage of coming launches.

Our role as your pharmacy benefit manager is to support the optimal use of prescription drug therapies to:

- Help you control growth of drug spend
- Improve outcomes in your covered population
- Reduce your total healthcare cost

Specialty pharmaceuticals continue to play a significant role in drug spending growth. The sector's rate of growth has slowed, although it still outpaces the rest of the market. See pages 27–34 to learn more about developments in specialty pharmaceuticals in 2006, as well as our projections for the next 18 months.

The implementation of the **Medicare drug benefit** in 2006 made prescription drugs more affordable for millions of Americans. In many ways, the benefit also accelerated drug price consciousness and visibility in America, while highlighting the essential role pharmaceuticals play in the health and well-being of so many citizens.

For many Americans, pharmaceuticals and healthcare—their costs and the value received—remain top concerns despite recent slower rates of growth. Leaders of business and industry, health plans and government believe that **changing consumer health behaviors** is the key to taming cost growth. Pharmacy benefit management and pharmacy services will have crucial roles to play in the coming years in this transformation of the healthcare environment. At CVS Caremark, we look forward to working with you, the clinical community, and your plan participants and members to optimize the use of pharmaceuticals and healthcare services, thereby improving outcomes and maximizing the value of your healthcare investment.

Caremark BOB gross trend is the percentage change in gross drug spend year over year. It measures the components of gross cost change in price, drug mix and utilization over the previous year. Gross trend reflects total prescription cost, including both plan participant and payor portions. Trend is reported on a per member per year (PMPY) basis. All 2006 trend calculations are based on a *trend cohort group* which includes funded clients with integrated (mail and retail) benefit plans with claims from January 1, 2005 through December 31, 2006 (24 months of claims). Average eligibility must be within +/-15 percent period over period. Trend cohort group excludes Puerto Rico, Virgin Islands and Guam clients, and does not include Medicare Part D members. Gross trend calculations do not take into account projections related to the retiree drug subsidy, which will affect net trend for many of our clients. Calculations for trend without specialty pharmaceuticals exclude the Universal Specialty Drug List. 2007 BOB data, where cited, include Caremark and PharmaCare clients and Medicare Part D plans.

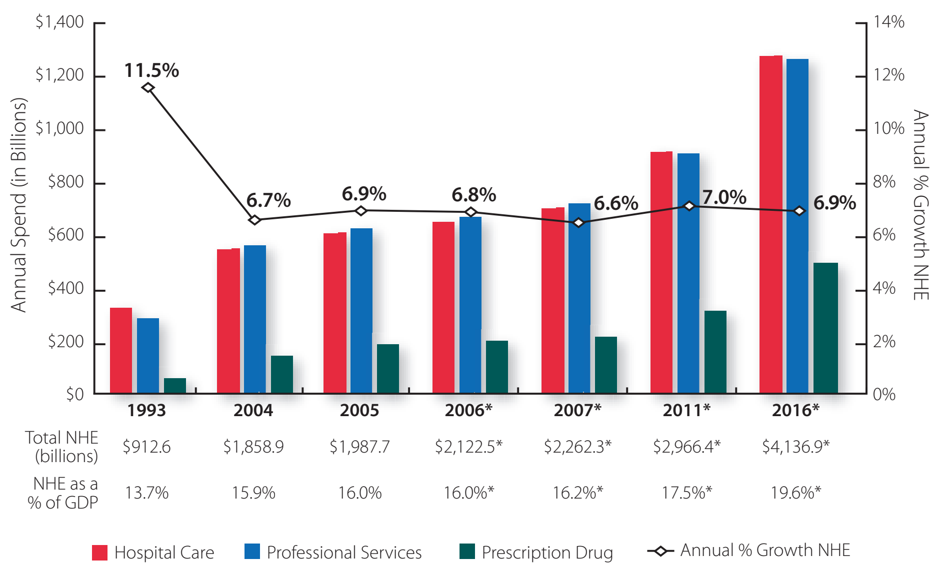
A New Approach to Care and Cost

There's no question that the United States devotes enormous resources to our healthcare system. The Centers for Medicare and Medicaid Services (CMS) estimate that **national health expenditures (NHE)** in 2006 exceeded $2.1 trillion and accounted for 16 percent of our gross domestic product (GDP). Per capita spending was just over $7,000. By 2016, the agency expects that the United States will spend more than $4 trillion on healthcare and that the sector will account for just less than 20 percent of GDP.[1]

Despite the magnitude of this investment, there is broad dissatisfaction. Payors recognize that current levels of **cost growth** are unsustainable, quality of care is inconsistent and access to care is an issue for tens of millions of Americans. **Healthcare coverage and costs** are the top domestic issue among consumers according to a recent Kaiser Family Foundation survey.[2] By and large, consumers experience the system as complex, impersonal, disconnected, reactive, and increasingly unaffordable.

Figure 1

CMS estimates that national health expenditures will exceed $4 trillion by 2016 and account for nearly 20% of gross domestic product.



* Projected

Source: "Health Spending Projections Through 2016: Modest Changes Obscure Part D's Impact," *Health Affairs*, February 2007. Data source: National Health Statistics Group, Office of the Actuary, Centers for Medicare and Medicaid Services; and U.S. Department of Commerce, Bureau of Economic Analysis and Bureau of the Census. Selected NHE components shown.

Market efforts have focused primarily on the "system" of healthcare, such as through vendor negotiations and efficient purchasing. Yet, at its core, healthcare happens between a patient and a provider.

Hewitt, The Road Ahead: Emerging Health Trends 2007

Prescription Drug Spending

Prescription therapies, of course, are a key factor in healthcare costs. In 2006, CMS estimated that prescription drug spending totaled approximately $214 billion, just under **10 percent of NHE**.[3] The prescription benefit is the healthcare benefit most used by consumers. In 2006, the average number of retail prescriptions per capita was 12.4. Fifty-nine percent of the population under 65 had a prescription drug expense in 2004, while 92 percent of those 65 and older had such an expense.[4]

Used appropriately, prescription drugs **reduce the incidence of complications** and delay or prevent the need for costly hospital, emergency and long-term care for people with conditions such as heart disease, asthma, AIDS, and diabetes. Additionally, these medications can **improve the quality of health and life** for individuals with cancer, rheumatoid arthritis, multiple sclerosis, schizophrenia, and depression, as well as many other conditions.

Less than 10 years ago, prescription drug spending was growing at double-digit rates. That rate of growth has slowed—largely through **more effective use of prescription benefit management programs** and strategies such as tiered co-payments, promotion of generic drugs when appropriate and utilization management.

Pharmaceutical breakthroughs that involve a precise diagnosis of a disease and an effective therapy save the system a tremendous amount of money even though the drugs may appear to be high-cost.

Clayton Christensen, professor
Harvard Business School, quoted in the
New York Times, December 31, 2006.

The Opportunity Ahead

As the **largest provider of pharmacy services** in the country, CVS Caremark plays a crucial role and has a critical opportunity to optimize our clients' investment in prescription therapies. As a key link in prescription benefit management, Caremark addresses both clinical and economic goals for our clients. Additionally, we are in contact with all stakeholders: consumers, pharmacists, physicians, and payors. **CVS** has the largest number of retail pharmacies in the country, a growing number of which contain on-site health clinics staffed by nurse practitioners—a delivery model with the potential to make care more convenient and reduce overall costs for consumers. In evaluating the potential contribution of our new organization, **Caremark** reviewed research about prescription utilization and disease incidence and found that:

- One in every four individuals at **risk for a chronic condition** such as hypertension is unaware of his or her risk. Individuals with diabetes may go as long as 12 years before the condition is diagnosed. Without treatment, these individuals can incur irreversible damage to their cardiovascular system.
- Of those who are diagnosed, we estimate that one in three **doesn't fill the prescription** received from his or her doctor.
- Of those who do fill the initial prescription, one in two **stops filling his or her prescription** within six months.
- Overall, our analysis indicates that as few as one of the four at-risk individuals (25 percent) is aware of his or her condition, receives a prescription early in the course of the disease and is **compliant with the medication prescribed**. However, among the 25 percent who have

begun and maintained appropriate treatment, some will be unaware of potential interactions with other medications or supplements or may otherwise compromise the efficacy of their treatment. Such lapses may be due to a lack of targeted education and counseling, low levels of health literacy, or other factors. Regardless of the cause, these individuals **may not be achieving the full benefits of appropriate condition management**.

Figure 2

Source: Caremark data combined with third-party references including the United States Census, Centers for Medicare and Medicaid Services (CMS), the World Health Organization (WHO) among others. Compiled by Jan Berger, M.D., Chief Clinical Officer, Caremark.

Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.

World Health Organization's 2003 Special Report, "Adherence to Long-Term Therapies: Evidence for Action."

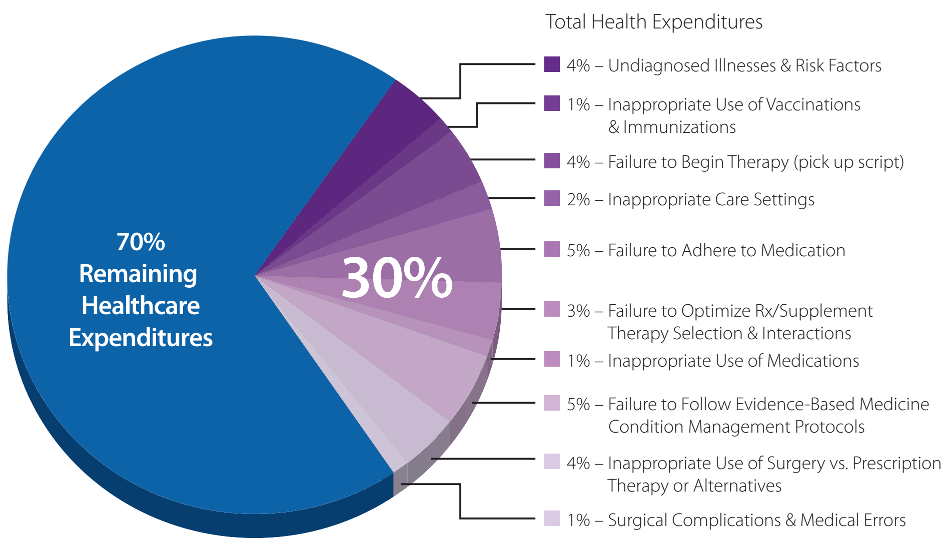
The 30% Goal

If fewer than one in four at-risk individuals is achieving the full benefits of appropriate condition management, the inevitable question is **'what is the cost, not only to the individual, but to the healthcare system as a whole?** And further, how much might all of us benefit from closing even some of those gaps?'

