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# SPECIALTY DRUG TREND REPORT



SPECIALTY PHARMACY

AN EXPRESS SCRIPTS COMPANY

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The CuraScript 2008 *Specialty Drug Trend Report* was produced based on research and analysis provided by CuraScript's parent company, Express Scripts, Inc.

**DEAR FRIENDS OF CURASCRIPT:**

Specialty medications used to treat complex and chronic diseases continue to be the fastest growing segment of overall drug spend. While traditional drug spend slowed to an increase of only 1.5% in 2008, specialty drug spend continued its steady climb, increasing 15.4%.

Now, more than ever, we must address the rising costs of specialty medications. Yet, we cannot sacrifice the comprehensive care and support specialty patients require. That's why plan sponsors turn to CuraScript, to get the savings and patient care they need.

Through our personalized patient care model and trend management tools, CuraScript helps to maximize the value of your specialty pharmacy benefit. Every day, we work in alignment with plan sponsors, members and healthcare providers to make the most of your healthcare dollars, while improving health outcomes.

CuraScript recognizes the importance of planning for tomorrow. We monitor important trends in the specialty drug landscape. And we're leveraging our parent company, Express Scripts, to develop new strategies that employ behavior-centric tools which will give us a deeper understanding of specialty patients and influence members to take charge of their healthcare. This will further fortify CuraScript's already strong abilities to drive therapy adherence, lower healthcare costs for plan sponsors and improve the quality of life for patients.

As always, we listen to those we serve. And we've heard what you need in your specialty pharmacy benefit:

*Better adherence*

CuraScript achieves improved therapy adherence by providing superior patient care and personalized education to members. We empower patients to maximize the benefits of their specialty medications, which creates healthier member populations and eliminates unnecessary healthcare costs.

*Innovative specialty solutions*

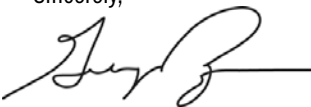
We see accelerated development of follow-on biologics and behavior-centric approaches to influence member choices as the best ways to deliver to patients the safest and most affordable specialty medications available.

*Zero waste*

CuraScript offers the latest patient-focused specialty care management, utilization management, and trend management tools. These evidence-based programs guide the safe and appropriate use of specialty medications and help you avoid wasted specialty drug spend.

In today's economic environment, you need us more than ever to optimize management of your specialty spend. As we look ahead to 2009 and beyond, we are proud to offer specialty solutions closely aligned with your health and savings goals.

Sincerely,



George Paz  
Chairman and CEO, Express Scripts

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# OVERALL TREND

2008 SPECIALTY  
DRUG TREND REPORT

## Overall Drug Trend

Continuing a pattern which began in 2003, per member per year (PMPY) pharmacy costs maintained their downward trend in 2008 to a rate of 3%, the lowest ever recorded by Express Scripts. All three components of overall trend — cost per prescription (cost/Rx), utilization and new drugs — were relatively flat at 2.3%, 0.4% and 0.2%, respectively. Utilization was moderated by multiple factors including movement of a popular brand, Zyrtec,<sup>®</sup> to over-the-counter (OTC) status, drug safety concerns and the economic downturn.

