TrendsRx® Report

2006

CAREMARK®
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2006 TrendsRx® Report

2006: The Challenge, The Opportunity

For the third year in a row, Caremark maintained single-digit pharmacy benefit trend in our overall Book of Business. At 7.9 percent per member per year (PMPY), trend in 2005 was lower than rates of annual growth for the previous six years. It's clear from our Book of Business (BOB) and from a review of national data that growth in prescription drug spending has moderated, in large part due to pharmacy benefit management techniques that impact consumer utilization and behavior as well as make effective use of marketplace opportunities.

2006 presents a mix of opportunities, challenges and uncertainty. A handful of key brand name drugs representing over $18 billion in sales will face **generic competition** for the first time. Analysts predict over 12 percent trend (year over year growth) in generic drug sales this year – a significant savings opportunity for plans in 2006 and beyond.

The year may provide real insight into the cost-cutting potential of two strategies favored by the administration in Washington. With the Medicare drug benefit now in place, there are 38 million Medicare beneficiaries who have drug coverage, And **consumer-directed health plans** have proliferated since first introduced, although the enrolled population is still a tiny fraction of the number of people in the United States with health benefits. In this report, we'll provide an overview of our participation in the Medicare drug benefit offerings, and you'll learn about the range of programs and strategies we've developed to support and encourage wise decision making by plan participants and members.

Specialty pharmaceuticals will present challenge and opportunity this year. New specialty pharmaceutical products are entering the market at a rapid pace, and many existing products are applying for and receiving approval for additional indications. Nationwide, specialty pharmaceutical utilization and spend are growing

Continued on next page

Caremark 2005 Book of Business Trend: 7.9% PMPY. Trend without Specialty Pharmacy: 7.0% PMPY.

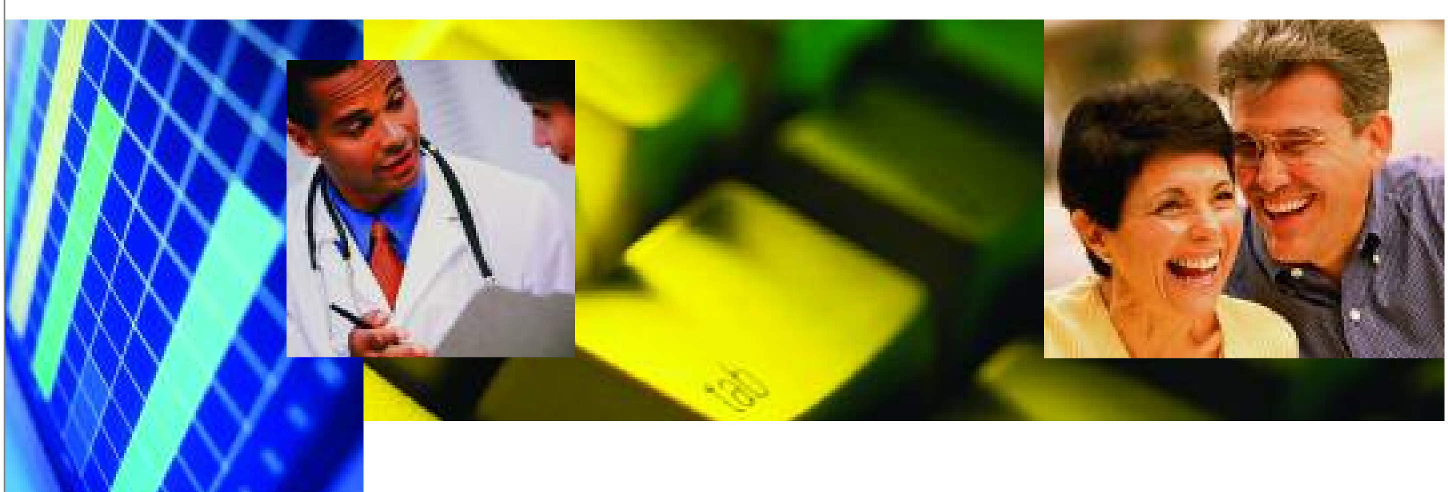
See pages 14–22.

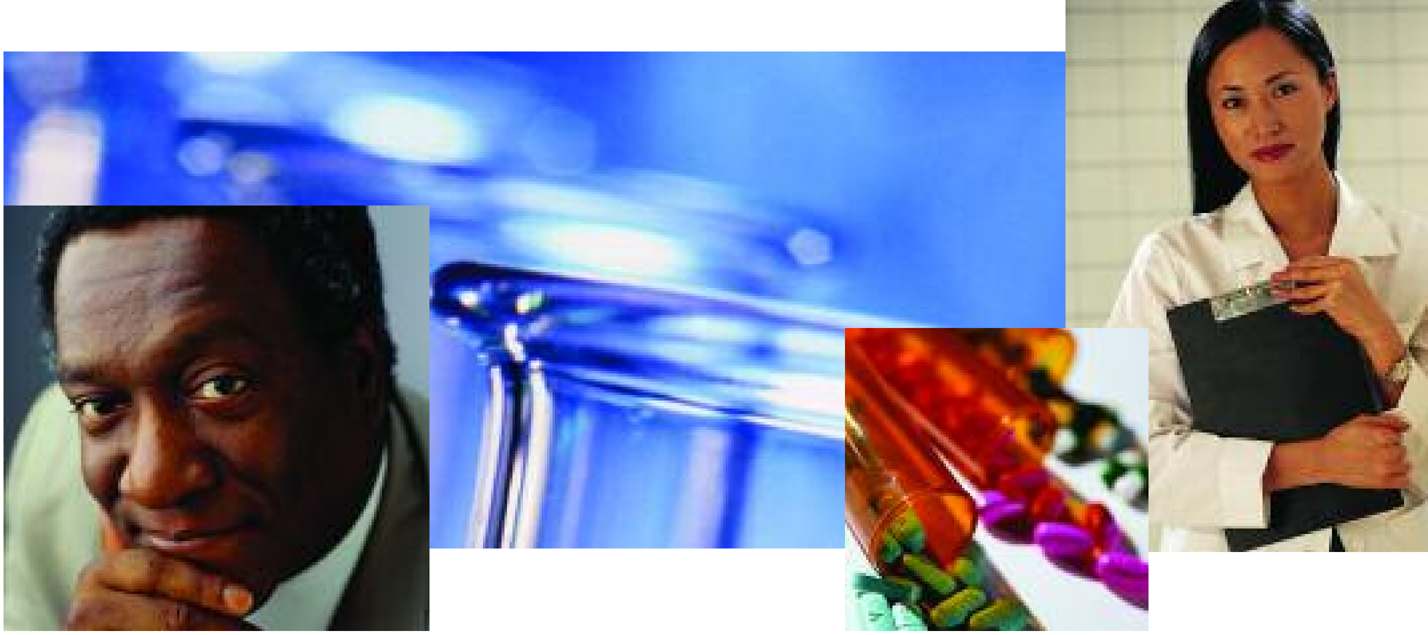
rapidly, presenting a challenge for payors, both public and private. At the same time, these pharmaceuticals often offer real advances in the treatment of complex conditions that are otherwise poorly controlled – tangible opportunities for improved quality of life and outcomes. *See our special section, pages 23-30, to learn more about the specialty pharmacy sector and its impact.*

Although prescription spending growth has slowed, **overall healthcare expenditures** consume more and more of our gross domestic product, with broad impact across society – on employers, insurers, payors, providers, and the general public. In terms of both cost and care, prescription drugs and the pharmacy benefit are crucial factors in the U.S. healthcare environment. Caremark is committed to helping our clients navigate this complex environment, manage their pharmacy benefit trend, support the health of plan participants, and help to reduce their overall healthcare costs.

In addressing the needs and goals of each specific plan population, Caremark takes a consultative, data-driven approach. Our unique suite of sophisticated, interactive assessment and planning tools, **CareSolutions**, makes it easy to select the right strategies to support your plan's success. CareSolutions helps identify opportunities to **optimize plan performance** through solutions in safety services, pharmacy trend management and comprehensive healthcare management. With CareSolutions analysis, you'll be able to focus on solutions that align with your plan's healthcare philosophy and business objectives, whether that is by impacting consumer behavior, influencing physician prescribing practice, increasing utilization of mail service pharmacy, or improving plan participants' compliance with condition management recommendations. You'll learn more about CareSolutions in the pages that follow – please consult your Caremark account representative to discuss how to implement these tools and apply these capabilities to optimize your plan management.

At Caremark, we recognize that careful and effective management of the pharmacy benefit has never been more important. We are continually evolving our services and expanding our capabilities to meet your current and future needs. The ***2006 TrendsRx® Report*** will introduce you to some of our new programs and innovative strategies to help you maximize generic utilization, manage your specialty spend, reduce your healthcare costs, and, above all, make the most of the opportunities that lie ahead.





The Rising Cost of Care

In 2005, healthcare cost growth slowed but continued to outpace inflation. Analysts anticipate ongoing growth of national health expenditures (NHE) at 7 percent or more a year for the next decade with healthcare costs claiming 20 percent of our gross domestic product (GDP) by 2015.[1] (*See Figure 1, page 4.*)

The Payor Shift in 2006

The major anticipated change in **national health expenditures in 2006** has to do with payors – where the money comes from. With the implementation of Medicare Part D in 2006, the Centers for Medicare and Medicaid Services (CMS) estimate that the rate of growth of public spending for personal healthcare will spike to 11.8 percent while projecting that growth in private spending will dip to 3.9 percent from a projected 7.2 percent in 2005. After 2006, public and private spending growth rates are both expected to return to a range of 6 to 7 percent.[2]

Despite lower rates of growth, CMS estimates that national health expenditures will double to $4 trillion over the next 10 years.

Impact on Benefit Costs

Inevitably, such cost growth has wide impact. Compared to 2000, employers in 2005 paid 78 percent more for healthcare while employees' costs increased 64 percent in the same period of time.[3] In one survey, half of large employers attributed slower profit growth to rising healthcare costs, and many felt that lower wage increases and reduced hiring were probable given continued double-digit growth in healthcare costs per employee.[4] The United States Government Accountability Office reported that rising benefit costs are forcing employers and their employees to make increasingly difficult **trade-offs between wages and benefits**. In fact, employer spending on benefits has grown faster than wages, due largely to rising costs for health insurance and retirement benefits.[5]

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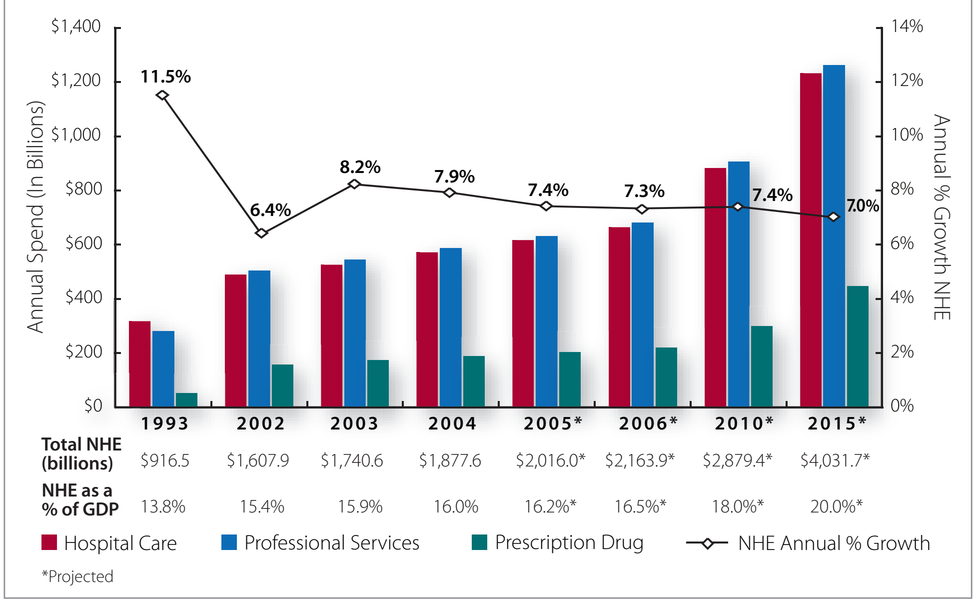
Figure 1

CMS estimates that national health expenditures will double to $4 trillion over the next 10 years and account for 20% of gross domestic product.



Source: "Health Spending Projections through 2015." Data source: Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Group; U.S. Department of Commerce; Bureau of Economic Analysis; and Bureau of the Census.

> CMS projects a slowdown in the growth of spending for hospital care and prescription drugs and a slight rise in spending for professional services.[6]

Other effects include reduced benefits and continued growth in the number of uninsured. A Kaiser Family Foundation survey found that 60 percent of U.S. businesses offered health insurance to workers in 2005, compared with 69 percent in 2000.[7]

Responses, But No Definitive Solution

Increasing the cost share borne by the consumer has been a widespread response to rising benefit costs for several years. **Cost share increases** have shown up as higher premiums, deductibles, co-pays, and "out-of-pocket" limits, but benefits administrators recognize that there are inherent limits to the strategy. Excessive cost share increases could make an employer less competitive in the labor market or drive employees to opt out of coverage altogether. Moreover, while changing cost share has helped to constrain costs somewhat, it has not had the hoped-for result of significantly reducing overall costs.

Consumerism is being championed as a way to address the more fundamental issue of cost reduction. The theory is that increasing consumer cost awareness and accountability will encourage consumers to make wiser, more economical healthcare decisions. That's the basis of the Bush Administration's continuing support of high deductible health plans (HDHPs) and tax-free health savings accounts (HSAs). In 2006, the President has advocated increasing the amount that can be deposited in HSAs and improving their tax advantages. Although the number of employers offering such plans is increasing, only a small percentage of the insured population currently has a consumer-directed healthcare (CDH) plan.