For the **individual consumer**, the opportunity is greater convenience, more personalized care and greater connection between the various parts of the system—physician, pharmacist and benefit provider—allowing a better healthcare experience, improved outcomes and lower costs.

Figure 3

We estimate that 30% of current healthcare expenditures could be eliminated through optimal prescription therapies.



Sources: Caremark data combined with third-party references including the United States Census, Centers for Medicare and Medicaid Services (CMS), the World Health Organization (WHO) among others. Compiled by Jack Bruner, FSA, Caremark.

As shown in the accompanying chart, Caremark has considered this question carefully. Our analysis leads to the estimate that, with consistent use of effective prevention, early intervention and adherence strategies, **30 percent of current healthcare expenditures** could be eliminated. The means to reach such a goal are varied and not necessarily complex in concept. They include increasing consumers' disease awareness through health risk assessments, supporting early diagnosis and treatment, as well as the appropriate use of vaccines and immunizations, helping people avoid the emergency room, providing counseling and monitoring to avert adverse drug events, and following the guidelines of evidence-based medicine—essentially doing what we know works.

Caremark is uniquely positioned to have a fundamental impact on the lives of those we serve by working to close the "gaps" and help the system and individuals do what works. We can accomplish this with a combination of world-class healthcare services integrated with industry-leading pharmacy services and consumer-focused health advocacy. The vision for our new organization includes providing:

- **Unprecedented consumer access**. With more than 6,200 locations and multiple touch points, we can interact with consumers face-to-face, by phone, over the Internet, or by mail—based on their preferences.

- **A patient-focused view**. Integrated services will allow the aggregation of information to provide a single view of consumers no matter where they enter the system, allowing us to personalize communications sharing savings opportunities, health improvement strategies and safety messaging.*
- **Point-of-care connectivity**. Our ePrescribing capabilities bring physicians information on their patients' prescription history—including whether previous scripts were filled—and formulary and benefit strategies at point-of-prescribing. At the pharmacy counter, we provide dispensing pharmacists information on benefit designs, formulary and therapeutic alternatives on a real-time basis.
- **Personalized health advocacy**. Importantly, with the alignment of these capabilities, we will be able to offer personalized counseling on prescription-related and other health behaviors though a variety of outreach media, including face-to-face counseling from a pharmacist or nurse practitioner—two of the most trusted health advisors according to numerous consumer surveys. Moreover, we provide a point of entry for disease management programs, health assessments and other services that will make the healthcare experience less disconnected and impersonal for the consumer.

For the **benefit provider**, the opportunity is better generic utilization and formulary compliance, improved adherence, fewer adverse drug events, better outcomes, lower costs, and improved employee/member satisfaction.

Figure 4

Balanced Health Scorecard
High Performance Results and Priorities

Cost Efficiencies	Health Value
• Higher generic substitution rate	• Proactive compliance and adherence interventions
• Greater formulary compliance	• Consistent delivery of quality care
• Accessible evidence-based care at lower cost	• Reduced incidence of medication-related adverse events
• Consumer education and counseling	• Improved consumer awareness and rates of diagnosis
Consumer Support	**Operational Excellence**
• Face-to-face counseling	• Retail/mail choice enhancements
• Increased access for interactions with pharmacist	• Personal health record database
• Personalized multi-channel communications	• Enhanced connectivity across all healthcare constituents
• Decision-making aids with aligned incentives	• Personalized feedback systems

*Any sharing of personally identifiable information will be done in accordance with contractual obligations, HIPAA and other applicable privacy laws.

A New Approach

CVS Caremark is committed to **creating flexible solutions** to meet each client's unique needs and goals, and we recognize that performance in any business environment is determined by more than financials. We developed the Balanced Health Scorecard (see page 7, based on concepts originally published in the *Harvard Business Review*) to reflect the broad key areas in healthcare where clients need to balance their specific value strategies. We're targeting immediate, near-term and long-term priorities to drive lower costs, desired consumer behaviors, improved health value, and overall operational excellence. Some of the initiatives under consideration include:

- **Optimized core pharmacy services**. Flexible prescription fulfillment, improved therapeutic interchanges and optimal use of cost-effective alternatives
- **Improved access, greater convenience**. Web ordering; retail, mail and specialty pharmacy fulfillment; a choice of counseling venues: face-to-face, telephonic, Web—in sum, "making it easier" for consumers
- **Data integration/mining**. Supporting risk identification and improved compliance and adherence

Our goal is to make healthcare simpler, more personal, affordable, proactive, and connected.

Meaningful Change, One Person at a Time

We believe our new organization is ready to lead a needed change in healthcare. CVS Caremark will become **the easiest, most effective and most accessible healthcare entity** for consumers. As trusted advisors with access to integrated data, our clinicians will provide the support consumers need to make positive behavioral changes that will favorably impact their health outcomes and overall costs. We look forward to leading the change with—and for—you.

Single-Digit Trend Continues in 2006: Making the Most of Market Opportunities

5.2% PMPY Book of Business Gross Trend

The Caremark BOB posted its **fourth straight year of single-digit prescription drug trend** in 2006. Growth in spending declined by well over 2 percent—from 7.9 percent in 2005 to 5.2 percent per member per year (PMPY). At 4.0 percent, price (average cost per unit) was the major driver of prescription drug trend in 2006. The **price of brand name drugs**, on average, increased at a rate three times greater than the consumer price index in 2006—the **highest increase since 2002**.

During the same time period, **prices for generic drugs decreased**, on average, by 1.2 percent. Generics were a major factor in inhibiting drug trend in 2006. Caremark clients took advantage of our consumer-focused generic initiatives and careful plan design to make the most of a wave of **new generic opportunities**. Strength in generics and a **scarcity of high-impact new drugs** helped to limit the impact of product mix as a trend driver to 0.5 percent.

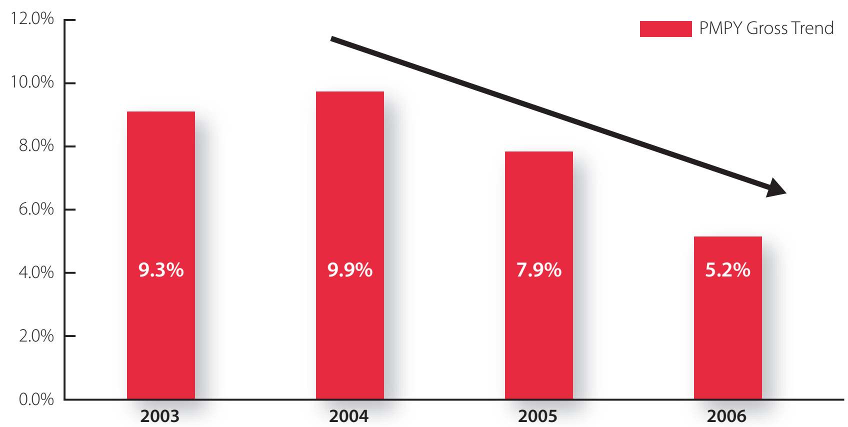
Our 2006 BOB **utilization** trend, calculated as days' supply per member per month, was 0.7 percent. This is a significant drop from the 2005 utilization trend figure of 4.1 percent. Utilization management, ongoing safety concerns and the lack of high-performing new brands helped slow growth in utilization.

2006 Caremark Book of Business Gross Trend without Specialty Pharmacy: 4.3% PMPY

Specialty pharmaceuticals continue to play a significant role in drug spending growth. See page 27 for specialty pharmaceuticals trend and spend.

Figure 5

Caremark maintains single-digit trend in 2006.



Source: 2003, 2004, 2005, 2006 BOB data Caremark BOB trend cohort, including specialty pharmaceuticals. 2006 trend does not include Medicare Part D plans. January 2007, Industry Analytics.

Figure 6

Caremark management strategies effectively emphasize preventive care and management of chronic conditions.

Trend Impact: 0.6% Acute or Life-saving	Trend Impact: 3.4% Chronic, Preventative, Maintenance or Symptomatic
Cancer treatments, Infections, HIV, Hepatitis	Cardiovascular diseases, Neurologic disorders, Asthma, Neurologic disorders, Arthritis, Osteoporosis, Depression, Diabetes, Hemophilia
Trend Impact: 0.1% **Lifestyle or Cosmetic**	**Trend Impact: 1.1%** **Potential for Over-utilization**
De-pigmentation and Acne, Fertility, Male pattern baldness, Smoking cessation, Weight management, Age-related wrinkles, Sexual dysfunction	Growth hormones, Narcotic analgesics, ADHD treatment, Sleep aids, Heartburn

Source: Caremark 2006 Book of Business, February 2007, Industry Analytics. Category lists are representative, not inclusive.

Optimizing the Value of the Prescription Benefit

Today's pharmacy benefit is finely tuned to focus on optimizing access to **therapies that improve health, save lives and substantially improve quality of life**—the treatment categories represented in the top two quadrants of the accompanying table (above). These two quadrants account for the major portion of our 2006 gross trend—4 percent of the total 5.2 percent. Appropriate management strategies for these categories drive adherence to treatment guidelines and medications with the goal of improving total health and preventing disease progression.

Therapies in the lower two quadrants account for the remaining 1.2 percent. These categories are generally considered in the healthcare industry as either non-essential to health status or as having overuse or abuse potential. For these categories, in our BOB, clients have chosen to focus on tools that ensure that **the right person receives the right drug** and maintains therapy for an appropriate duration. Such careful management of utilization helps to control drug trend and spend, as well as overall healthcare costs while supporting better outcomes in the covered population.

What Drove Pharmacy Trend in 2006?