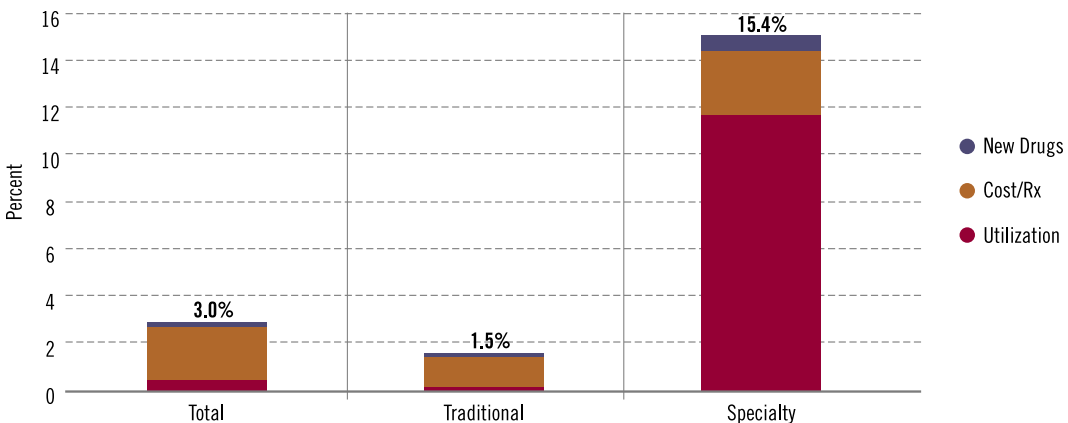
Trend for traditional (nonspecialty) drugs fell to a record low of 1.5%. Following a pattern similar to total trend, traditional trend components changed little — 1.3% for cost/Rx, 0.1% for utilization and 0.2% for new drugs.

However, spending for specialty drugs continued to grow at a double-digit rate. The specialty trend of 15.4% was driven by an 11.7% increase in cost/Rx, which was largely due to 9.4% price inflation. A modest 2.7% increase in utilization also contributed. Influencing the increase in specialty utilization were market-share shifts out of medical benefits into pharmacy spend and changes in prescribing practices away from traditional drugs as indications expand and newer specialty drugs enter the market. In 2008, new drugs added only 0.7% to specialty trend.

Beginning in 2008, the way we determine therapy categories has changed to mirror the classification system used in our plan-sponsor reporting. We moved to a proprietary system — most common indicators (MCIs). Developed by our clinical team, MCIs are named not for the type of drugs they contain (for example, anticonvulsants), but for the condition being treated (seizures). In addition, some nomenclature has changed for 2008. Classes previously named “nonspecialty” have been renamed “traditional.”

### EXHIBIT 1

#### Components of Total, Traditional and Specialty Trend



## SPECIALTY TREND

At 11.7%, increased cost/Rx was the main factor contributing to the 15.4% specialty-drug trend for 2008. The major driver was price inflation of 9.4%, a rate three times greater than for traditional medications. As was seen for traditional medications, though, the rate of utilization growth for specialty medications dropped by over 40% to 2.7%.

### EXHIBIT 2

#### Components of PMPY Specialty Cost Trend 2006 to 2008\*

	Ingredient Cost	Ingredient Cost Net of Rebates
	2006 vs. 2007	2007 vs. 2008
Price Inflation	7.3%	9.4%
X Units per Prescription	-1.3%	-0.4%
X Brand/Generic Mix	0	0
X Therapeutic Mix	2.2%	2.6%
<b>= Cost/Rx</b>	<b>8.2%</b>	<b>11.7%</b>
X Utilization	4.7%	2.7%
<b>= Common Drugs</b>	<b>13.3%</b>	<b>14.4%</b>
+ New Drugs	0.7%	0.7%
<b>= All Drugs</b>	<b>14.0%</b>	<b>15.4%</b>

\* The percentage contribution of each factor does not total to the All Drugs percentage increase. The calculation takes the base cost for a given year and multiplies it by one plus the percentage contributed by the first factor (price inflation). The resulting total is then multiplied by the percentage contributed by the second factor (number of units dispensed), and so on for each Common Drugs factor. The percentage contribution of the New Drugs is then added to the total Common Drugs percentage, to yield an All Drugs percentage increase. Final results may differ due to rounding.