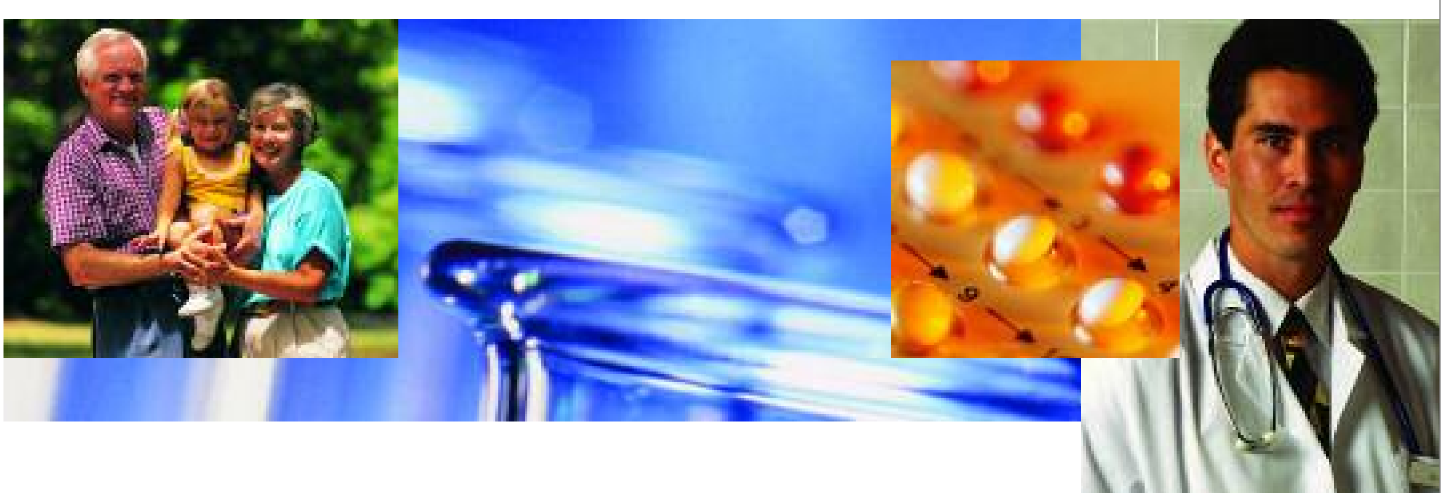
In the Caremark Book of Business, the number of clients offering a high deductible health plan increased substantially and the number of covered lives in such plans tripled in 2006. Despite this surge in growth, HDHP-covered lives are still a tiny fraction – less than one percent – of our entire population of plan participants. It's important to note, however, that there are a number of ways to increase consumer cost awareness and accountability through pharmacy benefit plan design, and the Caremark client base is increasingly adopting strategies – such as **co-insurance, iBenefit™ reporting and plan participant education** – intended to influence consumer behavior.

It remains to be seen whether consumers in these new plans will alter their health-related behavior. Perhaps more importantly, given the small number of enrollees currently, it will likely be some time before it can be determined how such behavior change will impact overall healthcare spending.

Consumerism depends upon informed healthcare decision making. Health plans and payors are making significant efforts to **educate plan participants** in regard to quality care and costs (why and how to evaluate a healthcare provider) and health advantages and health risks (why it's a good idea to continue to take your antihypertensives). **Disease management programs** are being more widely adopted in an effort to control healthcare costs for the highest cost plan participants with chronic illnesses. Two-thirds of large employers now offer one or more disease management programs.[8]

Helping consumers recognize **quality care** depends upon data – reporting on clinical practices and evaluating outcomes according to accepted measures of quality. The Bush Administration is also supporting wider use of **electronic medical records** (EMR) and **health information technology** (HIT). These measures are expected to reduce costs, improve quality and reduce the incidence of medical errors. The government and some health plans are also investigating pay-for-performance measures, wherein providers are rewarded for following standardized treatment guidelines.

In the Caremark Book of Business, the number of participants in HDHPs tripled in 2006.



Disease Management Helps Cut Healthcare Costs

A large employer client wanted to reduce overall healthcare costs and empower plan participants to make better healthcare decisions. A Caremark data analysis revealed higher than average utilization in some therapeutic classes. Using the client's medical and pharmacy claims data, Caremark identified individuals with **targeted disease states** who could benefit most from a disease management program. For this client, targeted disease states included diabetes, asthma, coronary artery disease (CAD), heart failure and ulcers. The **CarePatterns® disease management program** was offered to these individuals, and 2,500 plan participants enrolled.

The CarePatterns program was customized to meet the needs of the client and plan participants. Information was provided on appropriate management for the individual conditions in a variety of ways, including **direct coaching and counseling by CarePatterns nurses**. For example, nurses counsel plan participants with diabetes using the American Diabetes Association's standards of care recommendations on medication and clinical test compliance, and diet, exercise and lifestyle changes.

Twelve months after implementing the CarePatterns program, analysis of medical and pharmacy claims data showed that the client realized **more than $5 million in savings in overall healthcare costs**. This represented a return on investment exceeding 150 percent. Moreover, there was significant improvement in clinical measures across all CarePatterns programs for this client.

Condition Management – Promoting healthier outcomes for higher risk plan participants.

Figure 2

CarePatterns disease management program helps save more than $5 million in healthcare costs.

Disease State	Enrollees	Projected Medical Spending PPPY	Actual Medical Spending PEPY	Medical Savings PEPY	Total Savings
Asthma	275	$4,711	$3,098	$1,613	$444,000
CAD	679	$12,408	$7,307	$5,101	$3,464,000
Diabetes	1,031	$6,293	$4,963	$1,330	$1,371,000
Heart Failure	142	$8,904	$6,608	$2,296	$326,000
Ulcer	151	$5,414	$4,649	$765	$115,000
Total					**$5,720,000**

Projected medical spending per plan participant per year (PPPY) was estimated from calculating expended trend of baseline medical costs per targeted plan participant per month before the program year. Savings based on the difference between projected and actual targeted costs per enrollee per year (PEPY).
Source: Caremark Book of Business data

National Prescription Drug Spending

CMS provides an annual report on health spending, looking at gross expenditures. CMS analysts identified a slowdown in the growth of prescription drug spending in 2004 and 2005 and lowered their estimate on annual spending growth for prescription drugs by two percentage points, to an average 8.2 percent through 2015.

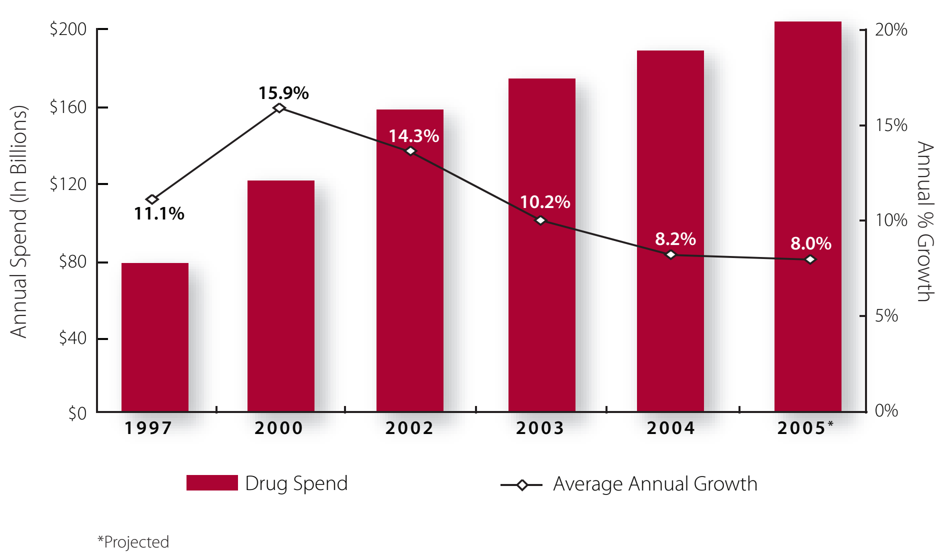
CMS analysts cited the following as factors contributing to the slowdown in overall prescription spending growth:

- Deceleration in drug utilization related to cost share shifts and other **pharmacy benefit management strategies**
- Rapid growth in the use of lower-price generic drugs driven by **tiered benefit plan designs**
- Increased use of **over-the-counter medications**, particularly anti-ulcer drugs and antihistamines
- A shift toward greater **mail service dispensing**
- Reduced consumption of certain drugs because of **safety concerns**
- Higher than expected discounts and rebates associated with **Medicare Part D**[9]

Caremark maintained single-digit trend in 2005. To learn more, see pages 14–22.

Figure 3

National expenditures for prescription drugs continue to grow, though at a slower rate.



Source: "National Health Spending in 2004." Data source: Centers for Medicare and Medicaid Services, Office of the Actuary; January 2006

Looking ahead for the long term, CMS forecasters see two primary factors that will increase drug spending – practice patterns wherein larger segments of the population will be treated with prescription drugs and **greater utilization of high-cost specialty drugs**. Greater utilization of generics and increased cost sharing in the form of higher co-payments and deductibles are expected to have a constraining effect on growth in drug spend. Overall, it's expected that these factors will offset one another, leading to relatively stable growth in the range of 8.0 to 8.4 percent from 2007 through 2015.[10]

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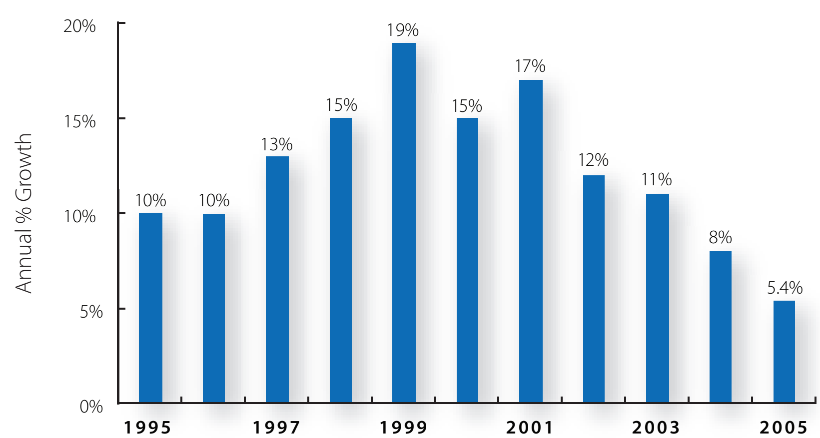
IMS, a leading resource for pharmaceutical industry information, also reports on gross spending. This year, IMS reported that U.S. drug sales grew 5.4 percent in 2005, a significant drop from their reported 8.2 percent growth in 2004. Growth factors cited by IMS include:

- **Generics** sales growth of 20.6 percent, driven by a number of significant and aggressive generic launches and the effective promotion of the use of lower-cost therapies by payors
- Lackluster performance of **traditional brand name drugs**, marked by fewer approvals of new drugs, lower-performing product launches and decreasing use of COX-2 products
- **Biotech** sales growth of 17.2 percent, marked by successful launches and expanding indications particularly in the rheumatoid arthritis class[11]

Figure 4

IMS reports that prescription dollar sales growth continues to slow.



Source: IMS Health

The Reasons Behind the Rise

America is spending more on healthcare in large part because people are using more healthcare. According to one study, between 1987 and 2002, the number of people per 100,000 treated for pulmonary conditions nearly doubled; the number treated for mental disorders more than doubled; and the number of people treated for high cholesterol increased by more than 400 percent.[12]

Many of these changes reflect **increases in disease prevalence** and changing population **risk factors** such as aging and obesity. But the increases in disease treatment also reflect changing standards and awareness – for example, greater emphasis on **earlier diagnosis**, **stricter guidelines** for cholesterol levels and greater social acceptance of treatment of depression. **Advances in pharmaceutical science and diagnostic and treatment technology** also contributed to our increased utilization of healthcare.

Figure 5

In the U.S., more people are being treated for many diseases.

	Treated Prevalence per 100,000		Cost per Treated Case	
Medical Condition	**1987**	**2002**	**1987**	**2002**
Cancer	2,710	3,666	$3,081	$3,999
Pulmonary Conditions	9,294	17,699	$507	$639
Arthritis	4,573	7,640	$701	$1,282
Mental Disorders	4,658	10,984	$1,242	$972
High Cholesterol	1,383	7,427	$278	$618
Hypertension	9,372	11,988	$456	$664
Back Problems	4,581	8,144	$1,457	$1,202
Upper Gastrointestinal	2,618	7,042	$854	$769

Source: "The Rising Prevalence of Treated Diseases." Health Affairs, 27 June 2005

Treatment of **chronic conditions** dominates our healthcare spend. Eighty-eight percent of prescriptions written, 72 percent of physician visits and 76 percent of inpatient stays involve treating chronic disease. Furthermore, the more chronic conditions a person has, the greater the utilization of healthcare services. Spending on people with five or more chronic conditions is about 14 times greater than for someone without chronic conditions. Individuals with multiple chronic conditions account for two-thirds of all prescriptions filled.[13]

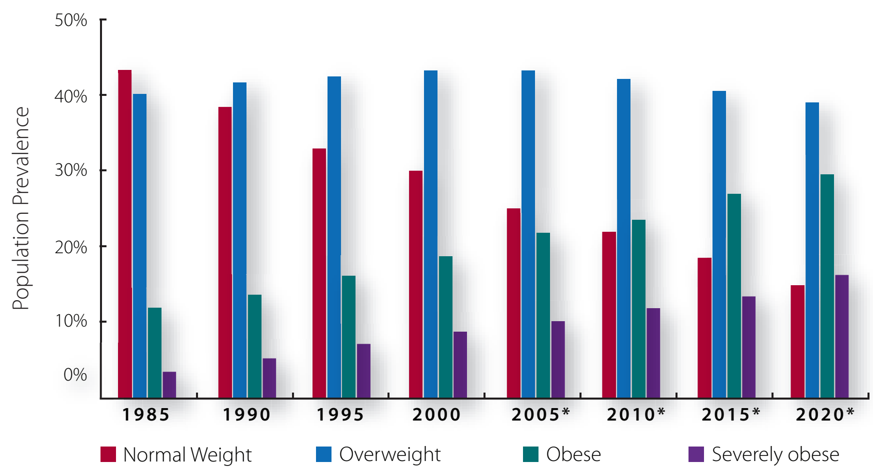
The Health of Aging America

Is this investment in care paying off? According to a recent report from the U. S. Census Bureau, the **health of our older citizens** is improving. Life expectancy is increasing, chronic disability among the elderly has declined and the prevalence of chronic disease conditions among the elderly has dropped. In fact, about three-fourths of non-institutionalized persons aged 65 to 74 consider their health to be good, very good or excellent. Commenting on the report's findings, the Director of the Behavioral and Social Research Program at the National Institute on Aging, said our image of aging may be "20 years out of date."[14]

As the first Baby Boomers near their 60s, this news is encouraging. However, it's important to recognize that there will be **inherent healthcare costs for maintaining quality of life** throughout those additional years of life expectancy. In fact, the greatest rate of increase in health spending has been among those with no limitations in activities of daily living. This could reflect increased spending to preserve and restore health.[15] Moreover, Caremark 2005 Book of Business drug utilization data indicates that the various generations may have distinct attitudes and expectations about health and healthcare. (*See pages 12-13.*) Current data may not reflect future health behavior trends.

Figure 6

Trends in weight among men ages 50-69, selected years 1985-2020.



Notes: Normal Weight: body mass index (BMI) greater than 18.5, less than 25; overweight: BMI greater than 25, less than 30; obese: BMI greater than 30, less than 35; severely obese: BMI greater than 35. Predicted values holding sociodemographics (age group, race/ethnicity) constant at 2002 level, based on ordered logit model of weight class.
* Data for 2005-2020 are extrapolated.

Source: "The Effects of Obesity, Smoking and Drinking on Medicaid Problems and Costs."
Data source: Behavioral Risk Factor Surveillance System, various years

Acomplia™, with an indication for obesity, is one of the few anticipated blockbuster launches of 2006.

The Obesity Epidemic

Between **3 and 7 percent of healthcare costs** in the U.S. are attributable to overweight- and obesity-related diseases such as osteoarthritis, heart disease, hypertension, high cholesterol, stroke, diabetes and certain cancers.[16] Moderate to severe obesity is associated with an average increase of 44 percent in healthcare costs[17] and a 77 percent increase in medication costs compared to people of normal weight.[18] Of particular concern are rising rates of childhood obesity and overweight. As with adults, obesity increases the risk of hypertension, elevated cholesterol and type 2 diabetes in children. Moreover, obesity in childhood is a key predictor of adult obesity.