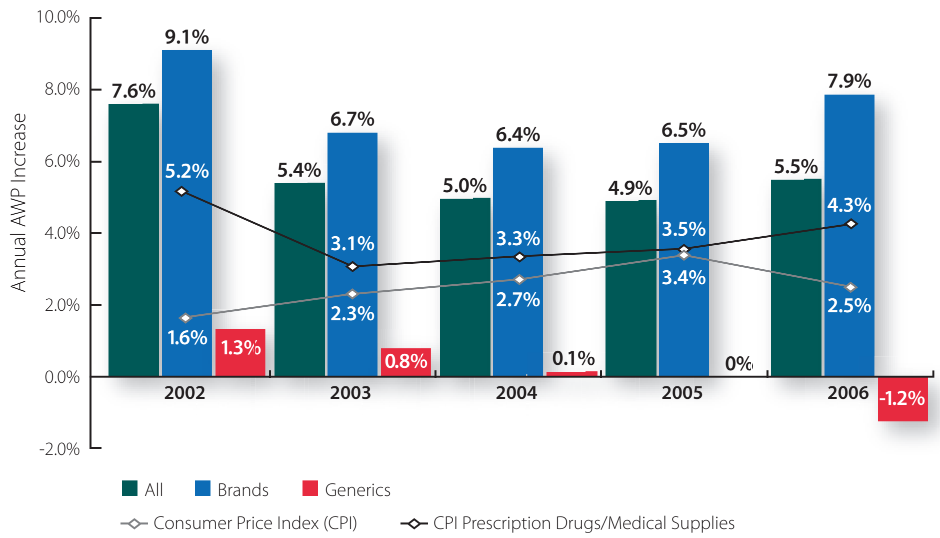
Price 4.0%

Price (average cost per unit) was the major driver of prescription drug trend in 2006. In evaluating price as a driver, Caremark analysts consider both average wholesale price (AWP) inflation and contract pricing. The price of **brand name drugs**, on average, increased at the highest rate since 2002—7.9 percent. During the same time period, **prices for generic drugs decreased**, on average, by 1.2 percent.

For several years, overall AWP inflation has consistently and significantly outpaced the "market basket" consumer price index (CPI). However, the Bureau of Labor Statistics also indexes **consumer prices for medical care**—prescription drugs, medical supplies, physician and hospital services, and related expenses. The CPI for the medical care category has consistently been higher than that for the overall market basket.

Figure 7

AWP Inflation: Brands outpace CPI, but generics decrease in price.



Source: AWP data from First Data Bank and Medispan. Consumer price index from Bureau of Labor Statistics, "Consumer Price Index: December 2006." *News*, United States Department of Labor, January 18, 2007. Caremark Internal Analysis.

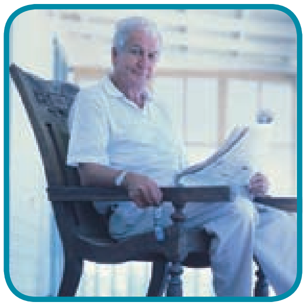
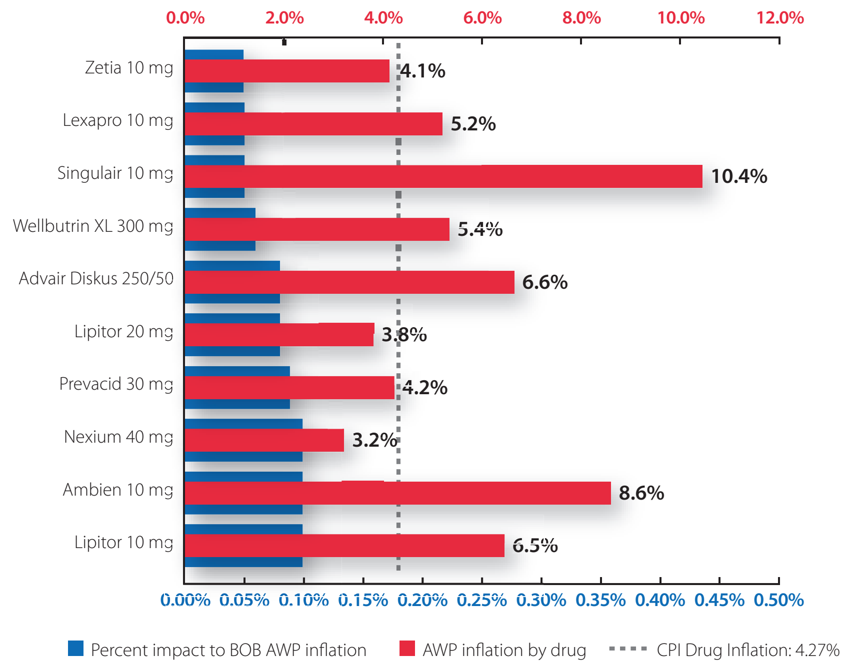


Figure 8

Price as Trend Driver: 10 drugs with highest AWP inflation significantly impact BOB AWP inflation.



Source: Caremark BOB data, Industry Analytics.

The accompanying chart demonstrates the impact just a few drugs can have on overall trend. The 10 drugs shown contributed 0.8 percent to the 5.5 percent AWP inflation. Of these, Singulair (the 13th most utilized drug for 2006) shows the largest year-over-year increase in AWP, with 10.4 percent. The resulting contribution to Caremark overall AWP inflation for this drug was 0.05 percent. Note that two category leaders for asthma—**Singulair and Advair Diskus**—are in the top 10 for AWP increases. The antiasthmatic category posted double-digit trend in 2006—growth in utilization of the category is also related to increasing disease incidence and changing treatment guidelines. Singulair, originally indicated for asthma alone, has received additional indications (e.g., allergy) and has posted high trend for several years.

Cholesterol leader Lipitor, the world's most utilized drug, experienced a more modest increase in AWP, but contributed a larger share of the BOB AWP inflation, close to 0.20 percent for the two dosage forms.

Of the 10 drugs shown, five—including the two forms of Lipitor, Ambien, Prevacid, and Wellbutrin XL—are expected to have **generic equivalents by 2010**. Price increases are not uncommon before a drug loses its patent protection as manufacturers attempt to capitalize on market exclusivity while it lasts.

Product Mix: 0.5%

Product mix evaluates the **impact of new products and changes in the balance between generics and brands, and between more expensive and less expensive drugs in a category**. As a driver, product mix was favorably impacted in 2006 by a number of significant generic launches. Moreover, new drug approvals continued to stall. The U.S. Food and Drug Administration (FDA) approved 18 new molecular entities (NMEs) in 2006, the same number as the previous year. In contrast, 31 NMEs were approved in 2004. Moreover, few new brand launches have proven to be blockbusters. Continuing a trend from the last few years, new biotech/specialty products figured prominently among the top performing launches in 2006.

In 2006, some of the major influencers of product mix included:

- ↓ Launches of generic alternatives in top categories
- ↓ Ongoing scarcity of new blockbuster brand drugs
- ↑ New specialty products on the market
- ↑ Direct-to-Consumer (DTC) advertising

Over the past several years, large increases in the percentage of generic prescriptions dispensed were a major contributor to the decelerating drug spending growth rates.

John A. Poisal, et al. Health Spending Projections Through 2016...*Health Affairs*, February 2007.

Figure 9

How New Brand Drugs and Generics Impacted Trend in 2006

New Product Impact	Average Gross Cost per Day	% BOB Gross Cost	Gross PMPM Trend Impact
2004- 2006 New Brands Antiasthmatics, Anticonvulsants, Antidepressants, Antidiabetics, Antihyperlipidemics, Antineoplastics, Antivirals, Endocrine, Hypnotics, Psychotherapeutic and Neurological Agents	$4.14	5.2%	**3.3%**
2004- 2006 New Generics Analgesics and Anesthetics, Cardiovascular Agents, Central Nervous System Drugs, Endocrine and Metabolic Drugs, Neuromuscular Drugs, Respiratory Agents	$2.31	5.5%	**- 1.7%**

Source: Industry Analytics

Figure 10

2006 Major Brand Drug Launches

Drug Name	Use
Exubera	Inhaled insulin for diabetes
Dacogen	MDS (myelodysplastic syndromes—a collection of disorders relating to the bone marrow)
Chantix	Smoking cessation
Gardasil	Human papilloma virus (HPV) vaccine
Januvia	Diabetes

2007 YTD Launches

Drug Name	Use	Market Outlook for Peak Sales
Invega	Schizophrenia	$1B US
Tekturna	Hypertension	$1.7B US
Veramyst	Allergic rhinitis	$750M US

Figure 11

Brand Drugs Pending 2007 Approval

Drug name	Use	Market Outlook for Peak Sales
Arxxant	Diabetes-related nephropathy and retinopathy, including macular edema	$1B global
Sulodexide	Diabetes-realted nephropathy	$1B US
Neramexane	Alzheimer's disease	$750M US
Asoprisnil	Endometriosis and menopausal syndrome	$700M US
Galvus	Type 2 diabetes	$1B global
Xaliproden	Alzheimer's disease	$1B global
Cervarix	Prevention of cervical cancer caused by human papilloma virus (HPV)	$4B global

Forecast References: Ixis Securities "Pharmaceutical Sector Report", S.G. Cowen "Therapeutic Categories Outlook", Equity Research, Credit Suisse, Lehmann Brothers, Morgan Stanley, Merrill Lynch, Bear, Stearns & Co., Rodman and Renshaw. AMN AMRO "GlaxoSmithKline: Improving Outcomes," June 2006. Detailed citations available upon request.

See page 32 for key products in the specialty/biotech pipeline.

Generics: What Happened, What's Next

The Forces Align

In 2006, five billion-dollar brands went generic, and plans and consumers reaped the benefits. Flonase, Mobic, Pravachol, Zocor, and Zoloft were the big names that went generic in 2006, but they were hardly the only brands to face first-time generic competition. With the 2006 launches, there are important generic options in all the top categories, offering more cost-saving alternatives to consumers and plans than ever before. The wave of significant generic launches is expected to continue as **many more high-performing brands face patent expiration** (see page 17).

Importantly, plans and consumers have never been better prepared to take advantage of these opportunities. **Pharmacy benefit design** incorporating features such as tiered formularies and step therapy have helped steer plan participants to cost-saving generics, as have careful determination of co-pays, consumer and physician outreach, and **greater price transparency through Web tools** and other communications. In the Caremark BOB, such factors helped push the generic dispensing rate (GDR) higher throughout the year, helping to reduce the effect of product mix as a driver and to keep gross trend low. Over the last three years, our overall **BOB GDR increased from 48.2 percent in 2004, to 52.6 percent in 2005, to 55.7 percent in 2006**.

