



# TrendsRx<sup>®</sup> Quarterly

DECEMBER 2006

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## Blockbuster Launches of 2006

As the wave of blockbuster patent expirations continues, payors face market uncertainty around high-stakes generic launches.

Some of the highest-impact drug launches this year don't have names that roll off the tongue, or advertising budgets to turn them into household names. But products like simvastatin, sertraline, clopidogrel, pravastatin, and meloxicam command attention all the same. They're the generics for Zocor, Zoloft, Plavix, Pravachol, and Mobic—just a few of the first-time generics that have been introduced in 2006. They represent some of the most highly utilized therapeutic categories, and each of their brand name counterparts drew more than a billion dollars in U.S. sales in 2005.

With today's heightened awareness of cost-effective generics, brand name drugs commonly lose substantial portions of their market share within days of the launch of their generic alternatives. This year, stakes are particularly high, and both generic and brand name drug manufacturers have been more aggressive in promoting their products and protecting their market.

**From a payor perspective.** For payors, the wave of new generics represents unprecedented opportunity and, given the current market environment, considerable uncertainty. For example, research shows that plan participants can save an average of 30 to 80 percent when they fill their prescription with a generic rather than the corresponding brand name drug. But a generic launched with **exclusivity** will not

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## Generic Launches: Washington is Watching as Well

Congressional interest in generic pharmaceuticals has accelerated in 2006 as blockbuster drugs lose patents and millions of Medicare beneficiaries enjoy a new federally funded prescription drug benefit. Congress has acted several times in the past few years to accelerate the availability of generics. Most recently, bills have been introduced to close legal loopholes in the Hatch-Waxman Act.

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*It all starts with care<sup>®</sup>*



## Blockbuster Launches of 2006...

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offer that level of savings during the first six months. An **authorized generic** adds competition to the market and can affect pricing favorably for buyers. At the same time, the authorized generic can reduce potential profits for the generic manufacturer and thereby reduce the incentive to launch. And, if a generic launches **at risk** and is later recalled, plan participants who have transitioned to the generic may find themselves “changing drugs” again before the various lawsuits are settled, resulting in disruption among member populations.

Moreover, the prescription benefit climate has changed considerably. As little as five years ago, a new generic might have been an option for those plan participants taking the reference brand. With current cost consciousness, greater consumer acceptance of generics and leaner prescription benefits, a generic launch can affect market share for more than just the reference brand. This year’s launches of generic versions of cholesterol drugs Pravachol and Zocor, for example, were seen as competition for market leader Lipitor and other statins as well as the reference brands. Analysts expected that prices and market share for all statins would be affected by these generic launches. Thus, a new generic may require evaluation of a plan’s strategy for managing the entire category.

### The Launch of Generic Plavix

Last summer’s at-risk launch of the generic form of Plavix illustrates the current high stakes atmosphere. Plavix, a blood thinner, is one of the world’s top selling drugs. It’s used to reduce the risk of heart attack or stroke in high-risk people and those who have had previous heart attacks or strokes.

In January, the Food and Drug Administration (FDA) approved a generic manufacturer’s application to market a generic version of the drug. Negotiation and litigation ensued between the generic and brand manufacturers. Weeks later, both parties announced a proposed out-of-court settlement granting the generic manufacturer a license to market a generic product in five years, several months in advance of expected patent expiration in 2011.

However, states Attorneys General reviewing the settlement rejected the agreement, which included a multimillion dollar payment to the generic manufacturer—a so-called **reverse payment**. A few weeks later, in August, the generic was launched at risk and gained market share quickly—an estimated 70 percent of all prescriptions written and over 80 percent of new prescriptions. A federal judge blocked sales of generic Plavix

## 2006 Blockbuster Generic Launches

Category	Brand	Generic	Annual Sales*	Generic Launch	Conditions at Generic Launch
Cholesterol lowering	Pravachol	pravastatin	\$1.8B	April	Generic exclusivity.
Cholesterol lowering	Zocor	simvastatin	\$4.5B	June	Defensive pricing for brand. Generic exclusivity (several mfrs., by strength). Authorized generic.
NSAID-analgesic	Mobic	meloxicam	\$1B+	July	Multiple generics at launch.
Antidepressant	Zoloft	sertraline	\$3B	August	Authorized generic.
Blood thinner	Plavix	clopidogrel	\$3.5B	August	At risk, w/exclusivity. Sales halted 3 weeks later.