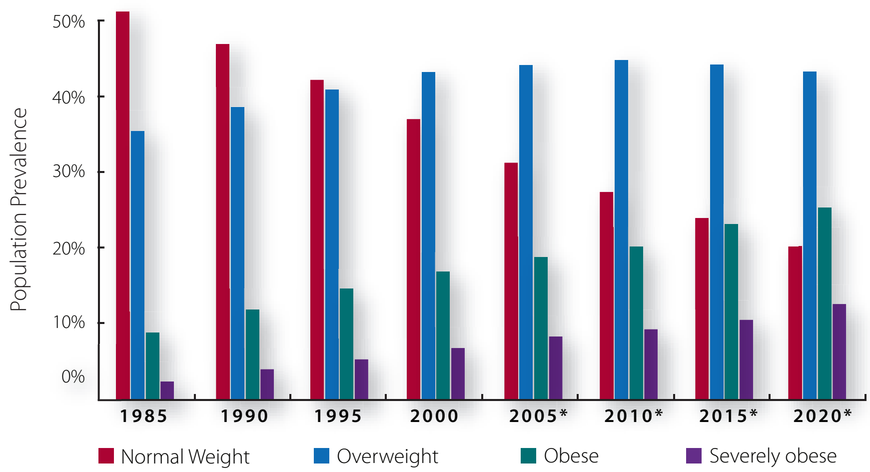
Caremark reports on the cost of obesity-related lost productive time.

A **recent Caremark study** provides the first national estimates that capture the cost of work loss resulting from both presenteeism (reduced performance) and absenteeism. Caremark analysts found that obese employees are about 20 percent more likely to lose productive time because of their health than their normal weight or overweight counterparts. Obese workers cost U.S. employers an excess of **$11.7 billion per year** compared with normal-weight workers, according to the study published in the *Journal of Occupational and Environmental Medicine* in December 2005.

Analysts also found that two-thirds of obese workers' lost productive time (LPT) occurred while they were on the job, demonstrating that reduced performance known as presenteeism has far more impact than absenteeism. The study also estimates that health-related LPT costs employers an average of $1,627 per obese worker per year.[19]

Figure 7

Trends in weight among women ages 50-69, selected years 1985-2020.



Notes: See Figure 6 for weight classification. Predicted values holding sociodemographics (age group, race/ethnicity) constant at 2002 level, based on ordered logit model of weight class.
* Data for 2005-2020 are extrapolated.

Source: "The Effects of Obesity, Smoking and Drinking on Medicaid Problems and Costs."
Data source: Behavioral Risk Factor Surveillance System, various years

The Year Ahead

While there were certainly implementation difficulties with the new Medicare drug benefit, a large number of beneficiaries had access for the first time to a range of choices for drug coverage. The experience with **Medicare Part D** and its impact on the marketplace will be closely watched in the months ahead.

2006 also promises **great gains on generics**. Brand name drugs with $10 billion in current sales are expected to face first-time generic competition in the first six months alone. **Specialty drugs** will continue to outpace the market with a pipeline rich with new products as well as the promise of expanding indications for existing top sellers. And **consumer-directed health plans** will be offered by more and more plan sponsors; how they affect consumer behavior and healthcare spending will be closely watched and evaluated.

Caremark, as one of the nation's premier health solutions providers, is committed to helping our clients make the most of the opportunities ahead. In this trend report, you'll learn about our Book of Business performance in 2005 and about our innovative and data-driven solutions to improve outcomes, reduce costs and achieve your benefit plan goals in 2006 and 2007.

Looking at Prescription Drug Utilization by Generation

Baby Boomers and their parents account for nearly two-thirds of the Caremark 2005 Book of Business spend, and they share the same top therapeutic category – the industry-leading antihyperlipidemics, the cholesterol lowering drugs that are also the top category for the oldest segment, the GI generation. Not surprisingly, Generation X and Millennials – today's children, adolescents and young adults – don't have the same health concerns and demonstrate different drug-related behavior.

Under-20 **Millennials**, the children of younger Boomers and Generation X, may not be making their own drug purchases but – with a generic dispensing rate (GDR) of 53.5 percent – clearly are becoming accustomed to utilizing generics. Their top three therapeutic categories include drugs used to treat asthma, attention deficit disorder and dermatological conditions. As might be expected, antibiotics also figure heavily in their top categories.

Antidepressants lead the therapeutic categories for **Generation X**, young adults (ages 21 to 41) starting out in life. Contraceptives account for the next largest group of claims for this demographic group, and anti-ulcer drugs, dominated by proton pump inhibitors, come in third. Availability of generics in each of these top categories probably bolsters Generation X's impressive GDR – 55.2 percent.

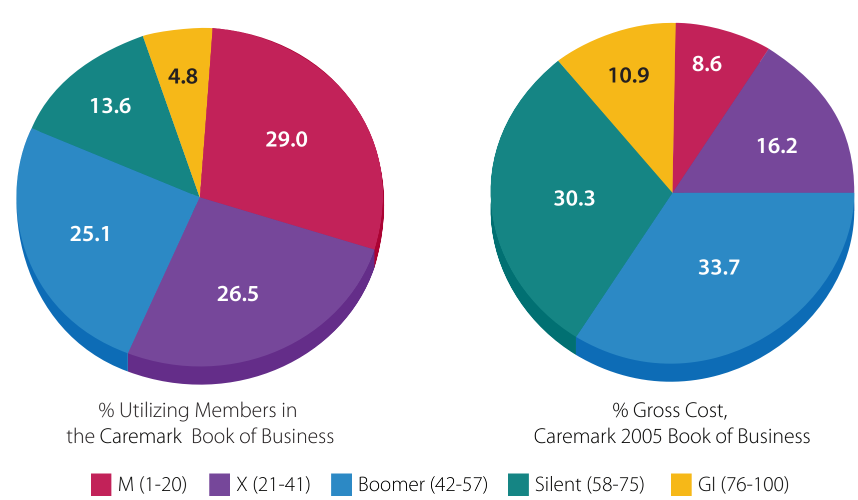
Boomers, ages 42 to 57, value quality of life highly and consider pharmaceuticals one route to achieve that quality. This generation is more likely to use antidepressants than their parents and less than their children; it's their number two category. Anti-ulcer drugs come in third for Boomers, the same ranking as for Generation X. Other top categories for Boomers – the cholesterol lowering drugs, antihypertensives and antidiabetics – are likely to continue to dominate drug spend as this group ages.

The **Silent Generation**, ages 58 to 75, were born between 1931 and 1948 and grew up during the Depression and World War II. Sandwiched between purposeful GIs and free-spirited Boomers, they're much less likely to use antidepressants than

The Baby Boomer population bulge – close to 76 million individuals – is a major component of the "Aging of America."

Figure 8

In the Caremark Book of Business, Baby Boomers represent 25 percent of utilizing members and about a third of gross costs.



Source: Caremark 2005 Book of Business data. Generations defined as in "Pharma 2005, Marketing to Individuals." PricewaterhouseCoopers, 1999.

Figure 9

Top 10 Therapeutic Classes by Generation

2005 Book of Business Rank	Therapeutic Class	X	Boomers	Silent	GI
1	Cholesterol lowering	10	1	1	1
2	Anti-ulcer	3	3	2	2
3	Antidepressants	1	2	6	10
4	Antihypertensives	18	4	3	3
5	Antidiabetics	11	5	4	5
6	Antiasthmatics/ Bronchodilators	6	9	7	6
7	Analgesics-Anti-inflammatory	9	6	5	12
8	Misc. Endocrine & Metabolic	20	15	8	4
9	Analgesics-Opioid	8	8	13	15
10	Anticonvulsants	5	10	14	19

Source: Caremark Book of Business data.

The top therapeutic categories of Millennials include: (1) antiasthmatics; (2) stimulants used for ADHD, narcolepsy, obesity, and anorexia; (3) dermatologicals; (4) endocrine and metabolic agents (growth hormone, for example); and (5) antipsychotics.

younger people. Antidepressants rank sixth among their top therapeutic categories. With that exception, their top categories closely follow those of their Boomer children.

Between 76 and 100 years old, the **GIs** are the eldest segment. Antidepressants drop to number 10 in utilization for this group. It's probable that economic concerns as well as product availability among anti-ulcer drugs, antihypertensives and anti-diabetics push their generic utilization higher, to 56 percent.

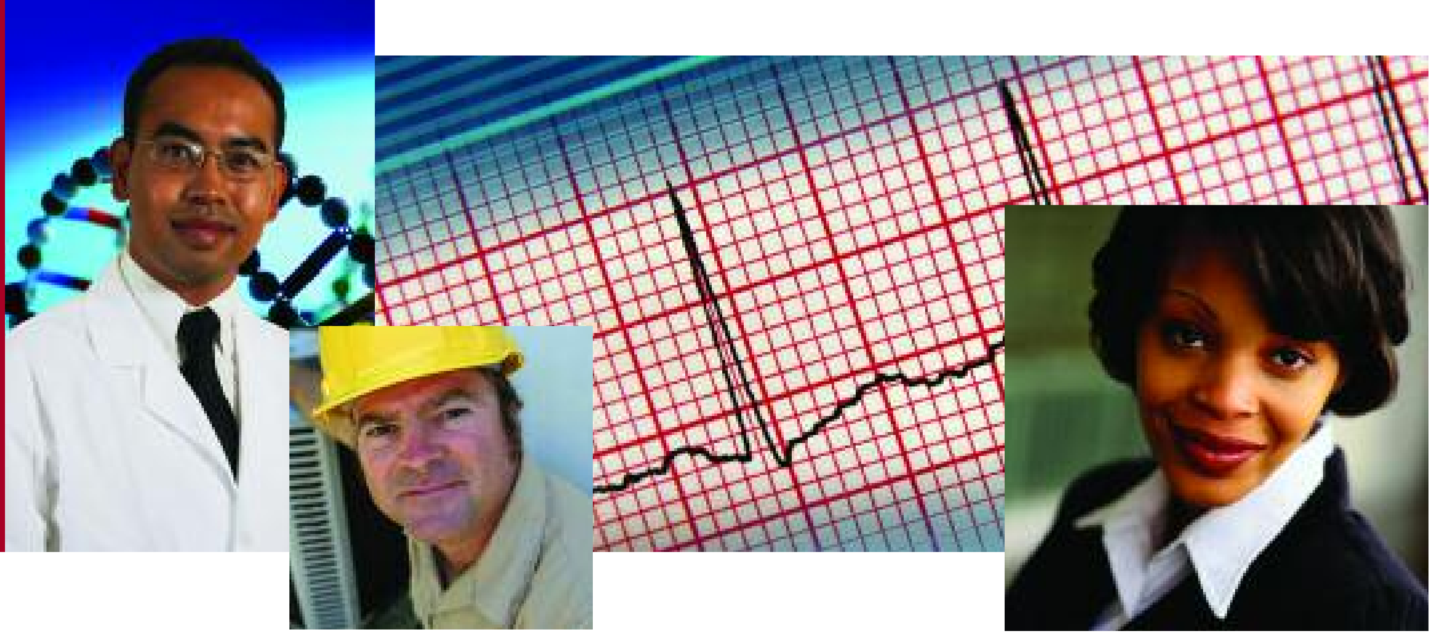
The U.S. Census Bureau predicts that by 2030 almost one out of five Americans, and all Boomers, will be 65 or older.

A generational perspective on managing prescription utilization and cost

The generations in their prime working years – Generation X and the Baby Boomers – grew up in an era of increasing availability and utilization of prescription drugs. As they age, it's reasonable to expect that they will continue to rely on pharmaceuticals to maintain their health and quality of life. Looking at long-term cost management, plan sponsors might ask:

- Is there more we can do to **promote utilization of generics**?
- How will the launch of **generic statins** affect this highly utilized class?
- How does our population compare in its **drug mix for antidepressants**?
- Are we adequately addressing **adherence to therapy**, particularly for individuals with asthma, diabetes and hypertension? Can we do more to support adherence and thereby better manage overall healthcare costs for the long term?
- Have we invested sufficiently in **wellness education and condition management** programs?

*Contact your Caremark account representitive to find out more about **CareSolutions** targeted for the needs of your specific population.*



Caremark 2005 Pharmacy Benefit Trend:
7.9% PMPY Book of Business

For the third year in a row, Caremark maintained a single-digit Book of Business (BOB) trend in 2005. At 7.9 percent per member per year (PMPY) our BOB trend* is significantly less than industry forecasts. In particular, Caremark trend management solutions helped our clients maximize the opportunities presented by the increasing availability of generics.

- Plans implemented recommended changes and programs that **encouraged utilization of generics and mail service,** and supported the rapid uptake of newly launched generics.
- Plans also took advantage of programs that **educated plan participants about generics and raised awareness** of their availability and savings potential.
- **Major launches included generic equivalents** for Duragesic, OxyContin, Ultracet (all analgesics); antibiotics Zithromax and Biaxin; and blockbuster antihistamine Allegra.
- With the increasing number of patent expirations and new generic launches, there are now **generic products in most of the major therapeutic classes**.

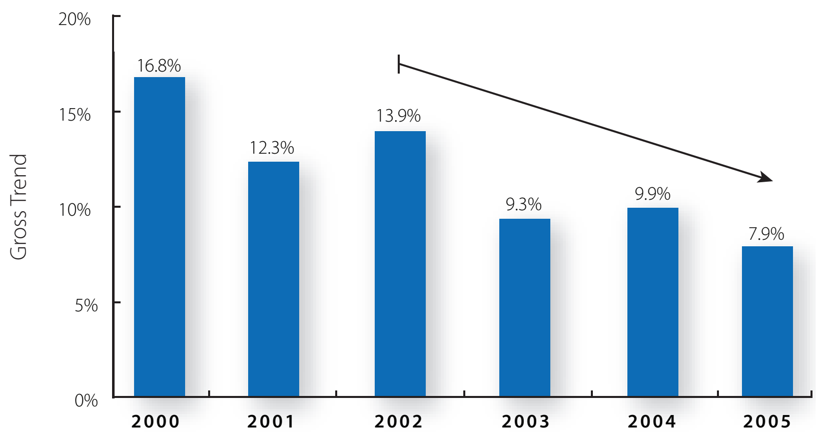
7.0% PMPY: Trend without Specialty Pharmacy

This year, for the first time, Caremark is reporting trend with and without specialty pharmacy to emphasize the significant growth of this distinct part of the pharmaceutical market. For a complete rundown on specialty pharmacy spend, trend and drivers, see pages 23-30.

*Caremark 2005 Book of Business (BOB) trend is the percentage change in gross drug spend from 2004 to 2005. The trend is based on 24 months of data, representing Caremark clients with integrated benefits and is reported on a per member per year (PMPY) basis. Gross spend is the cost to clients and their plan participants after discounts. Impact of drivers is determined multiplicatively for actuarial alignment according to industry standards.