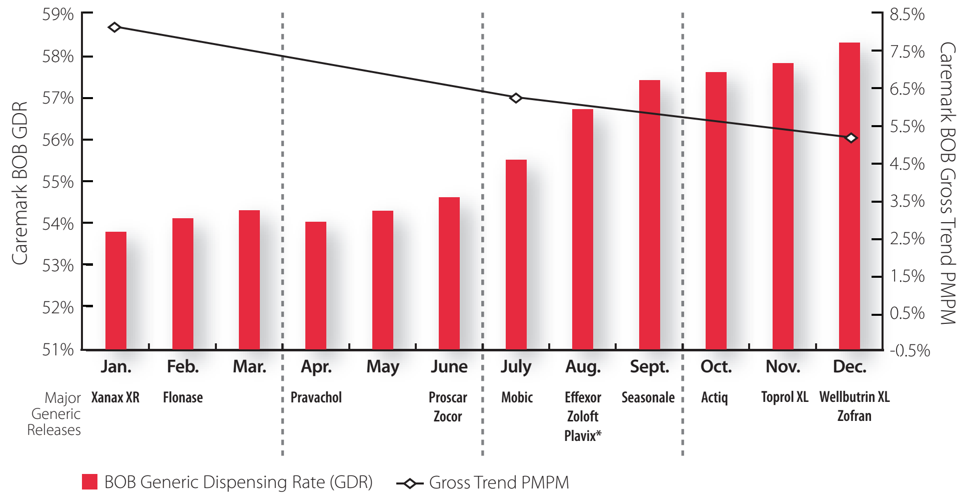
GDR Update 2007:

1Q GDR—58.8%

Clopidogrel, the generic form of platelet aggregation inhibitor Plavix, was launched at risk in 3Q 2006. This year, courts upheld the Plavix patent and the blood thinner is unlikely to face generic competition for another four years.

Figure 12

The top 14 generic launches in 2006 decreased product mix trend by 1.2% and helped lower gross trend.



* At-risk launch

Source: 2006 Caremark BOB data, generic release dates based on product availability. YTD trend based on cohort. February 2007, Industry Analytics.

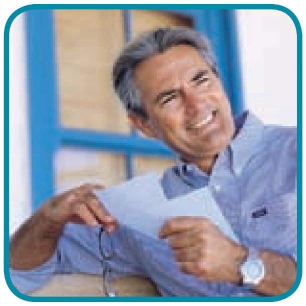


Figure 13

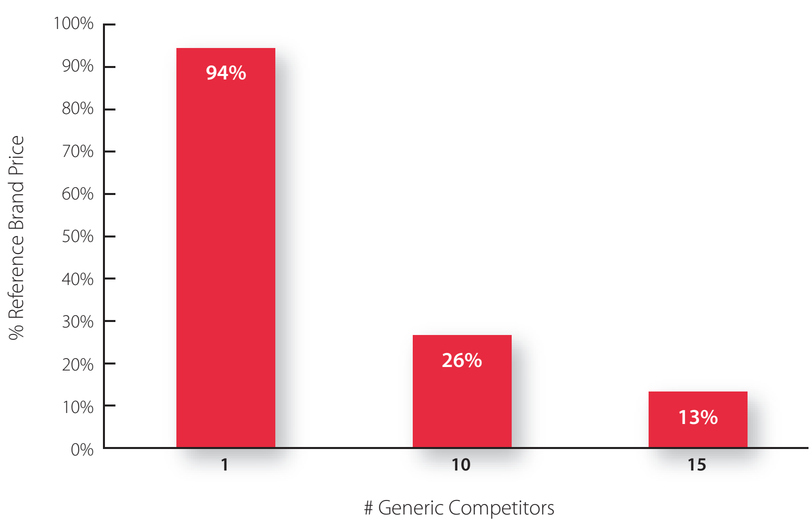
Generics helped Caremark clients save over 33% in 2006.

Generic Drug	Reference Brand	Use	Brand Gross Cost Per Day's Supply	Generic Gross Cost Per Day's Supply	BOB Spend % Reduction
fluoxetine HCL	Prozac	Depression	$6.82	$0.88	1.74%
metformin HCL	Glucophage	Diabetes	$2.33	$0.73	1.14%
hydrocodone w/ acetaminophen	Vicodin	Analgesics, narcotic	$4.13	$1.11	1.06%
atenolol	Tenormin	Hypertension	$1.72	$0.23	1.03%
lisinopril	Zestril	Hypertension	$1.31	$0.39	0.82%
All Other Generics					28.07%
Total					**33.9%**

Source: 2006 Caremark Book of Business, savings calculated at GPI14 and summarized to GPI8, April 2007. Industry Analytics.

Figure 14

Competition reduces prices for generic drugs.



Sources: Kaiser Family Foundation, Prescription Drug Trends, May 2007. Data from U.S. FDA, Center for Drug Evaluation and Research, "Generic Competition and Drug Prices."

Figure 15

New and Pending Major Generics, 2007-2010

Brand Name	Generic Name	Use	Launch Date	Industry Sales
2007 New Generics				
Ditropan XL	oxybutynin chloride	Genitourinary agents - bladder antispasmodics	2006	$332M
Inderal LA	propranolol HCL ER	Hypertension	Q1	$200M
Norvasc	amlodipine besylate	Hypertension	Q1	$2.7B
Ambien	zolpidem	Sleep Disorders	Q2	$2.18B
Omnicef	cefdinir	Anti-infective	Q2	$787M
Lotrel	benazepril / amlodipine besylate	Hypertension	Q2	$1.5B
Lamisil	terbinafine	Antifungal	Q3	$682M
Toprol XL (50, 100, 200 mg)	metoprolol succinate	Hypertension	Q3	$1.39B
2007 Anticipated Generic Launches				
Coreg	carvedilol	Hypertension	Q3	$1.54B
Zyrtec*	cetirizine	Antihistamine	Q4	$1.39B
2008 Anticipated Generic Launches				
Wellbutrin XL (150 mg)	bupropion	Antidepressant	2008	$844M
Fosamax	alendronate sodium	Osteoporosis	Q1	$1.9B
Risperdal	risperidone	Antipsychotic	Q2	$1.4B
Depakote, Depakote ER	divalproex	Anticonvulsant	Q3	$1.3B
Lamictal	lamotrigine	Anticonvulsant	Q3	$1.0B
Imitrex	sumatriptan	Migraine	Q4	$1.0B
2009 Anticipated Generic Launches				
Topamax	topiramate	Anticonvulsant	Q1	$1.0B
Prevacid ** (30 mg)	lansoprazole	Anti-ulcer	Q2	$3.2B
Valtrex	valacyclovir	Anti-viral	Q2	$800M
Adderall XR	amphetamine combination	ADHD/ADD stimulant	Q2	$780M
Altace	ramipril	Hypertension	Q2	$900M
2010 Anticipated Generic Launches				
Lipitor	atorvastatin calcium	Cholesterol-lowering	Q1	$7.7B
Cozaar	losartan	Hypertension	Q1	$1.2B
Flomax	tamsulosin	Benign prostatic hyperplasia	Q2	$691M
Protonix	pantoprazole	Anti-ulcer	Q3	$1.9B
Effexor XR	venlafaxine	Antidepressant	Q3	$2.5B
Aricept	donepezil	Alzheimer's agent	Q4	$1.0B
Levaquin	levofloxacin	Anti-infective	Q4	$1.3B

Source: Prospective Pipeline Analysis Summary. *Zyrtec will also be available over the counter. **Prevacid 15mg will also be available over the counter.

Information related to prospective drug launches is subject to change without notice due to events in the market, litigation, FDA delays, and other circumstances beyond our control. This information should not be solely relied upon for decision-making purposes.

(generics content continued on page 20)

Figure 16

Top 10 classes account for 53% of Caremark BOB spend.

Rank	Class	Gross Trend	Util Trend	% BOB Spend	Top Drugs	Recent or Pending Launches	Generics in Class
1	Cholesterol lowering	5.1%	4.3%	11.0%	Lipitor, Crestor, Vytorin		lovastatin, pravastatin, simvastatin
2	Anti-ulcer	4.0%	2.3%	7.1%	Nexium, Prevacid	Pylera	omeprazole
3	Antidepressant	4.9%	2.7%	6.5%	Lexapro, Cymbalta, Effexor XR	2007: Pristiq	citalopram, paroxetine, fluoxetine, sertraline, bupropion, venlafaxine
4	Antihypertensive	3.7%	0.1%	5.3%	Avapro, Cozaar	2007: Tekturna	lisinopril, fosinopril, felodipine, atenolol, propranolol, amlodipine besylate
5	Antidiabetic	10.0%	3.1%	5.2%	Actos	Exubera, Januvia 2007: Galvus	glimepiride, metformin, glyburide/metformin
6	Anti-asthmatic	10.9%	2.3%	5.0%	Advair Diskus, Singulair		albuterol
7	Analgesic, anti-inflammatory	-1.0%	-6.0%	3.7%	Celebrex, Enbrel, Humira, Orencia		multiple generics available, including meloxicam
8	Misc. endocrine, metabolic	1.9%	-5.1%	3.3%	Fosamax, Boniva, Actonel, Forteo		alendronate (daily)
9	Anticonvulsant	11.0%	5.9%	3.1%	Topamax, Lamictal, Lyrica		gabapentin, carbamazepine
10	Analgesic, opioid	3.2%	4.8%	2.8%	Vicodin, Oxycontin		oxycodone, hydrocodone
Total				**53%**			

Specialty drugs in blue.
This analysis is an estimate for informational purposes only. These estimates do not represent an existing or future contractual guarantee provided by Caremark.
This information is subject to change and will not represent any specific offer by Caremark or return on investment in the future.

See page 28 for Top Specialty Pharmaceutical Classes.