\*Estimated U.S. sales of the reference brand, 2005.

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.

**Exclusivity:** First-to-file generics are generally granted 180 days of market exclusivity before other manufacturers may launch their generics

**At risk:** Generic launched while brand name drug's patent is still in effect

**Authorized generic:** A generic authorized by the brand name drug manufacturer; generally launched simultaneously with the new generic

**Citizen petition:** Petition submitted to the FDA for review; originally intended to address possible safety issues; recently cited as a tactic used to delay launch of generic drugs

**Reverse payment:** Cash settlement to a generic manufacturer for entering into an agreement to delay a generic launch

three weeks later, but did not order a recall. The patent trial is scheduled for January. While generic clopidogrel offers savings over brand name Plavix, current supplies are limited. Pricing for clopidogrel will be lower after other manufacturers are able to launch their own generics. Caremark will continue to dispense clopidogrel through our mail service pharmacies until supplies are depleted.

**Other strategies which help counter generic competition.** Like other consumer products, pharmaceutical brands are managed to protect market share and increase brand loyalty. At the same time, these strategies can counter or delay the impact of generic competition. Effexor XR, for example, is a formulation that offers consumers greater dosing convenience than simple Effexor. Dosing convenience, in turn, offers the prescriber the potential of greater adherence and better clinical outcomes. With these attributes, Effexor XR has much more market share. Thus, the launch in August of the first generic serotonin-norepinephrine reuptake inhibitor (SNRI), venlafaxine (Effexor), was not expected to significantly impact upward trend in this category of antidepressants.

Combination products, offering two distinct drugs as a single product, can offer greater efficacy and convenience for appropriate individuals, as well as market share protection for the manufacturer. Other strategies that counter generic competition include application for additional indications, pediatric patent extensions (six additional months of patent protection) and the movement of a product from prescription to over-the-counter status. Several brand name drug manufacturers have now also acquired generic subsidiaries.

**Going forward.** In this uncertain market, Caremark advocates a case-by-case response to generic launches within an overall and longstanding commitment to maximize generic opportunities for our clients. We believe that defining generics as the first line of therapy translates into a simple, sustainable and easy-to-understand message for all.



Today,  
a generic  
launch  
can affect  
market share  
across an  
entire  
category.

## Significant Pending Generic Launches

Brand	Annual Sales*	Use	Generic	Estimated Launch	Anticipated Conditions at Generic Launch
Zofran	\$1.37B	anti-nausea (chemotherapy)	ondansetron	2006-Q4	Authorized generic.
Ambien	\$2.14B	sleep disorders	zolpidem	2007-Q2	Authorized generic. Pediatric extension granted. Multiple vendors expected.
Coreg	\$1.15B	high blood pressure	carvedilol	2007-Q3	Pediatric extension expected.
Lotrel	\$1.29B	high blood pressure	benazepril	2007-Q3	Authorized generic. Possible at-risk launch.
Norvasc	\$2.63B	high blood pressure	amlodipine	2007-Q3	Authorized generic. Possible at-risk launch.
Wellbutrin XL	\$1.48B	antidepressant	bupropion	2007-Q3	Once daily formulation. Possible at-risk launch.
Zyrtec	\$1.33B	antihistamine	cetirizine	2007-Q4	Multiple generic vendors. No exclusivity.



## Generic Launches: Washington is Watching as Well

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Bills have also been introduced to prevent brand name drug manufacturers from entering into agreements with generic manufacturers to delay the entry of generics, particularly those that involve cash settlements known as **reverse payments**. Other bills under consideration prohibit the marketing of **authorized generics** during the exclusivity period. The Federal Trade Commission has raised questions about both practices. Several members of Congress are also planning to introduce legislation intended to promote access to **generic, or follow-on, biologics**.

The **backlog of generic drug applications** has also drawn attention. There are over 800 such applications pending at the Food and Drug Administration (FDA), and it's expected that the number of such submissions will increase dramatically over the next several years. In July, the Senate Appropriations Committee approved a \$10 million boost in the budget of the Office of Generic Drugs, the part of the FDA that reviews applications from generic manufacturers.