Figure10

Caremark maintains single-digit trend for the third consecutive year.



Source: Caremark Book of Business data. Data for 2000-2004 reported per employee per year (PEPY). 2005 reported per member per year (PMPY). Trend numbers include Specialty/Biotech.

- With all these factors, **generic dispensing rates** improved throughout the year for the Caremark Book of Business, reaching 54.2 percent in December and **averaging 52.6 percent overall**, compared to 48.2 percent in 2004.
- With the increasing competition in the generic market, **price increases** for generics continued to lag significantly behind those for brand name drugs – 0.0 percent increase for generics while brand name drugs increased by 6.5 percent.
- While generic launches are increasingly aggressive, there have been fewer new brand name product approvals and **no blockbuster brand name drug launches** for the past few years.
- **Safety concerns** continued to decrease utilization in major therapeutic classes – the anti-inflammatory analgesics and the antidepressants.
- **A weak flu season** also helped to keep trend numbers down.

Impact of Trend Drivers – Drug Mix: 0.0%

Caremark strategies helped our clients maximize generic opportunities and derail drug mix as a driver. When we look at trend without specialty pharmacy, trend for drug mix was negative – a minus 0.7 percent.

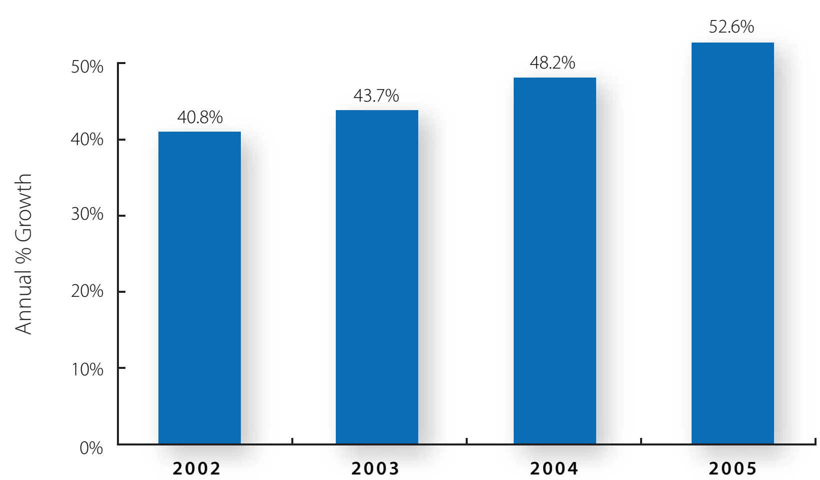
Over the last few years, an increasing number of blockbuster brand name drugs faced generic competition for the first time. Caremark clients benefited significantly from these opportunities by implementing benefit designs that encouraged utilization of generics and promoting plan participant education about these cost-effective alternatives. Our 2005 **generic dispensing rate rose to 52.6 percent**, up from 48.2 percent in 2004. Major first-time generics in 2005 included the non-sedating antihistamine fexofenadine (Allegra) and the antibiotic azithromycin (Zithromax).

Continued on next page

The impact of drug mix was also minimized by the **ongoing scarcity of blockbuster brand name drug launches.** As has been true for the last few years, the traditional brand name drug pipeline produced few high-impact new products in 2005. The FDA approved 18 new molecular entities (NMEs, or new drugs) in 2005. This was a nearly 42 percent decrease from the 31 NME approvals in 2004. Notable 2005 launches include the insomnia agents Lunesta (eszopiclone) and Rozerem (ramelteon); Lyrica (pregabalin), which is indicated for the treatment of pain associated with diabetic peripheral neuropathy; and several products for diabetes including Symlin (pramlintide) and Byetta (exenatide).

Figure 11

2005 overall generic dispensing rate (GDR) rose to 52.6%.



Source: Caremark Book of Business data.

Figure 12

Generics reduced Caremark clients' spend by 29% in 2005.

Generic Drug	Reference Brand	Therapeutic Class	Brand Gross Cost Per Day's Supply	Generic Gross Cost Per Day's Supply	BOB Spend % Reduction
fluoxetine HCL	Prozac	Antidepressant	$6.36	$1.00	1.75%
atenolol	Tenormin	Antihypertensive	$1.64	$0.27	1.09%
metformin HCL	Glucophage	Antidiabetic	$2.25	$0.87	0.95%
lisinopril	Zestril	Antihypertensive	$1.30	$0.48	0.87%
hydrocodone w/acetaminophen	Vicodin	Analgesics, narcotic	$3.64	$1.06	0.80%
All Other Generics					23.55%
Total					**29.0%**

Source: Caremark 2005 Book of Business data

CareSolutions

Targeted mailing increases generic utilization by 9% at mail. Encourages cost-conscious consumers.

A third party administrator (TPA) wanted to **modify plan participant behavior** through plan design change. Their experience demonstrates that targeted communications can effect change.

In this case, Caremark developed and sent personalized mailings to plan participants using a specific ACE (Angiotensin-Converting Enzyme) inhibitor for which there are no direct generic alternatives. The mailing alerted recipients to the availability of **indirect generic alternatives for their drug** – generic drugs in the same therapeutic class but not the same chemical product as their reference brand name drug. The mailing specified the projected annual savings afforded by using the suggested generic, provided education about the safety and value of generics and encouraged dialogue with their physician. The mailing also included physician-directed information about potential savings for the plan participant and the clinical rationale for evaluating the change.

Figure 13

Results: 9% increase in generic claims at mail service

Results of Targeted Mailings	% Generic Claims		Net Savings per Generic Conversion	
	Pre-mailing	Post-mailing	Plan	Plan Participant
Using mail pharmacy	0.8	9.8	$82.43	$16.53
Using retail pharmacy	1.3	6.1	$25.33	$11.62

Utilization and costs were compared for six months pre- and post-mailing.

Getting to The Right Drug through CareSolutions

- New in 2006: **Online – the Therapeutic Alternatives Database**
  Plan participants enter the name of a brand name drug on Caremark.com and find out in a few seconds what clinically appropriate, same and related class as well as generic and over-the-counter alternatives are available.
- **ePrescribing**
  Caremark delivers information about generic and preferred drug options right to the physician's hand using iScribe®, the Caremark ePrescribing formulary tool.
- **Count on Generics®**
  Ready-to-use communication tools educate plan participants on the safety, value and efficacy of generic medications.

Ask your Caremark account representative to learn more about all the generic maximization programs available through CareSolutions.

The Right Drug – promoting lower-cost, clinically appropriate drugs.

Impact of Trend Drivers – Price: 3.7%

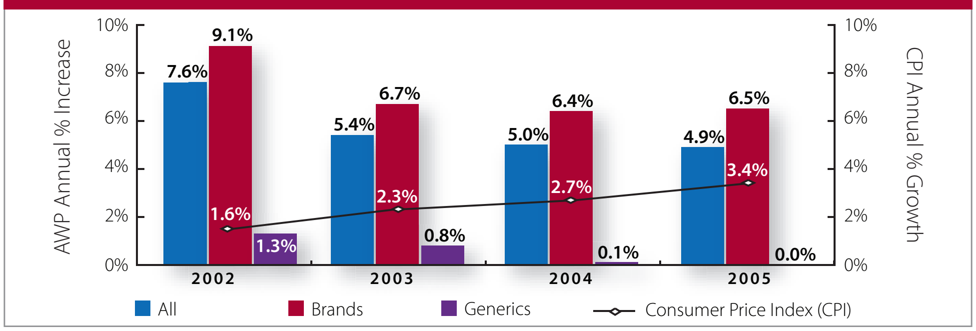
Overall price inflation has held fairly steady for the last three years, with increases for brand name drugs averaging around 6.5 percent. Inflation for generics has decreased in the same period; in 2005, increases for generics were negligible – 0.0 percent. The prescription marketplace continues to present many challenges and uncertainties for brand name drug manufacturers – the effects of the Medicare drug benefit, safety concerns, greater FDA caution, pricing pressure from payors, a less-than robust pipeline, and impending patent expirations for top-selling products. These pressures may well result in accelerated manufacturer price increases in the coming months.

From 1994 to 2004, the number of prescriptions purchased increased 68 percent, compared to a U.S. population growth of 12 percent.

Kaiser Family Foundation, using data from IMS Health and the U.S. Census Bureau

Figure 14

Average Wholesale Price (AWP) inflation: generics hold the line.



Source: Caremark Book of Business data.

Impact of Trend Drivers – Utilization: 4.1%

Utilization was again the major driver of trend in the Caremark 2005 BOB, as it was throughout the United States. Factors that drive utilization increases include:

- The **aging** of our population
- The increased incidence and treatment of **chronic conditions**
- **Long-term use** of drug therapy to manage chronic conditions
- **More aggressive guidelines** for disease diagnosis and treatment
- **New drugs**, particularly those that represent breakthrough therapies or new benefits
- Approval of **additional indications** for existing drugs
- **Direct-to-consumer (DTC) pharmaceutical marketing**, which can effectively promote specific products, increase disease awareness and promote long-term product utilization

Figure 15

Drug use rises dramatically as people grow older.

Age Range	Annual Average Drug Cost
Under 65	$620.00
Over 65	$1,754.30

Source: Caremark 2005 Book of Business data

Figure 16

Caremark 2005 Top 10 Therapeutic Classes

2005 Rank	2004 Rank	Therapeutic Class	Gross Trend	Utilization Trend	% of Total Spend	Comments
1	1	**Antihyperlipidemics,** cholesterol-lowering agents, dominated by statins	13.7%	10.5%	10.6%	Treatment guidelines promoting aggressive lowering of LDL (low density lipoprotein) continue to drive utilization. Projected availability of generic statins in 2006 should help moderate trend.
2	3	**Anti-ulcer Agents,** dominated by proton pump inhibitors (PPIs)	5.0%	2.3%	7.5%	Utilization trend and gross trend increased in 2005, in part due to use of PPIs in combination with NSAIDs as replacement for COX-2 therapy.
3	2	**Antidepressants,** leading categories include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs)	-0.3%	1.3%	7.0%	Generic SSRIs have helped lower trend, as have safety concerns related to increased risk of suicidal thinking, particularly among pediatric utilizers. SNRIs (Cymbalta, Effexor) have a different mode of action and no generic versions and are expected to increase in utilization.
4	4	**Antihypertensives,** includes ACE Inhibitors, Angiotensin II Receptor Antagonists (ARBs)	8.6%	5.3%	5.3%	Incidence of hypertension is related to aging and obesity of population. Generic ACE inhibitors have helped lower trend since 2004. ARBs and ARB combination drugs have no generic equivalents and have contributed to upward trend.
5	6	**Antidiabetics,** includes insulin, insulin sensitizing agents and other antidiabetic drugs	14.1%	9.7%	4.9%	Diabetes has been termed an epidemic in the U.S. and is often poorly controlled. New products – including Symlin, Byetta, Levemir, and Exubera, an inhaled insulin – may offer hope of better control for some patients.
6	7	**Antiasthmatic and Bronchodilator Agents,** includes inhaled corticoseroids, various bronchodilating agents and a biotech product, Xolair	17.6%	8.9%	4.9%	Asthma drugs, led by Singulair and Advair Diskus, posted the highest gross trend of the top therapeutic classes. Among the reasons: Current treatment guidelines stress the utilization of chronic medications to prevent exacerbation of the condition. Singulair received approval for expanded indications – allergy treatment. Also, class includes Xolair, a specialty asthma product, and Spiriva, which offers once-a-day dosing for chronic obstructive pulmonary disease. However, the FDA recently added a black box warning to Advair and Serevent related to increased risk of asthma-related death. Such warnings typically have long-term effects on utilization trends.
7	5	**Anti-inflammatory Analgesics,** includes NSAIDs, COX-2 inhibitors and biotech agents used for rheumatoid arthritis	-13.6%	-23.2%	4.1%	Declining utilization of COX-2 inhibitors dropped this class from #5 in 2004. However, the class includes specialty products for rheumatoid arthritis, and these products have demonstrated trend near 40 percent, largely related to expanding indications.
8	8	**Misc. Endocrine and Metabolic Agents,** led by calcium/bone regulators (osteoporosis drugs), also includes specialty products: growth hormone agents and fertility drugs	13.2%	5.3%	3.1%	Aging of the population, new products, and increasing disease awareness have led to continued increases in the treatment of osteoporosis.
9	9	**Analgesics, Opioid,** narcotic agonists	6.0%	10.6%	2.9%	A greater focus on pain treatment and chronic pain management is increasing utilization of this class. Gross trend was lowered in 2005 due to launches of generic forms of Duragesic (fentanyl) and OxyContin (oxycodone).
10	10	**Anticonvulsants,** anti-seizure agents	5.1%	6.5%	2.9%	Off-label but acceptable use for pain and neuropathic pain have driven trend for this class upward for several years. Launch of the generic for Neurontin (gabapentin) was a major contributor to reducing trend in the class (19% in 2004 to 5.1% in 2005). New product Lyrica (pre-gabalin), an anticonvulsant with an indication for neuro-pathic pain, is expected to bolster the class.
Top 10 Therapeutic Classes, % of Total Spend					**53.2%**	

Classes ranked by gross cost in the Caremark 2005 Book of Business.

Caremark Mail Service pharmacy supports pharmacy and healthcare cost management

Promoting the utilization of the **lowest cost delivery channel** is a fundamental strategy in pharmacy trend management, but the benefits of mail service utilization go beyond the cost savings of improved discounts and reduced administrative fees. Mail service supports the use of lower cost, clinically appropriate drugs, facilitates clinical management and reinforces overall healthcare management.

Benefits to the plan increase when plan participants access **Caremark.com** to order refills through the mail service pharmacy. While on the Web site, they can compare costs and access drug and health information. A new feature on Caremark.com – the Therapeutic Alternatives Database – provides information on clinically appropriate over-the-counter, generic and preferred brand name treatment options available in the same and related therapeutic classes and encourages plan participants to discuss these options with their physician as potential cost-saving options.

The Right Place – Supporting the lowest-cost delivery channel.