▲ Estimated greater than 4% increase ⊖ Estimated flat trend ▼ Estimated greater than 4% decrease

Pending Generics	Trend Projection	Key Trend Factors
	▲	New generics dampened trend, but utilization continues to grow due to more stringent treatment guidelines and significant DTC advertising, especially for combination products Vytorin and Caduet.
Aciphex (at-risk), 2009: Prevacid	▼	Utilization management strategies that promote OTC options help to lower trend.
Wellbutrin XL (150 mg)	⊖	Top classes—SSRIs and SNRIs—have different modes of action. Generic SSRIs help to lower trend. However, utilization of SNRIs, with no generic availability, is increasing.
Coreg, Lotrel, Norvasc 2009: Altace, Aceon	▲	Incidence of hypertension increases with age, and patients often need a combination of drugs to achieve blood pressure control. Antihypertensives are also used in the treatment of other conditions, such as heart failure. Adherence measures and disease management can help to control the condition and healthcare costs, but may drive utilization increases. Current and pending generics can help to control costs in the class.
	▲	Ongoing increase in disease incidence and new drugs drive utilization growth. New drugs with novel mechanisms of action and more favorable side effects profile may offer better hope of control but do not replace older therapies. Emerging safety concerns about Avandia may drive more utilization of older drugs.
	▲	Increasing disease incidence, new drugs, and a multi-pronged approach to therapy drive trend. Also prices for top drugs—Singulair and Advair Diskus—saw significant increases. Phase out of CFC-containing inhalers—all generic—in 2007 also expected to drive trend. Replacement inhalers with albuterol are branded products. Disease management programs emphasize use of maintenance products and help to limit use of rescue drugs and additional healthcare costs.
	▲	Declining utilization of COX-2s due to safety concerns continues to reduce trend, but growth in use of DMARDs, which include biologic agents such as Enbrel, Humira and Orencia, will continue, due in part to expanding indications. DTC advertising of these biologic agents likely also contributed.
2008: Fosamax (weekly)	▲	Class is dominated by drugs for osteoporosis and includes hormone replacement therapies (HRT). As population ages, awareness and treatment of osteoporosis are rising. Also, specialty osteoporosis product Forteo trended in the double-digits in 2006. Trend in the class may be affected by recent news regarding benefits of HRT for certain age groups.
2008: Depakote, 2009: Topamax	▼	Double digit trend relates to cost increases and utilization, particularly use of drugs in the category for pain and increased use of single source brands—Topamax, Lamictal and Lyrica. Generics for Neurontin continue to help to dampen growth.
	▲	A greater focus on pain treatment and chronic pain management is increasing utilization of this class although generic availability has slowed trend.

DMARD-disease modifying anti-rheumatic drug
OTC-over-the counter
SNRI-serotonin norepinephrine reuptake inhibitor
SSRI-selective serotonin reuptake inhibitor.

Caremark has a comprehensive portfolio of programs that optimize generic utilization. With our generic awareness programs we can reach out to plan participants, as well as physicians, to communicate the benefits of choosing generics. Our goal is to help you manage your total healthcare spend by leveraging all the marketplace opportunities afforded by the ongoing wave of new generic launches.

Our consumer-directed solutions engage, encourage and empower plan participants to make the right prescription decisions. On Caremark.com, for example, plan participants can check drug costs and find out about potential savings opportunities including generic alternatives for their prescriptions. The iBenefit™ Report identifies for plan participants the most cost-effective options and shows actual and potential savings by using generics.

Innovative options now available include the Co-pay Waiver Program, which targets plan participants on selected multi-source or single-source brand drugs and offers them a waiver or reduction in co-pay if they move to the recommended generic product.

A plan design innovation is our Narrow Formulary, which combines formulary, plan design and utilization management to create a highly generics-focused benefit option for clients. Each drug class is clinically reviewed, and higher cost brand agents are placed in tier three with limited clinical exceptions. Multi-source brand medications with generic equivalents available are completely blocked.

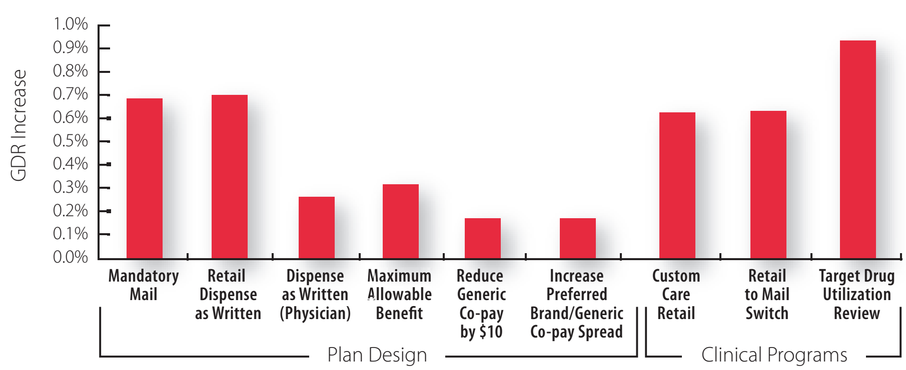
At the point of prescribing, the iScribe® ePrescribing tool reaches physicians with targeted generic messaging. Our clinical consultants also provide information on generic opportunities on-site and in-person. In addition, Caremark can provide patient-specific mailings to physicians alerting them to alternative, cost-saving therapies.

All told, nearly half of the 60 most commonly prescribed drugs will become available over the next four years at prices that could save health plans and consumers a potential $49 billion by 2010.

Wall Street Journal, October 31, 2006

Figure 17

Increasing GDR: Top Plan Design and Clinical Program Drivers



Note: The averages above are based on Caremark BOB results in 2006 comparing clients with and without the programs. Actual client-specific results will vary based on plan design, pricing, demographics, and drug mix.

Source: 2006 Caremark BOB data, Industry Analytics.

Generics on the National Stage

Rising drug prices, Medicare Part D and the many generic launches helped put generics on the center stage in 2006. **Medicare Part D plans** promoted both price transparency and generics. A year after the implementation of the Medicare Part D drug benefit, generic drug utilization among beneficiaries hovered around 60 percent.[5]

Medicare Part D, of course, increased the portion of national prescription spending paid by public funds. Medicare, Medicaid and other public payers now fund 40 percent of our national prescription drug spend.[6] Generics are widely viewed as a means to make the most of these public dollars. Thus, a variety of proposals have been introduced in **Congress** to improve consumers' access to generics. These include the development of an approval pathway for generic versions of biotech drugs and restrictions on tactics used to delay or defuse generic launches such as authorized generics and pediatric extensions. The **Federal Trade Commission** (FTC) is looking into reverse payments ("pay to delay") cash settlements paid to generic manufacturers by brand drug manufacturers in exchange for delaying the launch of generic competitors.

Caremark was the first PBM to promote legislation to reduce **patent expiration "loopholes"** and is now working with the Coalition for a Competitive Pharmaceutical Marketplace (CCPM) to help reduce prescription costs by:

- Encouraging legislation to codify a legal pathway for FDA approval of generic versions of biologic drugs
- Ensuring that the pediatric exclusivity provision is being applied to appropriate drugs
- Removing a roadblock to the entry of generic versions of certain antibiotics
- Clarifying the use of the 30-month stay of effectiveness period to limit its use as a tactic to delay entry of generics

Figure 18

Caremark Forecast: GDR to grow in the coming years.

GDR	2007	2008	2009	2010
Mail	44-48%	50-54%	52-56%	58-62%
Retail	57-61%	60-64%	62-66%	64-68%
Overall	55-59%	59-63%	60-64%	63-67%

These forecasts reflect anticipated generic launches and ongoing generic maximization programs. Note that drug mix varies significantly between mail and retail. Chronic maintenance medications dispensed through mail service pharmacies are less likely to have generic equivalents than the acute medications dispensed through retail outlets. Thus, retail GDR is typically higher than mail GDR.

Source: Industry Analytics

This analysis is an estimate for informational purposes only. These estimates do not represent an existing or future contractual guarantee provided by Caremark. This information is subject to change and will not represent any specific offer by Caremark or return on investment in the future.

Utilization: 0.7%

Our 2006 BOB utilization trend, calculated as days' supply PMPM, was 0.7 percent. This is a significant drop from the 2005 utilization trend figure of 4.1 percent. In the Caremark BOB, clients have implemented **careful utilization management strategies**, emphasizing the appropriate use of medicines targeting chronic conditions (see page 10). In addition, utilization growth continues to be dampened by **safety concerns** about some drug classes and by the ongoing lack of blockbuster new brand drugs. Our 2006 low utilization trend also reflects the composition of our trend cohort group, which excluded Medicare Part D plans. In its first year, Medicare Part D plans could not provide the 24 months of claims data needed for year-over year comparison.

As noted earlier, the bulk of Caremark BOB prescription drug spending (3.4 percent of trend) was driven by **drugs used for the treatment for chronic conditions** and diseases, such as cardiovascular disease, asthma, depression, diabetes, and arthritis. As the U.S. population ages, incidence of chronic conditions increases—both factors are primary drivers of the growth in utilization. Increasing utilization in these categories is also related to an **increased focus on appropriate treatment, adherence and achieving desired clinical goals**—such as specified hypertension, blood glucose and cholesterol levels. See the Top 10 Therapeutic Class table (pages 18–19) to review factors impacting utilization and overall trend for the most utilized therapeutic classes in the Caremark BOB. Much of the spend in these categories, of course, helps keep people well and productive and avoid costly medical events, thus **helping to manage overall healthcare costs**. Direct-to-consumer (DTC) advertising can also have an impact on utilization. For example, although sleep agents account for less than 2 percent of BOB spend, the category had a very high gross trend in 2006 at 34.0 percent with a utilization trend of 15.6 percent. Lunesta and Ambien CR, two newer sleep agents, were heavily advertised and had a combined 2006 DTC spend of more than $413 million.

In 2006, some of the major influencers of BOB utilization trend included:

- ↓ Ongoing scarcity of new blockbuster brand drugs
- ↓ Safety concerns about specific categories including anti-inflammatory analgesics, antidepressants and hormone replacement therapy
- ↑ DTC advertising

The Generational Perspective

Looking at drug spend by generations provides insights into both health status and health concerns. The three oldest population segments in our BOB account for 50 percent of utilizers and 75 percent of our 2006 drug spend.