**Citizen petitions** are believed to have contributed to the backlog. Citizen petitions can be initiated by anyone and were originally intended to raise questions of safety. The FDA must review these petitions, and during that review, the generic application does not move forward. Critics cite citizen petitions as delaying tactics used by brand name drug manufacturers and have requested reform of the process.

**Caremark** has been a leader in bringing generic drug issues to the forefront in Washington. We are currently leading a coalition of employers, health plans, pharmacies, and pharmacy benefit managers (PBMs) to educate and encourage Congress to take action on legislation supporting generics. To learn more about the **Coalition for a Competitive Pharmaceutical Marketplace**, visit the Web site: <http://www.therightprescription.org>.

### Impact of Generics on Medicare Part D.

As anticipated, managers of Medicare Part D prescription drug plans promote utilization of generics, and an estimated **60 percent of prescriptions under Medicare Part D** are filled with generics. In testimony before the Senate Special Committee on Aging, the president of the Pharmaceutical Care Management Association (PCMA), Mark Merritt, cited a study on potential savings to Medicare from pending generic launches. Looking at 14 drugs commonly used by seniors, PCMA calculated that the Medicare Part D program and seniors could save an estimated \$23 billion if

generics for these drugs came to market as scheduled over the next five years. Furthermore, generics have been cited as one way to delay beneficiaries' entry into the donut hole. Merritt also noted that adoption of a uniform ePrescribing standard would likely result in an increase in generic drug utilization.

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

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# TrendUpdate

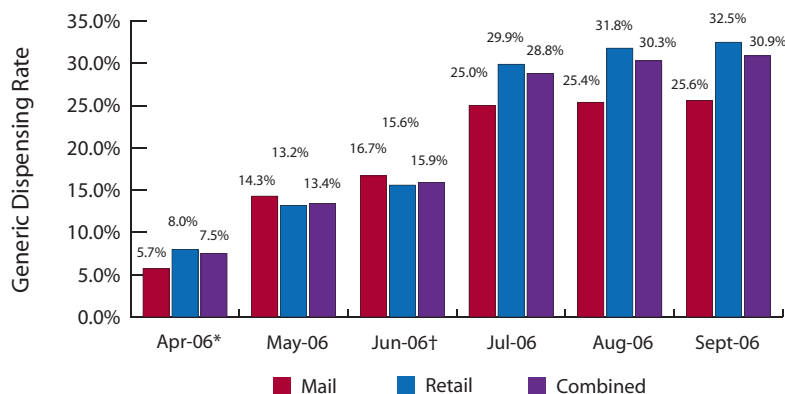
## Book of Business Gross Trend: 5.1% PMPM

In the Caremark Book of Business, the **generic dispensing rate (GDR)**—55.6 percent YTD through Q3, **56.1 percent in Q3**—continues to climb as clients and plan participants take advantage of this year's wave of new generic launches. Our gross trend, at 5.1 percent PMPM, also benefits from an exceptionally low utilization trend, which is related to the impact of Medicare Part D on the demographics of our BOB population. For the first half of 2006, **specialty/biotech trend declined** from 2005 trend levels—20 to 17.4 percent PMPM. However, as a percentage of spend, specialty/biotech continued to rise—8.0 to 8.5 percent.

Cholesterol-lowering drugs remain the top category by gross spend—8.3 percent of overall spend. Several factors are impacting trend in this therapeutic category. Importantly, the launches of new generics pravastatin and simvastatin have increased GDR and caused market share shifts. More aggressive treatment guidelines continue to drive utilization and the prescription of combination therapies and newer alternatives to statins.

Among the top therapeutic categories, **anticonvulsants** have the highest gross trend at approximately 14 percent. Trend in this category is related to decreasing use of generics (especially gabapentin, generic for Neurontin) and increasing use of single-source brands (Topamax, Lamictal and Lyrica).

Statin Class Generic Dispensing Rates



\* pravastatin launch † simvastatin launch

Three classes within top categories had **double-digit trends over 15 percent**: SNRI antidepressants (Cymbalta, Effexor XR), antihypertensive combinations, and non-barbiturate hypnotics, which include the heavily promoted new launches Lunesta and Ambien CR. Each of these categories represents less than 2.5 percent of BOB spend.