Mail Service Pharmacy – The Right Drug

Mail service pharmacy provides

- Greater than 95 percent generic substitution rate (2005)
- Rapid availability and dispensing of new generic launches
- Auto substitution (generics for brand name drugs) when appropriate

Mail Service Pharmacy – The Right Way

Mail service pharmacists support plan participant adherence

- When there is a potential drug interaction
- When a change in prescribing guidelines may affect dosing or other aspects of the prescription
- When the plan specifies prior authorization for a particular drug
- To request permission to substitute a generic for a prescription designated as "dispense as written"

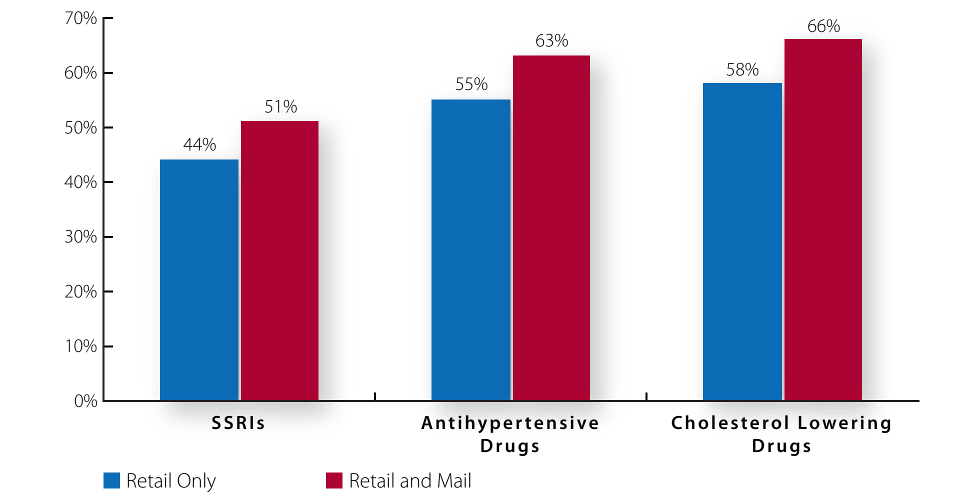
Mail Service Pharmacy – Adherence to Care

Mail service pharmacy supports plan participant adherence

- Providing e-mail reminders when it's time to order refills
- Making prescriptions more affordable
- Providing relevant drug and health information to help manage plan participants' conditions

Figure 17

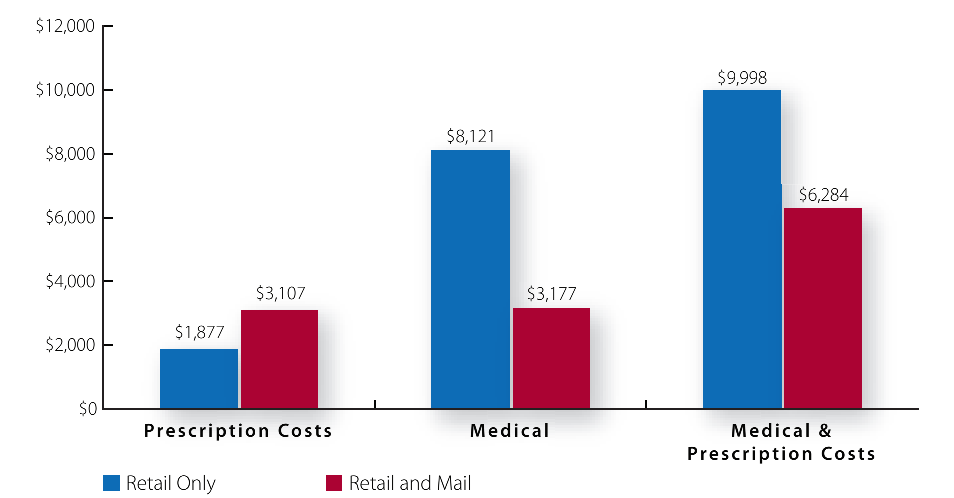
Plan participants who use Caremark Mail Service pharmacy have higher persistency than those who use only retail pharmacies.



Source: Caremark 2004-2005 Book of Business data
Note: Persistency provides one measure of compliance. Specifically, persistency measures duration of therapy by evaluating number of days supply of medication over a specific period. Overall compliance can result in significant reduction in preventable complications and associated medical costs.

Figure 18

Plan participants who take antihypertensives and use Caremark Mail Service pharmacy have lower overall healthcare costs than these who use only retail pharmacies.



Source: Caremark 2005 Book of Business data

Caremark Mail Service pharmacy helps manage pharmacy trend three ways – it supports utilization of lower-cost, clinically appropriate drugs; enhances opportunities for clinical management of prescriptions; and provides a low-cost delivery channel option. *Contact your Caremark account representative to discuss the benefits mail service pharmacy offers for your plan and plan participants.*

Figure 19

Forecasting Trends
Top 20 Therapeutic Categories*

Therapeutic Categories	Primary Use	2006 Expected Trend†	Recent and 2006 Anticipated Brand Launches	Anticipated Generic Launches	Current Generic Opportunities	OTC Opportunities
Cholesterol-Lowering Agents	high cholesterol	▲	Vytorin, Caduet	Zocor	lovastatin, pravastatin	
Proton Pump Inhibitors	anti-ulcer	▬			omeprazole	Prilosec OTC
SSRIs	depression	▼		Zoloft	fluoxetine, paroxetine, citalopram	
Sympatho-mimetics	asthma	▲			albuterol, terbutaline	
NSAIDs	pain	▬	Arcoxia, Dynastat	Mobic	ibuprofen, naproxen, nabumetone	Advil, Motrin, Aleve
Calcium Channel Blockers	hypertension	▬			cartia XT, verapamil SR, nifedical XL	
Anticonvulsants	pain	▲	Lyrica, Rufinamide	Trileptal, Zonegran	gabapentin, carbamazepine, primodone	
Calcium Regulators**	osteoporosis	▲	Boniva, Fosamax Plus D, Actonel with Calcium, Oporia, Preos	Miacalcin Nasal	none available	
Antihistamines Non-Sedating	allergy	▼	Allegra-D 24 Hrs	Allegra-D	fexofenadine	Claritin, Claritin-D, Alavert
Insulin Sensitizing Agents	diabetes	▲	ACTOplus met		none available	
Platelet Aggregation Inhibitiors	anti-clotting	▲			cilostazol, dipyridamole, ticlopidine	
Narcotic Agonists	pain	▲			tramadol, fentanyl, morphine sulfate, oxycodone	
ACE Inhibitors	hypertension	▬			lisinopril, enalapril, quinapril	
Multiple Sclerosis Agents**	MS	▲	Tysabri (relaunch)		none available	
SNRIs	depression	▲	Cymbalta		none available	
Rheumatoid Arthritis Agents**	RA	▲	Orencia		none available	
Angiotensin II Receptor Antagonists	hypertension	▲			lisinopril, enalapril, quinapril	
Insulin	diabetes	▲	Apidra, Byetta, Exubera, Levemir, Symlin		none available	
Non-Barbiturate Hypnotics	insomnia	▲	Ambien CR, Lunesta, Indiplon	Ambien	temazepam, triazolam, flurazepam	
Nasal Steroids	allergy	▼			flunisolide, fluticasone propionate	Claritin, Claritin-D, Alavert

▲ Estimated greater than 4% increase

▬ Estimated flat trend

▼ Estimated greater than 4% decrease

* Top 20 Caremark Book of Business selected therapeutic categories.

** Category contains specialty products.

† Expected trend is projected based on marketplace events only and is void of plan design, clinical programs and other initiatives that may impact trend.

This analysis is an estimate for information 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 of return on investment in the future.

2006 — Focus on Specialty Pharmacy

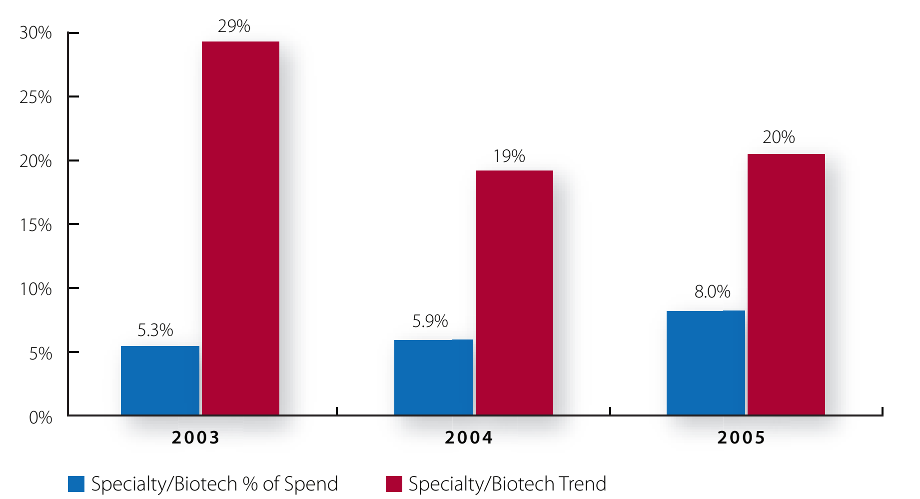
Biotech and specialty pharmaceuticals offer groundbreaking medical advances in the treatment of complex illnesses. These products are high cost, but have made the most profound difference to individuals with conditions such as multiple sclerosis (MS) and rheumatoid arthritis (RA), reducing pain and discomfort, improving quality of life and slowing the progression of disease. With a flourishing pipeline and multiplying indications for products already on the market, the sector is seeing an astonishing growth in utilization. There's no question that specialty pharmaceuticals are changing standards of care and will play an ever-greater role in our nation's healthcare in the years to come.

"Specialty drugs… are taken by just 1 percent of Americans, yet account for 15 percent of total U.S. drug spending."

Crain's Chicago Business, January 2, 2006

Figure 20

In the 2005 Caremark Book of Business, Specialty/Biotech Spend reached 8 percent.



Source: Caremark Book of Business data

Figure 21

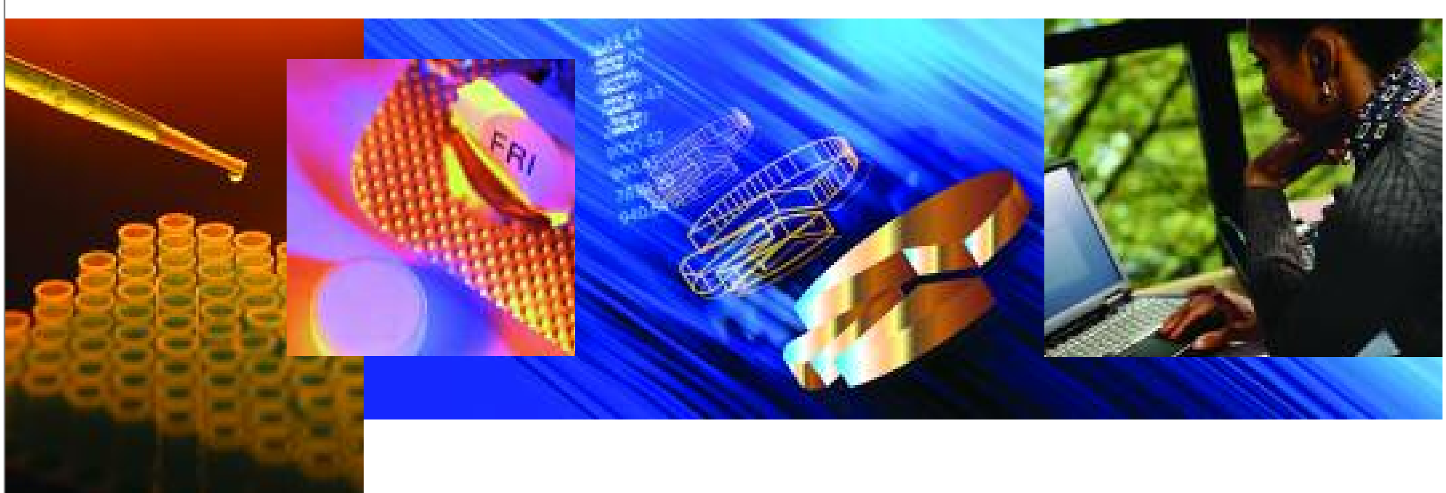
2005 Top 10 Specialty/Biotech Products

2005 Rank	2004 Rank	Drug	Common Indication	Drug Utilization Trend
1	1	**Enbrel**	Rheumatoid arthritis	26.6%
2	2	**Avonex**	Multiple sclerosis	-5.7%
3	4	**Humira**	Rheumatoid arthritis	38.4%
4	3	**Copaxone**	Multiple sclerosis	12.5%
5	5	**Procrit**	Hematological used for anemia	6.5%
6	6	**Cellcept**	Immunosuppressive used with organ transplants	12.3%
7	8	**Gleevec**	Antineoplastic used to treat a rare cancer	16.0%
8	9	**Rebif**	Multiple sclerosis	25.0%
9	7	**Prograf**	Immunosuppressive used with organ transplants	13.5%
10	10	**Betaseron**	Multiple sclerosis	2.2%

Source: Caremark 2005 Book of Business data
Drugs ranked by gross cost in the Caremark 2005 Book of Business
Utilization Trend = 2005 Days Supply Per Month (PMPM) ÷ 2004 Days Supply PMPM

Caremark 2005 Specialty/Biotech Trend: 20.4%, Driven by Utilization

Growth in utilization is the major driver behind specialty's double-digit trend. Despite significant launches and the approval of additional indications for existing products, Caremark Specialty Pharmacy management programs kept specialty trend to 20.4 percent in 2005 – below industry forcasts. Over the year, specialty pharmaceuticals grew from less than 6 percent of our gross Book of Business (BOB) spend to 8 percent – more than a 30-percent increase. Growth in utilization, at 11.4 percent, was consistent with market rates although it was more than twice the overall Caremark BOB rate.



The Specialty Pipeline – New Drugs and Indications Fuel Growth in Utilization

While the specialty segment currently accounts for about 15 percent of pharmaceutical spending in the United States, the specialty pipeline is approaching parity in terms of the number of potential new products. The pipeline is expanding in scope as well as volume. An increasing number of products are aimed at **chronic conditions** – RA, psoriasis, asthma – with **higher incidence rates** than the "orphan" diseases that first dominated the specialty sector. For example, three products for macular degeneration are expected to win FDA approval this year, and there are seven additional drugs for the condition in earlier stages of development. More than two million people in the U.S. have wet age-related macular degeneration (AMD), and approximately 200,000 new cases are diagnosed each year. As our population ages, AMD incidence is expected to increase. Products in the pipeline are expected to offer better outcomes than the few treatments currently available.

Continued on next page

Figure 22

Top 10 Specialty Therapeutic Classes

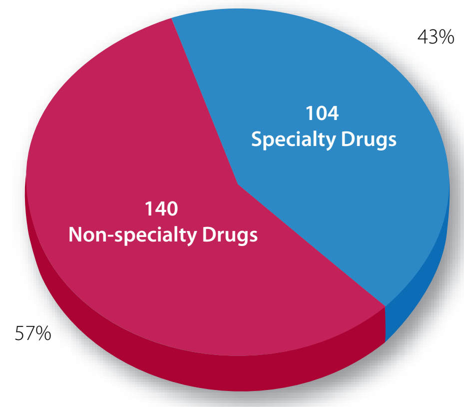
Therapeutic Class	Leading Specialty Drugs	Average Annual Cost of Therapy
Rheumatoid Arthritis	Enbrel, Remicade, Humira, Kineret, Orencia	\$15,000 - \$20,000
Multiple Sclerosis	Betaseron, Avonex, Rebif, Copaxone	\$20,000 - \$24,000
Oncology	Gleevec, Tarceva, Nexavar, Revlimid, Sutent, Iressa	\$40,500 - \$95,000
Hematopoietics (used as an adjunct to cancer and other therapies)	Procrit, Epogen, Neupogen, Neulasta, Aranesp	\$5,000 - \$20,000
Immunosuppressants (used with organ transplants)	Cyclosporine, Cellcept, Zenapax, ATGAM	\$10,000 - \$45,000
Human Growth Hormone	Nutropin, Humatrope, Genotropin, Norditropin, Tev-Tropin	\$18,000 - \$20,000
Hepatitis C	Rebetron, Pegasys, Peg-Intron, Infergen	\$24,000 - \$30,000
Infertility	Gonal F, Follistim	\$10,000 - \$20,000
Hemophilia	Recombinant Blood Factor Products	\$150,000 +
Osteoporosis	Forteo	\$9,000

Ranked by gross cost in the Caremark 2005 Book of Business

This page contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with Caremark.