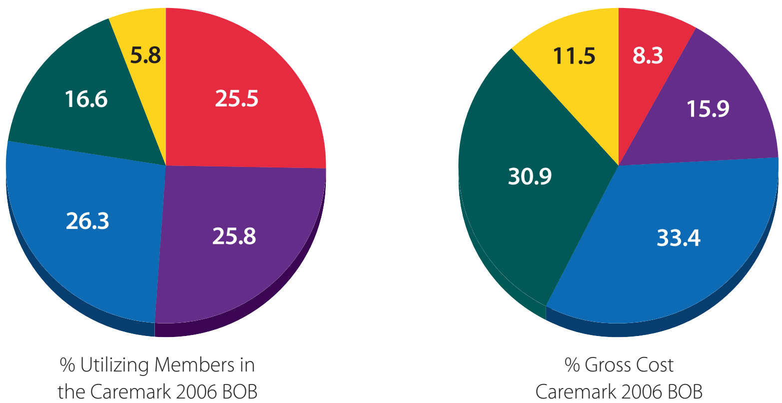
The **Baby Boomers (age 43 to 58)** lead the way, representing slightly more than a quarter of the BOB utilizing population and a third of overall spend. Boomers are beginning to face the health issues of aging and have embraced pharmaceuticals to help them maintain their quality of life. Leading classes for the Boomers include the cholesterol-lowering drugs, anti-ulcer agents and antidepressants. The top therapeutic classes for **Millenials (birth to age 21)** include antiasthmatics, stimulants (used for ADHD, narcolepsy, obesity, and anorexia), and dermatologicals.

Perhaps the younger **Generation X (age 22 to 42)** has taken fitness recommendations to heart. Cholesterol-lowering drugs and antihypertensives don't yet figure in their top 10. Their leading classes include antidepressants, contraceptives and anti-ulcer agents.

The **Silent Generation (age 59 to 76)** grew up during the Depression. The **GIs (age 77 and older)** came of age during World War II. Antidepressant use drops out of the top five in these two groups, replaced by antihypertensives at the number three slot.

Figure 19

In the Caremark BOB, plan participants over the age of 43 account for almost 50% of the population and more than 75% of drug costs.



	M (Age <21)	X (Age 22-42)	Boomer (Age 43-58)	Silent (Age 59-76)	GI (Age 77-101)
2006 GDR	59.6%	59.5%	54.2%	53.2%	56.9%

Source: 2006 Caremark BOB data, Industry Analytics.

Trends in Pharmacy Benefit Design

Pharmacy benefit design strategies are becoming more targeted and sophisticated. Rather than relying on increasing consumer cost share to reduce spending, plans are implementing **programs that incentivize use of generics**, sometimes distinguishing between higher and lower cost generics in a class, and otherwise increase cost awareness. To **support adherence** and help manage overall healthcare costs, some plans lower or have no co-pays for certain chronic medications or provide a co-pay allowance for certain classes.

Traditional Pharmacy Trend Strategies

- Three- and four-tier plan designs
- Larger spread between co-pays
- Programs that drive mail service utilization
- Restrictive coverage on lifestyle medications
- Dispense as written (DAW) penalties on brand drugs

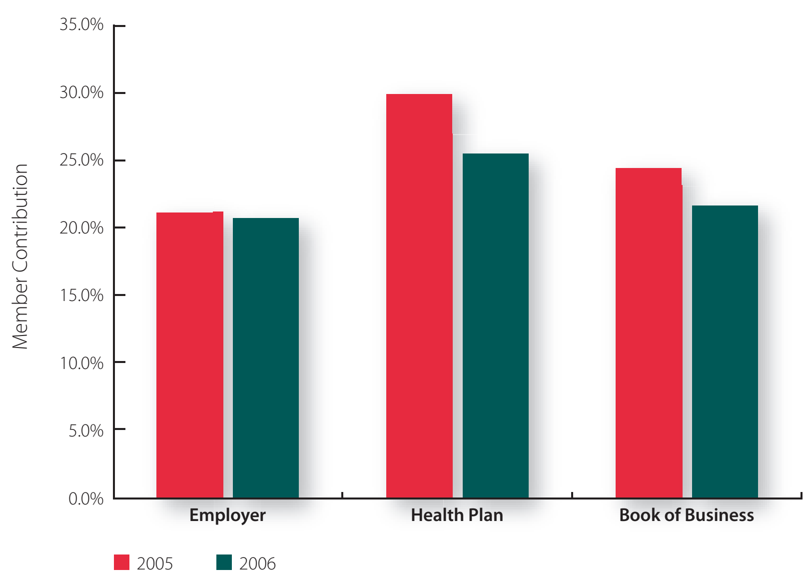
Innovative Trend Strategies

- Narrow formulary to promote generics
- Stepped co-pays
- Zero co-pays for generics
- Dual co-pays for generics
- Drug class co-pay allowance
- Coupon and rewards programs
- Pharmacist-directed generic launch messaging at point-of-sale
- Consumer-directed health programs
- Preventative drug list plan designs
- Health and wellness incentives

Ask your Caremark account representative about new ways to achieve your plan goals and help manage your pharmacy and healthcare costs.

Figure 20

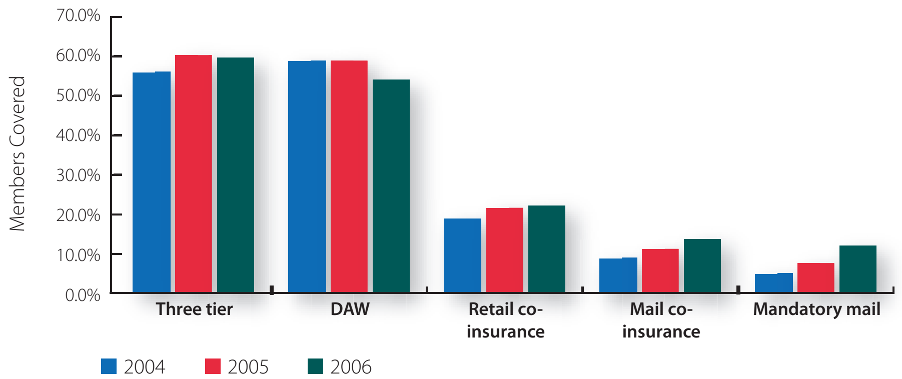
Decreases in member contribution vary by market segment.



Source: Caremark BOB data, January 2007, Industry Analytics.

Figure 21

Plan design changes continue to support greater cost awareness.



Source: Caremark BOB data, January 2007, Industry Analytics.

Forecasting National Prescription Drug Trend

The **Centers for Medicare and Medicaid Services (CMS)** annually evaluate national health expenditures and provide forecasts of expected growth. Their evaluations look at aggregate figures—overall spend rather than per capita—and consider the factors that drive or inhibit growth.

The implementation of the **Medicare Part D drug benefit** in 2006 brought significant changes to the prescription drug marketplace, most importantly providing many seniors with greater access to needed medications. CMS expected the benefit to increase senior drug utilization and utilization of generics. In economic terms, CMS anticipated that the benefit would substantially increase the portion of drug spend paid by public funds. While final numbers have not been reported, all of these expected effects have been realized. Despite these changes, the benefit is expected to have little impact on overall rate of spending growth.

The factors that CMS does expect to drive growth rate include a leveling off of the generic dispensing rate and increased utilization due to new drugs and new indications for existing drugs. When 2006 numbers are finalized, CMS expects a **drug spending growth rate of 6.5 percent** and expects an acceleration to a growth rate of 7.4 percent in 2007. Thereafter, CMS forecasts steady increases over time to a growth rate of 9.7 percent in 2016.[7]

BOB Prescription Drug Trend Forecast

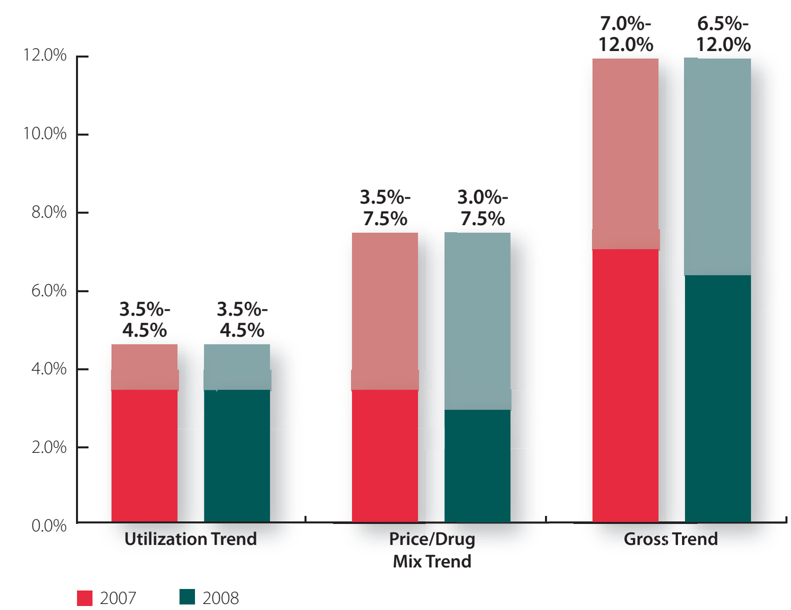
Caremark Analytics Services anticipate **relatively stable growth in utilization, price and drug mix** over the next 18 to 24 months with the impact of generic launches being somewhat offset by new drugs and expanding indications, especially in the specialty sector.

Caremark clients have experienced several successive years of single-digit pharmacy benefit trend based on **careful, proactive plan management and maximization of market opportunities**. The same approach can help plans reduce trend below our forecasted levels, which assume a continuation of current plan design and demographics in the plan populations.

Importantly, while management of the prescription benefit by itself is essential, no one today can overlook the vital role the benefit plays in **controlling overall healthcare costs**. Appropriate drug utilization helps to control exacerbations and limit complications related to major cost drivers in U.S. healthcare—heart disease, diabetes, asthma, osteoporosis, multiple sclerosis, and more. We look forward to working with you over the months ahead to manage your prescription benefit, improve outcomes and reduce overall healthcare costs.

Figure 22

Caremark Gross Trend Forecasts



Forecasts based on Caremark Book of Business and represent future overall underlying secular gross drug trend; that is, the PMPY gross cost increase that would prevail if no plan design or demographic changes occur. Trend forecasts include specialty pharmaceuticals. This analysis is an estimate for informational purposes only. These estimates do not represent an existing or future contractual guarantee provided by Caremark. This information is subject to change and will not represent any specific offer by Caremark or return on investment in the future.