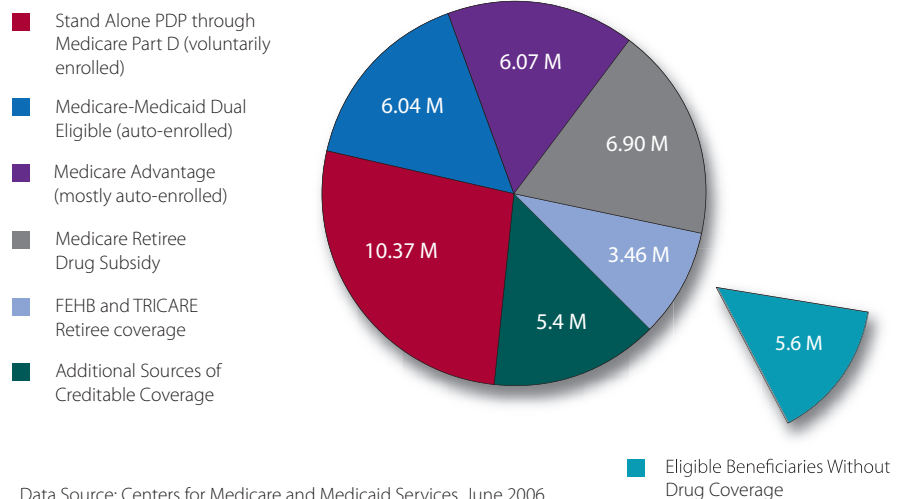
Most pharmacists and physicians believe the Medicare Part D drug benefit is helping seniors save money.

## Progress Report on Medicare Part D

The Medicare Part D drug benefit implemented in January was the largest expansion of Medicare in 40 years. Despite a bumpy start, the program has had notable success.

According to studies completed this summer by the Kaiser Family Foundation, eight out of 10 seniors are satisfied with the Medicare Part D benefit. The majority of pharmacists and physicians acknowledge administrative problems but believe that Medicare Part D is helping seniors save money. At summer's end, as more seniors entered the donut hole, there were some reports of beneficiary confusion and dissatisfaction. However, with this year's Medicare Part D experience and wider availability of donut hole coverage in 2007, next year should be much smoother. In the upcoming enrollment season, seniors will have more prescription drug plans (PDPs) to choose from as 17 companies are offering coverage nationwide with additional choices offered regionally. Plans offering some form of coverage in the donut hole will be widely available.

### Medicare Beneficiaries Drug Coverage By Type, In Millions



### The Coverage Gap – Communication and Information Reduce Frustration

Estimates on when and how many Medicare Part D beneficiaries will enter the coverage gap vary, and 2006 data is still forthcoming. Among beneficiaries who have reached the donut hole, some have reported that they have stopped filling prescriptions or have cut back. Many seniors have also indicated that they are willing to make the change to generics to cut costs.

Caremark subsidiary SilverScript<sup>SM</sup> Insurance Company has found that beneficiary confusion and frustration related to the donut hole can be alleviated by helping them anticipate out-of-pocket costs and making sure they are aware of the donut hole before they reach that coverage zone. The SilverScript Web site was designed to help beneficiaries make knowledgeable choices. Tools on the site can be used to project beneficiary costs over the entire year, find out whether their medications are on the formulary and locate in-network pharmacies. Moreover, SilverScript initiated outreach calls alerting beneficiaries to their potential entry into the donut hole shortly after receiving word about early entrants' confusion.

Starting in 2007, SilverScript will offer three Medicare Part D plans in every state, offering a range of deductibles, premiums and co-pays. The SilverScript Complete plan design includes coverage of generics in the donut hole. Also in development is a [single transaction Coordination of Benefits program](#) that would automatically adjudicate both the primary and secondary plans for a given beneficiary on one claim submission. Beneficiaries would be given just one prescription drug card to use at the pharmacy, eliminating a lot of confusion for beneficiaries and reducing paperwork for pharmacists.

Caremark has been an industry leader in developing and implementing Medicare Part D offerings. We are the only pharmacy benefit manager participating in three pilot projects to bring enhanced clinical management, health improvement and cost savings to the government-sponsored benefit. Moreover, we have developed a [range of modeling tools](#) to help clients evaluate different options and strategies for their retiree populations and can support whatever strategy they feel is best suited for their needs, whether they choose to take the retiree drug subsidy, provide wrap or secondary coverage or transition their beneficiaries into a PDP.