Figure 23

The Pharmaceutical Pipeline in 2006: Potential New Pharmaceuticals in Late-Phase Development



Source: RxPipeline Insider, February 2006

> "Experts estimate that 4 percent of Americans will be using [specialty drugs] by 2010, accounting for 60 percent of drug spending."
>
> Crain's Chicago Business, January 2, 2006

Also, an increasing number of specialty pipeline products – including oncologics such as the recently approved Sutent (sunitinib malate) – are being developed for **oral administration** rather than for injection, infusion or inhalation. While oral therapies provide easier administration than specialty injectables, many have complex side effect profiles, or are often used in conjunction with existing therapies, or are used as a first-line therapy before a more intense injectable medication is needed. The complexity of these therapies underscores the need for appropriate management of these individuals through specialty pharmacy services.

Oncologics continue to dominate the pipeline and present some of the most exciting new science. Products such as **cancer-preventive vaccines** and personalized drugs derived from an individual's own tumor are likely to have profound effects on cancer treatment.

Much growth in specialty utilization is related to **expanding indications** for existing products. For example, Humira (adalimumab) was approved in 2002 for the treatment of symptoms associated with moderate to severe RA. Today it has been approved for five additional indications, including the treatment of psoriatic arthritis. Additional indications for Humira are under consideration at the FDA.

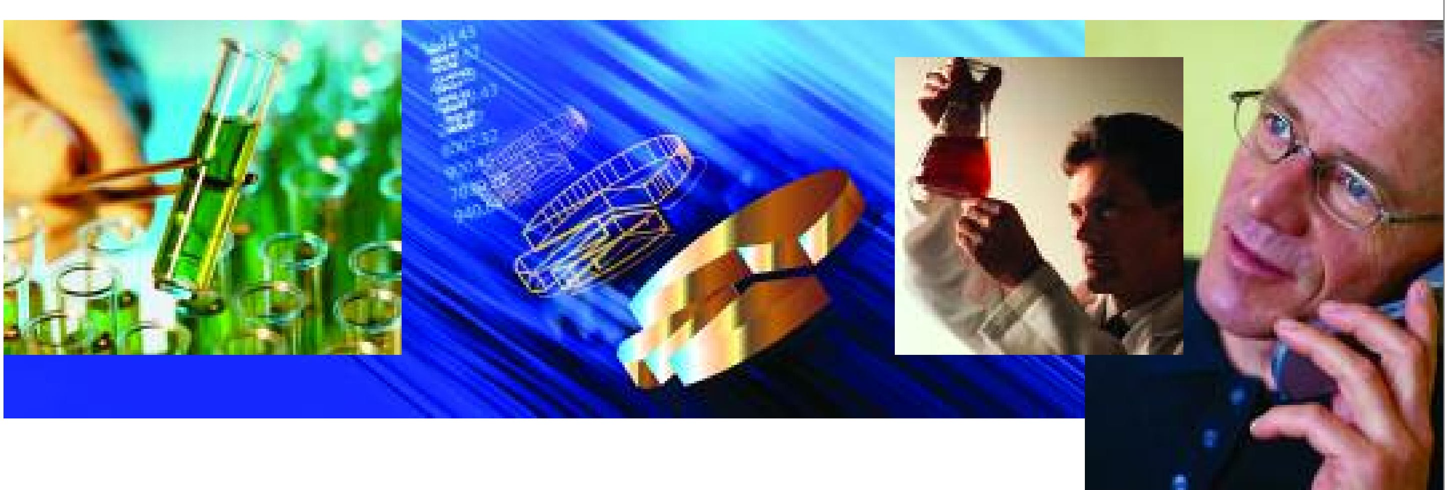
Utilization increases may also be related to the **expanding promotion of specialty pharmaceuticals**, including through direct-to-consumer (DTC) advertising. According to Verispan DTC audits, for example, DTC expenditures for Humira increased more than 80 percent from 2004 to 2005. DTC expenditures doubled for Neulasta, a drug used during chemotherapy to reduce the risk of infection by increasing white blood cells.

Figure 24

Significant Pending Launches, Specialty/Biotech Drugs

Brand Name (Generic)	Projected Launch	Estimated Peak Market Potential	Use	Comments
Gardasil (human papillomavirus vaccine)	2006	$2.5B US	Prevention of genital warts; cervical cancer	Short-term results from a recently released clinical trial showed this vaccine to be 100 percent effective in preventing pre-cancerous cervical changes and early-stage cervical cancer.
Orencia (abatacept)	2006	$600M US	Moderately to severely active RA	A biologic drug for the treatment of individuals who have failed other therapies; the first in a new class of drugs for this condition.
Provenge (sipuleucel-T)	2006	$1B US	Asymptomatic men with metastatic, androgen-independent prostate cancer	An injectable oncolytic that "attacks" only cancer cells; offers hope for treatment of certain types of prostate cancer.
Sutent (sunitinib malate)	2006	$750M global	imatinib (Gleevec)-resistant gastrointestinal stromal tumors (GIST); metastatic renal cell cancer	This oral therapy treatment could change the standard of care for the treatment of renal cell cancer.
Tysabri (natalizumab)	2006	N/A	Multiple sclerosis	Originally approved in 2004, Tysabri was withdrawn a few months later due to the development of fatal complications in individuals who used the drug in combination with Avonex. The drug presents a therapeutic advance for individuals with MS and has been approved for relaunch with tight restrictions around its use. Restrictions are expected to reduce sales from previous forecasts.

Caremark monitors the specialty/biotech pipeline continuously, evaluates the potential impact on utilization and spend and provides utilization management recommendations, where appropriate, for each pending launch. *Consult your Caremark account representative for recommendations for appropriate management strategies for pipeline products relative to your plan and plan population.*



CareSolutions

An Approach to Specialty Management – Better Outcomes, Lower Overall Costs and Appropriate Utilization

A comprehensive CareSolutions approach to specialty management leads to better outcomes, lower overall costs and the assurance that medications are used appropriately. Caremark Specialty Pharmacy management services go far beyond dispensing the medication.

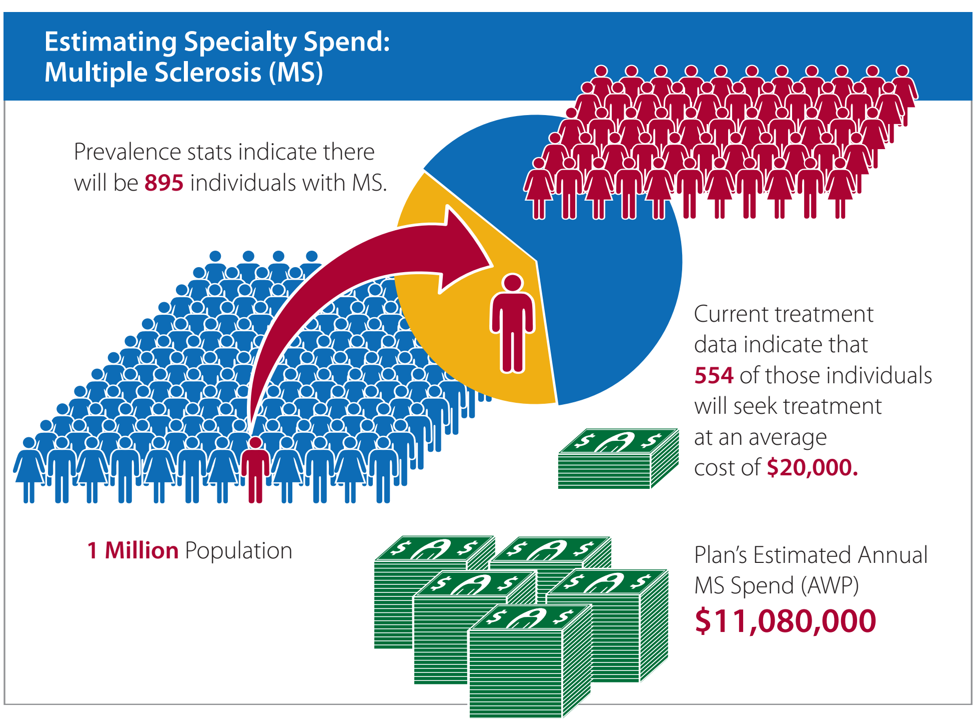
Understanding coverage and cost. Specialty pharmaceuticals may be administered in physician offices or bought at retail pharmacies or through a specialty pharmacy. Some drugs are commonly covered under the medical benefit, others under the pharmacy benefit. Due to all these factors, expenses related to specialty pharmacy costs can be hidden. A review of pharmacy and medical data can often uncover specialty utilization and allow for thoughtful consideration of management strategies.

Proactive pipeline management. Tracking the pipeline to anticipate prospective specialty launches allows proactive implementation of utilization management.

Utilization management. As specialty medications increasingly address more common chronic conditions, utilization management is essential to optimize the plan's investment and plan participant outcomes. Caremark also offers clients the option to apply clinical guideline management based on clinical practice guidelines and clinical trial literature to help ensure that the right candidates get the appropriate drugs. Once a plan participant is receiving therapy, our guideline management programs can help ensure that appropriate therapeutic endpoints are achieved.

Condition Management – Promoting healthier outcomes for higher-risk plan participants

Figure 25



Based on the Caremark prevalence of treatment model, updated January 2006.

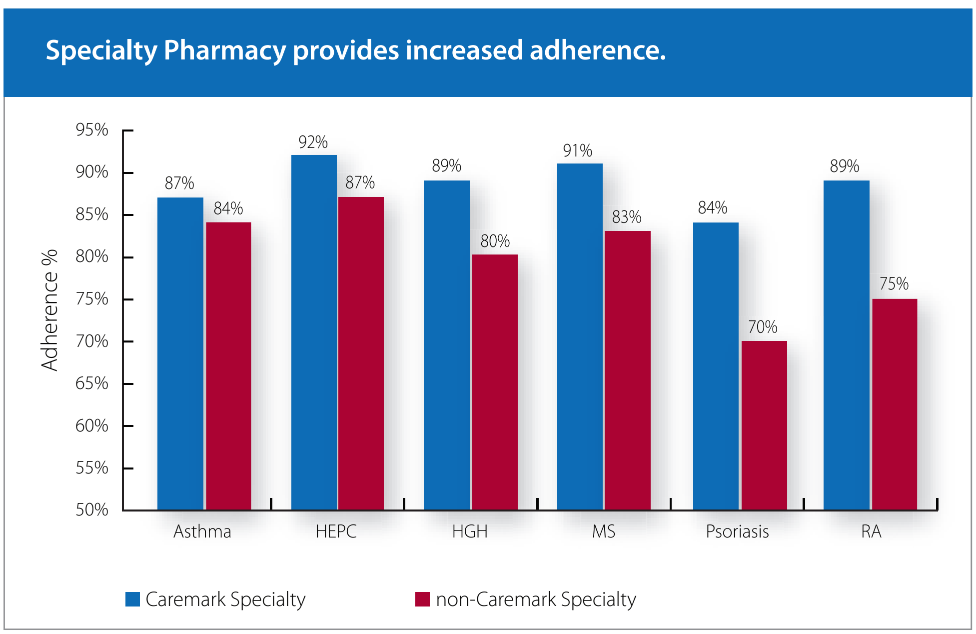
Supporting plan participant adherence. Appropriate, consistent use is essential to reap the full benefits of these costly medications, yet the difficulties of self-administration and troublesome side effects can discourage plan participants. Counseling from a health professional with special expertise with these therapies can support adherence. *See Figure 26*.

Providing extra support. CarePatterns® and Accordant® disease management programs are designed to help individuals understand their chronic conditions and properly use their medications. Through these programs, Caremark addresses a range of chronic conditions by working with patients, caregivers and providers. By combining the strengths of our Specialty Pharmacy services with disease management principles, Caremark offers an integrated delivery model that further enhances outcomes and decreases overall healthcare costs.

Caremark Specialty Pharmacy Provides More than Medication for Plan Participants

- Specialty drug fulfillment
- Convenient delivery
- Adherence management
- Proactive refill reminders
- 24/7 clinical support
- Care coordination
- Extensive education and counseling
- Self-injection training

Figure 26



Specialty Pharmacy provides increased adherence.

Source: Caremark Analytics and Outcomes analysis, 2005
Adherence – Plan Participant-Level Compliance + Plan Participant-Level Persistency. Compliance – How well a patient follows the physician's orders with a prescribed therapy regimen. Persistency – The duration that a patient follows the therapy regimen.
HEPC: hepatitis C; HGH: human growth hormone; MS: multiple sclerosis; RA: rheumatoid arthritis

Adherence to Care – Encouraging appropriate drug regimen adherence.

The Ongoing Challenges of Specialty Pharmacy Management

This year marked a major milestone in the specialty pharmaceutical market. In late May, **the FDA granted approval to a bio-generic** – Omnitrope, a human growth hormone product similar to Genotropin. While this is an encouraging development, it must be noted that human growth hormone products are among the few biologically derived drugs that are approved as chemicals rather than biologics. Furthermore, the FDA did not rate the generic product as equivalent to and freely substitutable for the brand.

Although patents for several biologically-derived pharmaceuticals have expired, or will expire soon, there is still **no clear regulatory pathway** that allows an abbreviated approval process for most bio-generics. Bio-generics present distinct approval challenges. More traditional "small molecule" drugs are typically combinations of chemicals. Biotech products are often large protein molecules derived from living cells – a much more complex manufacturing process. There are concerns that deviations from the current standard processes for specific biotech products will affect safety and efficacy. It is up to the generics manufacturer to demonstrate bioequivalence for potential bio-generic products. In turn, these demonstrations must be affordable to incent the manufacturer.

Market forces – notably increasing specialty utilization and the shift to public funding for a significant portion of our national pharmaceutical expenditure due to Medicare Part D – may come together to speed the development of a broader bio-generic approval pathway. With the expectation that such legislation will be enacted, some generics manufacturers are preparing to develop more bio-generic products for U.S. distribution.

IMS calculates that eight major molecules with global sales of $15 billion could potentially go generic by 2010.

As more specialty and biotech medications are introduced, plans may consider whether they could benefit from implementing traditional pharmacy benefit management strategies such as **formularies** to help control costs. However, the very differences that distinguish specialty pharmaceuticals from more traditional brand name products can make such a strategy problematic. Many specialty products act on a cellular level. Even within a therapeutic category, response can vary widely from person to person, as well as in a single individual over time. The complexity of the conditions being treated also complicates choice of therapies, increasing the need for careful one-on-one management of the plan participant. For all of these reasons, there are more limited opportunities for therapeutic interchange in specialty pharmaceuticals at the present time. Your Caremark account representative can work with you to explore specialty management strategies appropriate for your benefit plan and population.