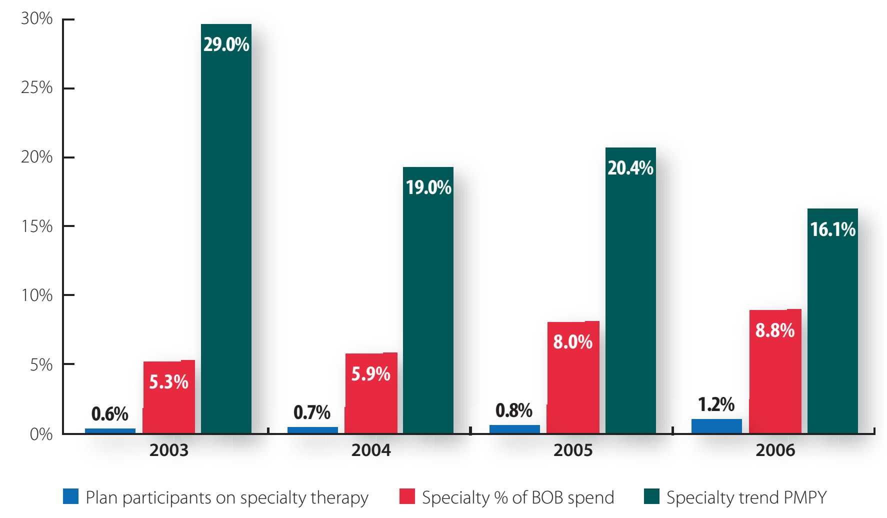
Source: Industry Analytics.

Specialty Pharmacy: 2006 Trend Analysis, 2007 Forecast

In 2006, specialty pharmacy trend in the Caremark Book of Business (BOB) slowed to its **lowest rate of growth in four years**. Nonetheless, with a gross trend of 16.1 percent per member per year (PMPY), the sector continues to outpace the rest of the pharmaceutical market by far. Specialty pharmaceuticals accounted for **8.8 percent of overall BOB spending**, compared to 8 percent in 2005. However, the portion of our BOB population using specialty pharmaceuticals increased significantly, from .8 percent to 1.2 percent. While this is still a small percentage of our overall population, it drives a **disproportionate amount of BOB spend**. Moreover, the growth is an indicator of specialty pharmaceuticals' broadening penetration into the pharmaceutical market.

Figure 23

Specialty pharmacy trend slows, but utilizing population grows.



Source: 2003-2005 Caremark historical. 2006 Caremark Book of Business trend cohort, which includes funded clients with integrated (mail and retail) benefit plans with claims from January 1, 2005 through December 31, 2006 (24 months of claims). Average eligibility must be within +/- 15 percent period over period. Trend cohort group excludes Puerto Rico, Virgin Islands and Guam clients, and does not include Medicare Part D members. Specialty trend calculations based on Universal Specialty drug list. February 2007, Industry Analytics.

What Drives Specialty Pharmacy Trend?

Specialty pharmacy, of course, is dominated by **biologically derived or "biotech" drugs**, many of which represent groundbreaking medical advances in the treatment of complex, rare or genetic illnesses. These drugs are often high cost—ranging from $10,000 to $250,000 and up per patient per year—and generally **require special handling or administration, patient-specific education, and close monitoring**. Specialty pharmaceuticals have made a profound difference in the lives of individuals with conditions such as cancer, multiple sclerosis (MS) and rheumatoid arthritis (RA).

These drugs can prolong life, reduce pain, improve quality of life, and slow the progression of disease. Such benefits obviously have a role in the sector's growth.

Other factors fueling growth include **a flourishing pipeline, expanding indications, earlier use of biologics in the treatment of some conditions, and expansion beyond treatment of rare diseases** to treatment of more common chronic conditions. In some classes, new launches are often adjunctive or **additive therapies** rather than replacements for existing specialty pharmaceuticals. Moreover, some specialty drugs are being **advertised direct to consumers**. All these factors increase utilization, and some specialty pharmaceuticals have now achieved blockbuster status. The cancer drug Avastin, for example, posted first-year sales of more than $1B. Other biotech blockbusters include hematological agent Procrit and RA drugs Enbrel and Remicade.

Specialty Pharmacy: Trend Drivers in 2006

Three of the top 10 specialty classes had double-digit utilization trend in 2006: drugs for RA (14.0 percent), cancer treatment (22.0 percent) and osteoporosis (23.6 percent). These classes illustrate some of the **major factors driving specialty utilization:** earlier and longer treatment, expanding indications, robust pipeline, and direct-to-consumer promotion. For example, drugs for RA, including Humira, Enbrel and Remicade, were among the most heavily advertised specialty drugs in 2006.[8]

Utilization, at 7.6 percent, and **price, at 6.3 percent**, were primary drivers of specialty pharmacy trend in the 2006 Caremark Book of Business.

Figure 24

Top 10 specialty therapeutic classes account for 7.5% of total BOB spend and 85% of total specialty pharmacy spend.

2006 Rank	Specialty Therapeutic Class	Gross Trend	Utilization Trend
1	Rheumatoid arthritis	19.6%	14.0%
2	Multiple sclerosis	17.5%	4.1%
3	Oncology	43.2%	22.0%
4	Hematopoietics	0.6%	2.4%
5	Transplant	4.7%	2.6%
6	Human growth hormone	8.9%	4.3%
7	Hepatitis C	-11.3%	-9.9%
8	Infertility	-4.0%	3.1%
9	Osteoporosis	33.2%	23.6%
10	Hemophilia	25.0%	-1.8%

Source: 2006 Book of Business, Specialty Universal Drug List, sorted by total gross cost. February 2007, Industry Analytics.

Expanding indications are more prevalent in the biotech sector than among pharmaceuticals overall and are a significant driver of utilization. In some cases, a new indication expands use of a drug to a new condition—Rituxan, for example, is indicated for several kinds of cancer and rheumatoid arthritis. In other cases, a new indication broadens the treatment parameters within which a drug is used—at an earlier stage of disease or in a broader patient population.

Figure 25

2006 Top 10 Specialty/Biotech Products

2006 Rank	Drug Name	Use	Gross Trend	Utilization Trend
1	Enbrel	Rheumatoid arthritis	11.3%	6.4%
2	Humira	Rheumatoid arthritis	46.1%	40.1%
3	Avonex	Multiple sclerosis	13.0%	-2.9%
4	Copaxone	Multiple sclerosis	19.3%	6.6%
5	Procrit	Hematopoietic	-6.2%	-0.9%
6	Cellcept	Transplant	9.2%	8.5%
7	Gleevec	Oncology	17.7%	7.9%
8	Rebif	Multiple sclerosis	27.8%	18.3%
9	Prograf	Transplant	7.7%	8.7%
10	Forteo	Osteoporosis	33.2%	23.6%

Source: 2006 Book of Business, Specialty Universal Drug List, sorted by total gross cost. February 2007, Industry Analytics.

Plan sponsors should anticipate that over time, as physicians and patients become familiar with newer drugs, prescribing rates and utilization may increase significantly, particularly if a product gains new indications.

Figure 26

Specialty Pharmaceuticals Receiving Supplemental Approvals (New Indications) in 2006

Drug	Primary Use(s)	# New Indications
Avastin	Cancer	2
Gleevec	Cancer	5
Remicade	RA, psoriatic arthritis, plaque psoriasis, Crohn's disease	3
Rituxan	Cancer, RA	3
Taxotere	Cancer	2

The following specialty drugs received one additional supplemental indication in 2006: cancer drugs Erbitux, Gemzar, Herceptin, Hycamtin, Revlimid, Taxotere, and Thalidomid; MS drugs Betaseron and Tysabri; RA drug Humira; transplant drug Prograf; and hematopoietic agent Aranesp.

Source: Caremark Pipeline Services.

Figure 27

Drugs for cancer, MS, and RA were the top drivers of price inflation among specialty pharmaceuticals in 2006.

Drug	Use	2006 AWP Inflation
Thalidomid (50 mg cap)	Cancer	42.9%
Thalidomid (100 mg cap)	Cancer	38.2%
Copaxone (20 mg injection)	MS	18.1%
Avonex (30 mcg syringe)	MS	16.8%
Pegasys (180 mcg/0.5 ml conv pk)	Hepatitis C	12.2%
Betaseron (0.3 mg vial)	MS	11.8%
Rebif (injection 44/0.5)	MS	9.6%
Enbrel (25 mg kit)	RA	6.1%
Humira (40 mg/0.8 ml pen)	RA	5.4%
Enbrel (50 mg/ml syringe)	RA	5.0%

Source: March 2007, Industry Analytics.

Challenges of Managing Specialty Pharmaceuticals

Specialty pharmaceuticals present a unique set of challenges to payors as well as plan participants. Management is complicated by **rapid growth in utilization**, the launch of new drugs, expanding indications, off-label use, multiple points of access, and varied forms of coverage, as well as by the pharmaceuticals' high cost. **Adherence** is key to achieving desired outcomes, yet patients can be deterred by methods of administration (such as injection or infusion), difficult side effects and complicated treatment regimens.

Caremark Specialty Pharmacy Services can help both payors and plan participants achieve the benefits of the investment made in specialty pharmaceuticals. Our new organization provides one of the broadest, most accessible networks with **61 specialty pharmacies** across the country.

Caremark Specialty Pharmacy Services are designed to maximize outcomes and the cost-effective use of specialty medications for plan participants. Our trusted Care Team conducts live pharmacist-patient and pharmacist-physician consultations to **support optimal medication use**. We continuously integrate learnings from these consultations to refine and improve our support services to create a better patient experience. These services **drive increased adherence** to therapy which can potentially reduce your total healthcare costs by decreasing the number of hospitalizations, emergency room visits, physician office visits, complications, and the use of adjunctive medications.