The Medicare Part D drug benefit has made needed prescription drugs more easily available for millions of Americans. As anticipated, 2006 has been a year of learning and adjustment for both beneficiaries and providers. Caremark and SilverScript are committed to bringing maximum value, enhancing the beneficiary experience and ensuring beneficiary satisfaction as we help them make the most of this important addition to their healthcare benefit package.

Medicare Part D Standard Benefit Parameters	2006	2007
• Deductible	\$250	\$265
• Initial Coverage Limit	\$2,250	\$2,400
• Out-of-Pocket Threshold	\$3,600	\$3,850
• Total Covered Medicare Part D Drug Spend at TROOP Threshold	\$5,100	\$5,451.25



Confusion and frustration related to the coverage gap can be alleviated by helping beneficiaries anticipate out-of-pocket costs.

*To learn more about SilverScript Insurance Company's offerings and to preview beneficiary tools, please visit [www.silverscript.com](http://www.silverscript.com). You can also ask your Caremark account representative for full details on 2007 program offerings and financial modeling support tools.*

# Expanding indications are a significant driver of biotech growth...

## But what drives the growth in indications?

**B** iotech drugs for rheumatoid arthritis (RA)—specifically tumor necrosis factor (TNF) inhibitors—have been among the highest trending pharmaceuticals in recent years. In fact, Enbrel was the fastest growing pharmaceutical brand—specialty or non-specialty—in 2005, when sales increased 42 percent over the previous year.<sup>1</sup> Enbrel—like RA drugs Humira and Remicade—is approved for the treatment of psoriatic arthritis and ankylosing spondylitis as well as rheumatoid arthritis.

Other conditions for which biotech RA drugs have been approved, or are pending approval, include plaque psoriasis, Crohn's disease, osteoarthritis, ulcerative colitis, chronic obstructive pulmonary disease, severe asthma, and breast cancer.

While TNF inhibitors have been especially successful in gaining new indications, expanding indications are more prevalent in the biotech sector than among pharmaceuticals overall. In 2004, of the 101 late-stage biopharmaceuticals in clinical trials for 169 indications, 27 percent were already approved by the FDA.<sup>2</sup> A number of factors specific to biotech products support this process of growth.

**Biotech Drug Development.** Historically, biotech drugs were aimed at rare diseases. But the same groundbreaking research that supported drug development also increased understanding of disease processes. Now researchers know that many diseases have common physiologic pathways. If a biologic therapy has been found to be effective for one condition, there frequently is reason to investigate it for another, similar condition.

**Drug Approvals.** Small biotech firms may not have the resources to initiate large-scale trials, so they apply for (and may get approval for) quite specific indications. For example, a drug may be approved for use with a defined population subgroup, or at a specific stage of disease, only in combination with another drug, or only when other treatments have failed. Drug developers seek to expand indications, of course, to expand the drug's use. They may subsequently try for an indication for use earlier in a disease, or in an additional population, for example.

**In the Prescriber's Office.** Physicians are not restricted to the approved use once a drug has received FDA approval. Motivation to prescribe outside of approved indications can be stronger when physicians deal with diseases that are often inadequately controlled, where treatment is evolving rapidly or when patients have few other clinical options. For all these reasons, off-label use of biologics is widespread and often related to ongoing clinical trials being done to investigate additional uses for a drug.

For plans and payors, the situation is challenging. Expanding indications and off-label use complicate utilization management. For example, a drug can have different dosing regimens and routes of administration for different therapeutic uses.

**Caremark Specialty Pharmacy Services** can help address these complexities. Our comprehensive services are designed to improve medication therapy adherence and outcomes. Our utilization management and clinical programs help to ensure that plan participants are managed according to current standards of medical practice. Then, depending upon benefit plan design, our clinical team will consult with the prescribing physician regarding any prescription that falls outside those parameters. *To learn more about the benefits of using Caremark Specialty Pharmacy services and Accordant® disease management services, contact your account representative.*

<sup>1</sup> MedAd News, June 2006

<sup>2</sup> Marc Cohen, MD; Thomas Morrow, MD and Peter Penna, PharmD; "Managing the Expanded Use of Biologics Across Therapeutic Areas: An Example from B-Cell Targeted Therapies." *The American Journal of Managed Care*, March 2006, pages s24-s37.



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