More Changes Lie Ahead

Beginning on January 1, 2006, with the implementation of the long-awaited **Medicare Part D drug benefit**, more than 40 million Medicare beneficiaries gained official access to prescription drug coverage. The benefit is sure to have long-term and wide-ranging impact on the healthcare environment. Multiple providers and a plethora of plans provided a competitive market environment, translating into lower than expected premiums and larger discounts and rebates, leading the Centers for Medicare and Medicaid Services (CMS) to lower its estimates on long-term costs.

With such a sweeping change, it's not surprising that the rollout was less smooth than had been hoped. Nonetheless, more than **38 million Medicare beneficiaries** had drug coverage by the mid-May enrollment deadline. This includes the nearly six million beneficiaries who were dually eligible for Medicare and Medicaid (often referred to as "duals") and therefore automatically enrolled into a plan. Also included in the 38 million figure: Just over eight million beneficiaries who enrolled in stand-alone prescription drug plans (PDPs); and nearly seven million beneficiaries who continue to receive drug benefits through former employers who have opted to take the Medicare retiree drug subsidy.

2006 will be a year of learning regarding the benefit; all stakeholders want to have a voice in refining the offering. Among the issues up for discussion: formulary requirements, pricing standards, reporting, and the number of plans that can be offered by a health insurer. Changes to Medicare have historically had a **ripple effect in the U.S. healthcare environment**. For example, the U.S. Food and Drug

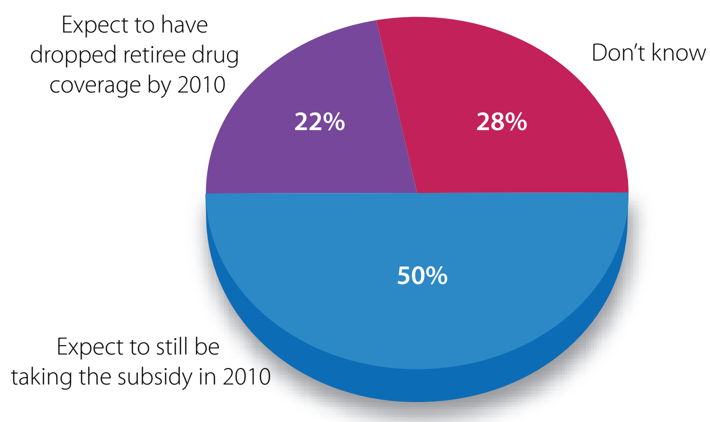
Continued on next page

Administration (FDA) is reviewing its regulations on generic drugs, including the provision of 180-day exclusivity, as part of its implementation of the Medicare Modernization Act, which included the Medicare Part D drug benefit.

Other changes associated with Medicare Part D that are already evident: increased emphasis on and investment in electronic medical records and **ePrescribing technology** and a drop in drug importation from Canada. The Canadian International Pharmacy Association reported a drop in cross-border sales of as much as 30 percent in the first month of 2006 when the Medicare drug benefit went into effect.[20]

Figure 27

Nearly four out of five employers took the Medicare Part D subsidy. Of employers who took the subsidy in 2006:



Source: Kaiser/Hewitt, December 2005

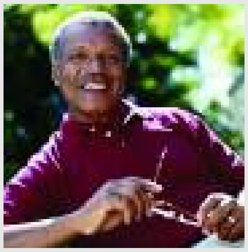
Waves of Change

While Medicare Part D has been termed the most significant overhaul of the U.S. healthcare system in a generation, rising healthcare costs have elicited calls for change and new solutions across the country. **Consumerism** has been broadly promoted in various forms – not only the Bush Administration-endorsed high deductible health plans with health savings accounts, but also increased emphasis on price and quality awareness and transparency, wellness education and disease management. **Health information technology**, electronic medical records and ePrescribing are seen as means to reduce costs and improve quality.

Rising insurance costs have reduced the number of employers offering **health coverage** and have led some workers to opt out of coverage altogether. Recognizing that providing care to the **uninsured** contributes significantly to the overall increase in healthcare costs, legislators at the state and national level have proposed solutions ranging from mandated nearly universal coverage at the state level to measures that

Continued on page 34

Caremark and SilverScript℠ serve Medicare beneficiary populations.



In support of our clients and Medicare beneficiaries, Caremark provides a full complement of services under Medicare Part D. SilverScript Insurance Company, an indirect wholly owned subsidiary of Caremark Rx, Inc., offers a **prescription drug plan (PDP)** in most CMS-designated regions, and will offer one in all regions in 2007. SilverScript Insurance Company is a Medicare-approved PDP providing a range of services for clients as well as individual Medicare beneficiaries.

Many Caremark **employer** clients offer retiree coverage that has been deemed creditable. In return for providing such coverage, the government has agreed to provide the sponsor with up to a 28-percent subsidy. For hundreds of clients seeking the 2006 subsidy, Caremark provides not only pharmacy benefit administration but also assistance with filing for the subsidy and CMS-required reporting, such as the provision of eligibility rosters and aggregate drug cost information. This option appeals to many employers, as it allows them to continue providing a valued benefit to their retiree populations at a reduced cost.

Still other beneficiaries who have been enrolled in Medicare health plans will simply remain in their **health plan** that now also offers prescription drug coverage (Medicare Advantage with Prescription Drugs – MAPD). Not all MA plans have to offer prescription drug coverage, but each sponsor with an approved MAPD must offer at least one plan that includes prescription drug coverage.

SilverScript also provides prescription drug coverage directly to the **dual-eligible and low income subsidy constituencies** as well as to other beneficiaries previously without coverage. Employers who did not elect to become a PDP on their own may provide **wrap-around coverage** to a beneficiary's PDP, such as SilverScript. Health and Human Services estimates that employers will provide wrap-around coverage for more than one million beneficiaries. Plan sponsors may also subsidize the monthly premium of a selected PDP.

Caremark and SilverScript combine to provide these types of services to nearly 50 clients, with Caremark administering the employer-provided wrap or secondary coverage, and SilverScript being the preferred PDP for the plan's Medicare-eligibles. SilverScript also provides services for several thousand beneficiaries who are part of our clients' waiver PDPs.

would make health insurance affordable for small business. More than 20 states have passed laws mandating that health insurers extend coverage for adult dependent children past college to age 25 or more. Mini (or limited benefit) medical plans providing **minimal, low-cost coverage** are being marketed as alternatives, particularly for low-income individuals, part-time employees and young people, who generally have few medical concerns and are just starting out in the job market.

Pharmaceutical Manufacturers Face Change

The implementation of Medicare Part D presents great change for pharmaceutical manufacturers as well – an enormous portion of drug spend will shift to the public sector. 2006 also marks the beginning of a wave of **patent expirations** on brand name drug blockbusters that extends over the next several years. Given the challenging market environment, manufacturers have developed a number of adaptive strategies, hoping to protect and extend patents, respond to safety concerns and improve perceptions of the industry. The industry has developed guidelines

Caremark participates in CMS ePrescribing demonstration.

Caremark ePrescribing programs will earn Congressional visibility as the company participates in the Centers for Medicare & Medicaid Services (CMS) demonstration project this year. The project results are to be presented to Congress in 2007 and will influence the final standards that will be adopted to create a robust system of ePrescribing for the new Medicare Part D prescription drug program.

As a participant in one of four coalition projects named by the CMS, Caremark will help measure the impact of electronic-prescribing data-transmission systems on patient safety and quality of care, evaluating ePrescribing utilization, changes in drug use, clinical outcomes, and patient satisfaction.

The coalition focuses on the Horizon Blue Cross Blue Shield of New Jersey (Horizon BCBSNJ) ePrescribing program, which in 2005 represented the country's largest electronic prescribing initiative. Caremark worked with its client to implement the iScribe® electronic prescribing system for 765 of its highest prescribing physicians in the state. Following on that success, Horizon BCBSNJ expressed interest in participating in the CMS projects. The competitively awarded project will take place in 2006 and will involve the Caremark iScribe system, the Caremark PBM plans and the Caremark Mail Service pharmacies.

around **direct-to-consumer (DTC) advertising**, including the implementation of waiting periods prior to the promotion of new products. Moreover, DTC advertising messages are shifting to reflect increasing focus on disease awareness and adherence messaging in line with the increased emphasis on the consumer in the marketplace.

A December 2005 court ruling could help **statin market leader Lipitor** avoid direct generic competition until 2011. Lipitor has led pharmaceutical sales in the U.S. for several years.

Challenges Facing Pharmaceutical Manufacturers

- Patent expirations and generic competition for many top-selling drugs
- Uncertainty around Medicare Part D regulations and enrollment
- Safety concerns about their products
- Greater caution at the FDA around new drug approvals
- Questions around comparative value of pharmaceutical products
- Scarcity of new blockbusters
- Governmental and public concern about drug prices
- Greater pressure on pricing from payors
- Consumer lack of trust in the industry
- ePrescribing, which provides reminders when generics are available
- Increasing costs of product development and promotion

Figure 28

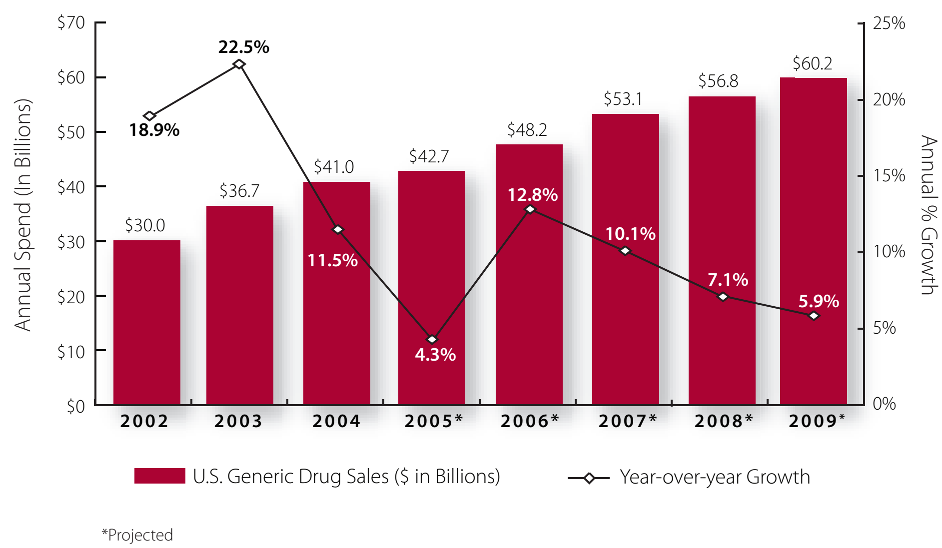
Significant Pending Launches: Brand Name Drugs

Drug	Projected Launch	Estimated Peak Market Potential	Use	Comments	CareSolutions
Acomplia (rimonabant)	2006	$1B U.S.	Weight loss	Orally administered; first in a new class of compounds called selective CB (cannabinoid receptor) blockers	AdvancedCare Weight Management program
Alvesco (ciclesonide)	2006	$1.2B global	Persistent asthma in adults, adolescents and children 4 years of age and older	A high potency steroid that is administered once daily via an inhaler	Drug limit (based on prescribed dose/frequency and package size); Utilization Review; CarePatterns
Asoprisnil	2006	$700M U.S.	Uterine fibroids	May show promise for treatment of endometriosis	Contact your Caremark Account Representative
desvenlafaxine	2006	$2.5B U.S.	Major depressive disorder; vasomotor menopause symptoms	SNRI related to Effexor	Prior authorization
Exubera (inhaled human insulin powder)	2006	$1.5B global	Type 1 and type 2 diabetes in adults	This inhaled insulin powder has the advantage that it could reduce or eliminate insulin injections for some individuals.	Prior authorization; CarePatterns
Levemir (insulin detemir [rDNA origin] injection)	2006	$1.2B U.S.	Type 1 and type 2 diabetes	Basal insulin analogue having a unique mechanism that results in a smooth and predictable effect. Offers a long duration of action (~ 20 hours) after injection.	CarePatterns
Oporia (lasofoxifene)	2006	$500M global	Prevention of osteoporosis	Orally administered, selective estrogen receptor modulator (SERM); the same class as other currently marketed drugs	CustomCare Retail osteoporosis (checks for off-label combination therapy)

See Figure 24, page 27 for information on pending launches in the Specialty/Biotech market.

Figure 29

Generic drug sales expected to rise sharply in 2006.



Source: IMS Health, Henry J. Kaiser Foundation, FDA, Centers for Medicare and Medicaid, and William Blair & Company, L.L.C. estimates

Generics – Numbers and News

In the U.S. in 2005, more prescriptions were filled with generics than with brand name products. **Generic market share** is expected to continue to grow as many high-profile brand name products lose patent protection over the next several years. *(See list, Figure 31, page 39.)* The FDA is reviewing more generic drug applications than ever before. In fact, **a backlog of generic applications at the FDA** is causing concern that generic launches will be delayed, potentially costing payors and consumers as they are forced to continue to pay higher prices for brand name products.

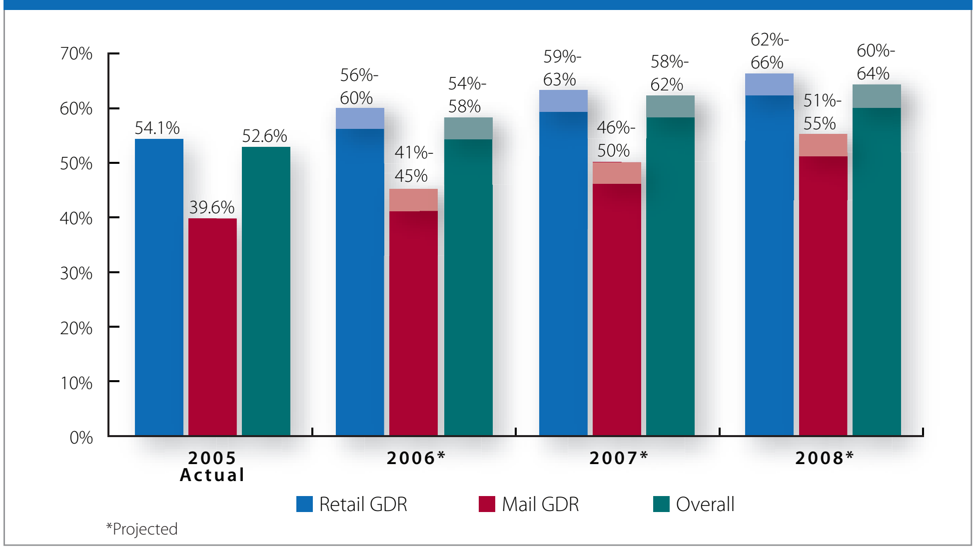
In 2005, more U.S. prescriptions were filled with generics than with brand name products.