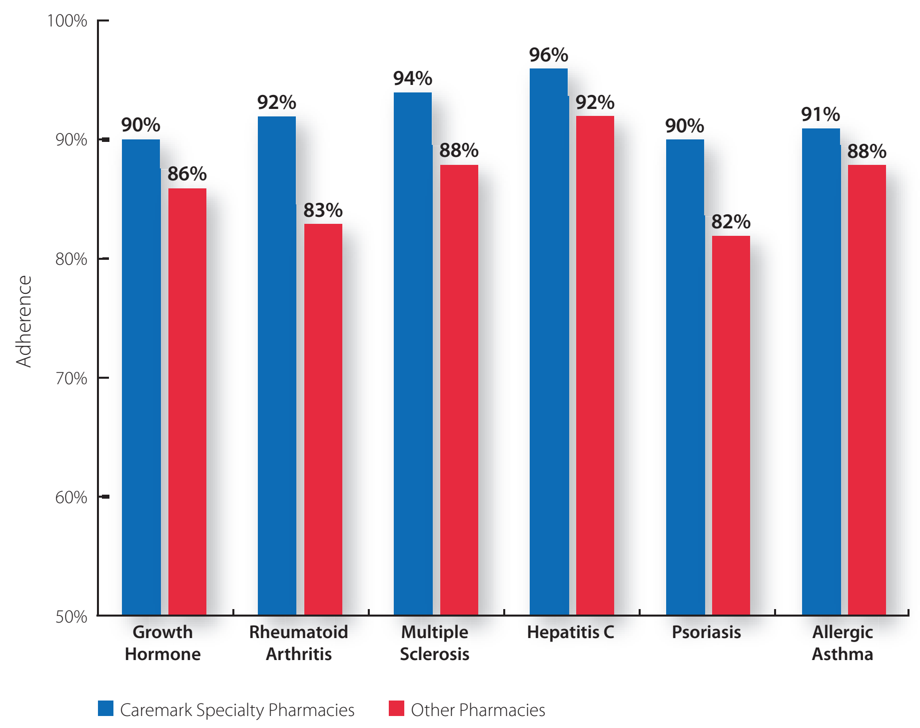
The **Caremark Specialty Guideline Management program** provides more comprehensive management. With this program, authorization for a specialty medication is obtained based on the application of currently accepted medical guidelines and consensus statements for appropriate use in a specific disease state. Moreover, each participant's progress is evaluated to determine whether expected outcomes are being met and appropriate therapeutic endpoints are achieved.

What's Ahead?

With a flourishing pipeline and multiplying indications for products already on the market, the specialty sector will continue to outpace the rest of the pharmaceutical market. It's estimated that **50 percent of drugs in development are biotech**, and that by 2020 specialty pharmaceuticals will account for about 37 percent of total drug expenditures.[9] Payors recognize that utilization management, therapy management and (increasingly) formulary management are key to maximizing the value received from their specialty investment. *(continued on page 33)*

Figure 28

Caremark Medication Management Services increase adherence to specialty medications.



Adherence: medication possession ratio (MPR)=days supply/days exposure to therapy.

Source: Caremark Analytics and Outcomes 2006 Analysis.

Multiple products within the same therapeutic class can increase competition and may lead to the possibility of the designation of preferred products. Classes with such potential currently include MS, RA, human growth hormone, and Hepatitis C.

Caremark clinicians monitor the specialty/biotech pipeline and review clinical trial literature continuously to make fully informed utilization management recommendations.

Figure 29

Key Products: Specialty Biotech Pipeline

Drug	Use	Estimated Peak Sales	Competitor Drugs
2007 YTD Launches			
Letairis	Pulmonary arterial hypertension (PAH)	$500M global	Tracleer
Supprelin LA	Precocious puberty	$28M*	Lupron
Tykerb	Breast cancer	$1.2B US	Herceptin
2007 Anticipated Launches			
Mircera	Hematopoietic	$900M US	Procrit, Epogen, Aranesp
Orplatna	Prostate cancer	$285M*	Eloxatin, Paraplatin, Platinol
Tasigna	Chronic meyloid leukemia (CML)	$400M*	Sprycel
2008 Anticipated Launches			
Cimzia	Crohn's disease	$525M US	Remicade, Humira
Icatibant	Hereditary angiodema	$100M (global)	First in class
Promacta	Idiopathic thrombo-cytopenic purpura (ITP)	$2.1B*	First in class
Retaane	Age-related macular degeneration (AMD)	$50M*	Lucentis, Macugen, Visudyne
Sarasar	Myelodysplastic syndrome (MDS); chronic myelomonocytic leukemia (CMML)	$75M*	Revlimid
Xenazine	Huntington's disease	N/A	First in class

This report contains brand name drugs that are registered or trademarks of pharmaceutical manufacturers that are not affiliated with Caremark. This page contains information compiled from a variety of sources and is provided for informational purposes only. Due to circumstances beyond the control of CVS Caremark, information related to prospective drug launches is subject to change without notice. This information should not be solely relied upon for decision-making purposes.

*Market unspecified

Source: Caremark Pipeline Services

Biogenerics—An Issue Under Consideration

While an approval process for generic versions of biotech medicines has generated considerable interest on Capitol Hill, the issue is complicated. Biologically derived medications often have multiple patents, many have multiple indications and there is a range of opinion on the need for additional human testing. Estimates on potential savings also vary widely. The issue remains on the agenda, but progress toward resolution has been slow.

Strongest category candidates for earlier biogeneric approvals include:

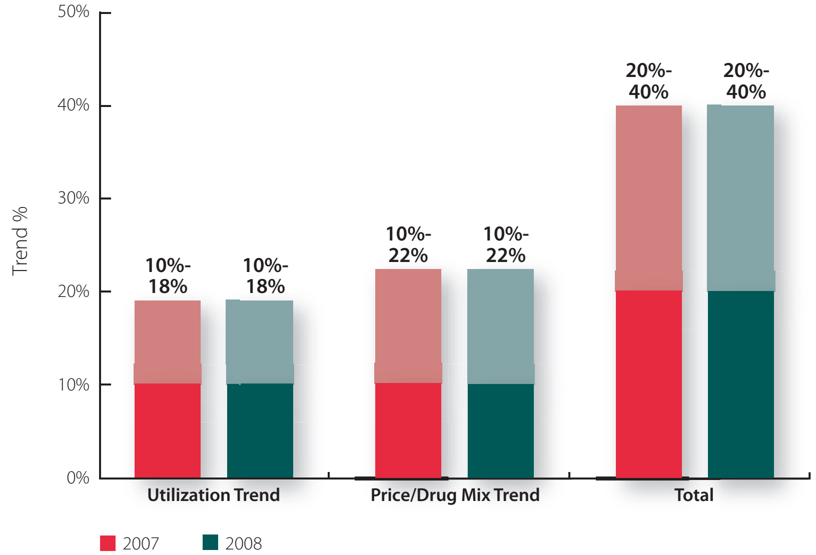
- Human growth hormone
- Insulin
- Interferons for multiple sclerosis
- Erythropoietin for anemia

Trends in drug research and development may help support such management. One of the most exciting areas of research is **pharmacogenetics**, which studies the effects genes may have on an individual's response to a drug. Pharmacogenetics may provide new ways to match medicine doses and medical treatments to individual groups of patients, increasing both the safety and efficacy of treatments by diminishing the trial and error for patients trying to find the optimal dose and treatment.[10] For example, the breast cancer drug Herceptin is being used to treat women who have a specific genetic marker present in approximately 20 percent of breast cancers; the drug has represented a significant step forward in the treatment of this population.

Risk maps are also expected to be used increasingly to improve the safety of specific drug therapies. Risk maps, or risk minimization action plans, are "strategic safety programs designed to meet specific goals and objectives in minimizing known risks of a product while preserving its benefits."[11] A risk map was a key component in the FDA's decision to allow the relaunch of the MS drug Tysabri, and the FDA is conducting hearings to assess the viability of making risk maps mandatory.

Figure 30

Caremark Specialty Pharmacy Gross Trend Forecasts



Trend forecasts represent per member per year (PMPY) cost increase that would prevail if no plan design or demographic changes were to occur. This analysis is an estimate for informational purposes only. These estimates do not represent an existing or future contractual guarantee provided by Caremark. This information is subject to change and will not represent any specific offer by Caremark or return on investment in the future.

Source: Caremark Trend Committee—Key metrics, February, 2007.

Figure 31

Balanced Health Scorecard for Specialty Pharmacy
High Performance Results and Priorities

Cost Efficiencies	Health Value
• Waste management	• Medication adherence
• Optimizing drug therapy	• Guideline management
• Prior authorization	• Improved health outcomes
• Competitive AWP discounts	• Reduction in relapse rates
• Reduction in healthcare costs	• Physician support and education through field-based experts
• Broad access for limited distribution products	• Medication therapy management
Consumer Engagement	**Operational Excellence**
• Patient-focused care	• JCAHO accreditation
• Welcome kits and patient education	• Full PBM integration
• Coordination of care with providers	• Disease management integration
• High member satisfaction	• Benefit management and investigation
• Broad access for limited distribution products	
• Online patient resources	

Such advances in **therapy management** may add to the cost of treatment with specialty pharmaceuticals. However, such measures are also expected to reduce inappropriate utilization and adverse drug reactions, and provide greater assurance that therapy goals are being realized. The complexities of management also underscore the need for specialized support, like that provided by Caremark Specialty Pharmacy Services, for these patient populations.

Specialty/biotech pharmaceuticals are the most dynamic element in today's pharmaceutical environment. The complexities of the conditions treated by these products, the challenges presented by a burgeoning pipeline and expanding utilization, and ongoing advances in drug development and therapy management—all these factors attest to the benefits of having expert support. **Caremark Specialty Pharmacy Services** take a comprehensive approach that leads to **better outcomes as well as lower overall costs** and provides the assurance that medications are used appropriately. Contact your Caremark account representative for recommendations on appropriate management strategies relative to your plan and plan population.

CVS Caremark—Partners in Health Advocacy

CVS Caremark is focused on building a new healthcare experience for consumers, an experience providing extraordinary access, personalized health information, improved value, and greater quality of care. For our PBM clients, this focus promises to drive improved outcomes and lower total healthcare costs—the benefits of a connected system that's less complex to navigate and eases access to trusted providers and advisors who can support improved health behaviors.

We invite you to learn more about our new initiatives and programs by contacting your Caremark account representative. All of us look forward to realizing this new vision with you.

Figures

References

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