The FDA backlog is only one potential challenge for generics manufacturers. As noted above, manufacturers of brand name drugs continue to make efforts to preserve and extend their patents and market share. One common tactic has been the brand name drug manufacturer's launch of an **"authorized generic"** version of a brand name drug facing first-time generic competition. These authorized generics can increase competition and decrease revenues for first-to-file generic manufacturers who have been granted exclusivity for their launch. **Governmental action** – such as the proposal to award patent extensions to brand name manufacturers for their Biodefense contributions, or the FDA's review of the 180-day exclusivity period typically granted to first-to-file generic manufacturers – could also upset the generic marketplace. All these forces could **negatively impact profitability for generics manufacturers** and reduce their incentive to bring new generics to market.

In the consumer marketplace, however, generic drugs have never been stronger. In the face of rising prices for brand name products, payors and consumers have been taking advantage of the increasing availability of generics. Caremark clients and plan sponsors nationwide have **incentivized utilization of generics** with lower co-pays and other benefit strategies. Moreover, widespread promotion and education about generic safety and effectiveness have helped increase **consumer confidence** in and acceptance of generic products. Generic utilization will also be positively impacted by Medicare Part D, increased use of ePrescribing technology and consumer-directed strategies to raise **cost awareness**. For all these reasons, along with an unprecedented number of anticipated generic launches, the generic market share is expected to top 60 percent in the next five years. Additional benefits may accrue from increased utilization of generics. In a recent study, patients started on generics were 12.6 percent more adherent than those started on non-preferred medications and had 62 percent greater odds of achieving adequate adherence.[21]

Figure 30

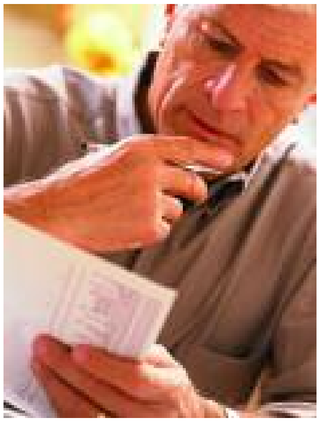
Generic Dispensing Forecast for the Caremark Book of Business



Book of Business GDR performance does not necessarily reflect individual client performance. Client specific projections will vary based on demographics, utilization, drug mix, benefit design, clinical programs, and changes in the marketplace. Based upon these variables, Caremark does not guarantee the estimated projections shown.

Drug mix varies significantly between mail and retail. Chronic maintenance medications dispensed through mail 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.

CareSolutions



CareSolutions can help you make the most of new generic launch opportunities

Caremark offers a wide array of options that work across the pharmacy care continuum to improve levels of generic drug dispensing. As part of our CareSolutions clinical strategy, Caremark analyzes a plan's pharmacy claims data to identify specific opportunities to impact prescription drug costs. Through the CareSolutions suite of tools, the client accesses a menu of solutions to support cost-effective and clinically appropriate drug care. Examples of CareSolutions that help maximize generic utilization include:

The Right Drug – Promoting lower-cost, clinically appropriate drugs.

Healthcare Provider Collaboration

- Electronic messaging at the point of prescribing through the iScribe ePrescribing tool
- Proactive consultations and communications on generic drug availability

Plan Participant Engagement

- Ready-to-use Count on Generics® communications tools
- Personalized communications highlighting generic savings opportunities
- Online interactive pricing tools to demonstrate pricing differences between generics and their brand name equivalents
- New generic launch alerts informing brand name drug users of the availability of new generic equivalents
- Coupons waiving co-pay at retail to encourage generic utilization

Plan Design Options

- Generic maximization programs such as mandatory generics, DAW cost shifts to plan participants, generic auto-substitution through mail service, and retail generic uptake programs
- Step therapy encouraging plan participants to try lower-cost therapies first
- Pipeline communications and modeling to enable proactive plan design adjustments

Contact your Caremark Account Representitive to find out more about CareSolutions targeted for the needs of your specific population.

Figure 31

Significant Pending Generic Launches 2006-2009

Brand	Annual U.S. Sales	Use	Generic	Estimated Launch
2006				
Allegra-D	$403 M	antihistamine and decongestant	fexofenadine/ PSE	Q3
Concerta	$958 M	ADHD/ADD stimulants	methylphenidate	Q2
Ditropan XL	$432 M	overactive bladder	oxybutynin	Q4
Flonase*	$1.06 B	respiratory anti-inflammatory	fluticasone propionate	Q4
Mobic	$1.05 B	analgesics – NSAIDs	meloxicam	Q3
Pravachol*	$1.88 B	cholesterol lowering	pravastatin	Q2
Xanax XR*	$90.9 M	anxiety	alprazolam	Q1
Zocor	$4.56 B	cholesterol lowering	simvastatin	Q2
Zofran Tabs/Inj	$700 M	anti-nausea (chemotherapy)	ondansetron	Q4
Zoloft	$3.0 B	antidepressant	sertraline	Q2
2007				
Ambien	$1.91 B	sleep disorders	zolpidem tartrate	Q4
Coreg	$899 M	high blood pressure	carvedilol	Q1
Geodon	$553 M	anti-psychotic	ziprasidone	Q1
Imitrex Tabs/Inj.	$1.08 B	migraine headache	sumatriptan	Q2
Norvasc	$1.88 B	high blood pressure	amlodipine	Q3
Risperdal	$1.43 B	anti-psychotic	risperidone	Q4
Toprol-XL	$1.07 B	high blood pressure	metoprolol	Q3
Viread	$641 M	HIV/AIDs	tenofovir disoproxil	Q4
Wellbutrin-XL	$949 M	antidepressant	bupropion	Q3
Zyrtec	$1.01 B	antihistamine	cetirizine	Q4
2008				
Advair Diskus	$2.32 B	corticosteroid bronchodilator combination used for asthma	fluticasone propionate/ salmeterol xinafoate	Q1
Depakote	$178.5 M	anticonvulsant	divalproex	Q1
Fosamax	$1.899 B	osteoporosis	alendronate sodium	Q1
2009				
Aciphex	$1.27 B	anti-ulcer agent	rabeprazole	Q2
Prevacid	$3.20 B	anti-ulcer agent	lansoprazole	Q2

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.
*Generic product already launched.

CMS analysts forecast that prescription drug spending will grow from an estimated $204 billion in 2005 to $446 billion in 2015.

National Trend Forecasts 2006, 2007

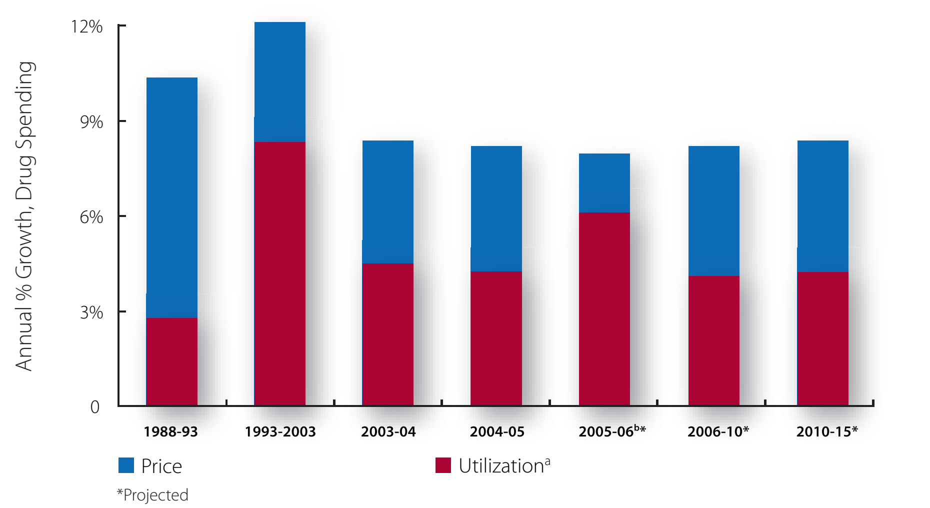
In their projections on national healthcare spending, analysts at the **Centers for Medicare and Medicaid Services** (CMS) predict an average annual prescription drug spending growth rate of 8.2 percent over the next ten years. They forecast a dip in prescription spending growth to 7.7 percent for 2006 – largely because **discounts and rebates associated with the Medicare Part D** drug benefit have proven to be larger than expected. These discounts and rebates are expected to nearly offset anticipated increases in utilization as seniors who had little or no drug coverage prior to 2006 make use of their Medicare Part D benefit. After 2006, CMS analysts anticipate that Medicare drug coverage will not have a major impact on the overall drug spending growth rate.

According to CMS, long-term growth drivers include healthcare practice patterns that involve prescribing existing drugs to a larger segment of the population and **increased utilization of high-cost specialty medications**.

Factors that are expected to constrain growth in spending include **increased use of generics and cost sharing** through rising co-payments and deductibles – management factors that impact both utilization and drug mix.

Figure 32

Utilization will be major driver of drug spending growth in 2005-2006 according to CMS estimates.



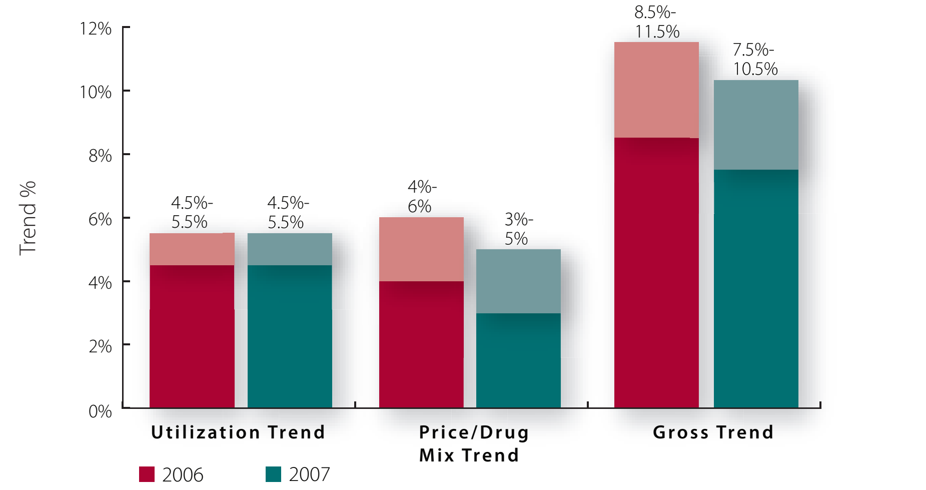
Source: "Health Spending Projections through 2015." Data source: Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Group

[a] Utilization also includes the effects of intensity and population growth.

[b] Without the effect of Medicare Part D, overall growth would be 8.1 percent (3.8 percent price, 4.3 percent utilization).

Figure 33

Caremark Gross Trend Forecasts



Forecasts based on Caremark Book of Business and represent gross trend per member per year (PMPY) if no plan design or demographic changes occur. This analysis is an estimate for information purposes only. These estimates do not represent an existing or future contractual guarantee provided by Caremark. This information is subject to changes and will not represent any specific offer by Caremark of return on investment in the future.

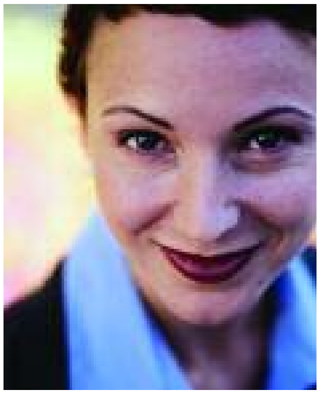
Caremark Trend Forecasts

Based on current Book of Business data, Caremark analytics services anticipate **relatively stable growth in utilization** over the next 18 to 24 months. The wave of **first-time generic launches** will have greater impact on drug mix and pricing over time as more generic manufacturers market competing versions of reference brand name products.

Caremark clients have experienced **three 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. 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 utilization of prescription drugs helps to control condition 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 our role in working with you over the months ahead to manage your prescription benefit, improve outcomes and reduce overall healthcare costs.

CareSolutions

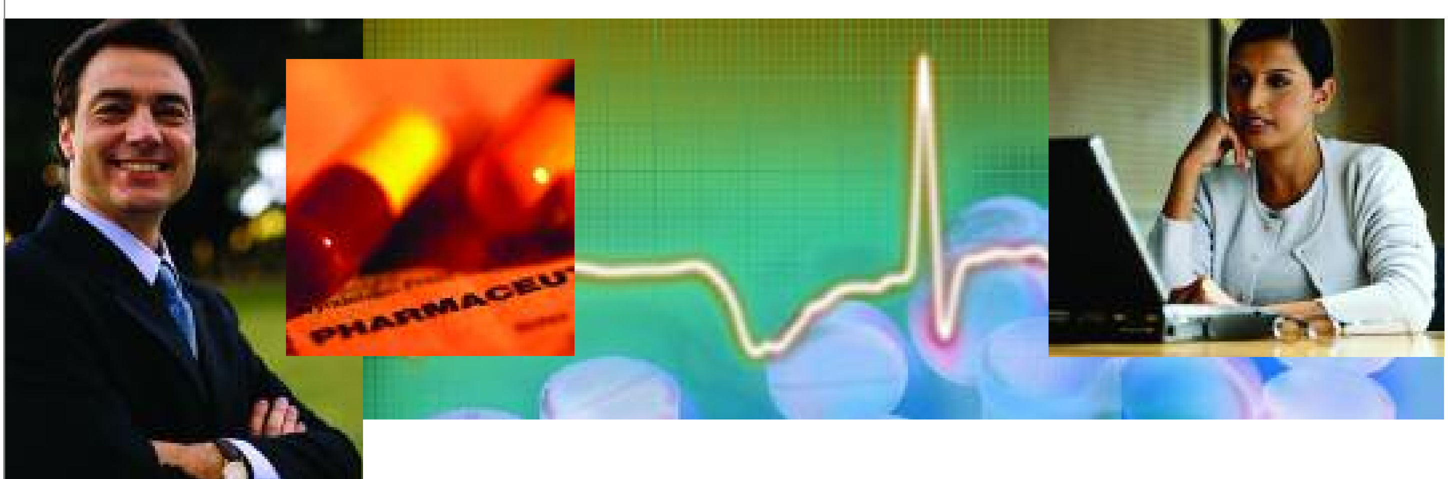
Pharmacy Trend Management – Reducing drug trend through proactive management.



What to Do Now – Top Tips to Reduce Your Plan's Pharmacy Benefit Trend

- Prepare to **take advantage of the coming generic opportunities** – see page 38 for a partial menu of CareSolutions related to generics.
- **Help plan participants become better consumers** – build in a cost structure that incentivizes lower-cost prescription options, increase consumer awareness of costs and educate them about the safety and effectiveness of generics.
- Consider how your prescription drug spend affects **overall healthcare costs** – evaluate management measures to support appropriate utilization, prescription safety and adherence.
- Invest in **disease and condition management programs** to help control overall healthcare costs for your higher risk plan participants.
- Identify **specialty utilization** and evaluate optimal management measures for plan participants with complex chronic conditions.

Investigate, quantify, identify, deliver, measure, report. Your Caremark account team is ready to help you select and implement data-driven solutions that align with your plan's healthcare philosophy and business objectives. We look forward to supporting you and your members and plan participants in this dynamic marketplace over the months ahead.



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Figures:

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