In 2008, taken together as a separate class, specialty drugs lead all therapy classes in terms PMPY spending. At \$98.77, PMPY spend on specialty drugs outdistanced \$68.68 PMPY for the leading traditional class (drugs to treat high blood cholesterol). The top specialty class, inflammatory conditions, was in the top 10 of all therapy classes (traditional plus specialty) based on PMPY spend in 2008. The top three specialty classes accounted for well over 60% of total specialty spend, with seven of the top 10 specialty classes having total trends of over 10%. Blood cell deficiency was the only class that showed a negative trend. For some classes, utilization increases were the major factors in driving up trend; for others cost/Rx had bigger impact. In one class, pulmonary hypertension, both utilization and cost/Rx had large increases.

**EXHIBIT 3****Components of Trend for the Top 10 Specialty Therapy Classes  
Ranked by Percent of Total Specialty Spend**

		<b>% of Total Specialty Spend</b>	<b>Total Trend</b>	<b>Utilization</b>	<b>Cost/Rx</b>	<b>New Drugs</b>
1	Inflammatory Conditions	27.5%	17.0%	10.5%	5.7%	0.2%
2	Multiple Sclerosis	20.2%	18.3%	-2.9%	21.9%	0
3	Cancer	16.0%	18.6%	2.0%	15.7%	0.7%
4	Growth Deficiency	5.2%	20.3%	12.9%	6.5%	0
5	Anticoagulant	5.2%	22.4%	14.0%	7.4%	0
6	Blood Cell Deficiency	4.3%	-11.4%	-17.3%	7.1%	0.1%
7	Infertility	3.6%	14.4%	-2.4%	17.2%	0
8	Respiratory Conditions	3.2%	-0.2%	-8.2%	8.8%	0
9	Hepatitis C	2.9%	-7.3%	-11.4%	4.6%	0
10	Pulmonary Hypertension	2.7%	59.2%	36.1%	17.0%	0
	Top 20	90.7%	15.4%	3.0%	11.8%	0.2%
	All Other	9.3%	14.8%	0.5%	9.0%	5.3%
	<b>Total</b>	<b>100.0%</b>	<b>15.4%</b>	<b>2.7%</b>	<b>11.7%</b>	<b>0.7%</b>

## Specialty Drug Spending Patterns Between Pharmacy Benefits and Medical Benefits

Management of specialty-drug spending is another area where untapped savings exist. Because specialty medications can be reimbursed through both medical benefits and pharmacy benefits, the economic impact of specialty spending may be hidden within medical benefits, which often are not well-managed. Express Scripts conducted a study to identify how specialty-drug costs are distributed between medical and pharmacy benefits. We used an integrated medical and prescription claims database to evaluate specialty-spending distributions for 22 conditions from 2005 to 2007. Results from the top 10 specialty classes are presented in Exhibit 4.

### EXHIBIT 4

*Proportion of Pharmacy Cost as a Percentage of Total Specialty Spend 2005 to 2007  
Ranked by 2007 Total PMPY Costs*

Rank	Disease State	2005	2006	2007
1	Cancer	15.5%	18.2%	18.9%
2	Inflammatory Conditions	65.8%	66.1%	65.3%
3	Blood Cell Deficiency	32.5%	17.4%	15.3%
4	Multiple Sclerosis	96.1%	97.2%	97.1%
5	Hemophilia	38.0%	33.9%	30.4%
6	Growth Deficiency	87.9%	92.5%	93.2%
7	Respiratory Conditions	69.9%	68.1%	69.1%
8	Immune Deficiency	60.6%	23.1%	20.4%
9	Anticoagulant	93.9%	94.5%	94.4%
10	Hepatitis C	98.0%	98.6%	98.3%
	Other	52.8%	52.6%	52.0%
	<b>Total</b>	<b>48.9%</b>	<b>45.2%</b>	<b>44.9%</b>

Source: MarketScan® Commercial Claims and Encounters Database: 2005 to 2007

By viewing total medical and pharmacy costs together, a more complete picture of specialty spending is presented. When total medical and pharmacy spending is considered, specialty drugs used to treat cancer was the number one class. However, cancer was the number three therapy class in terms of total pharmacy specialty spend — representing only 16%.

Our results show that 55% of the costs for specialty medications in 2007 was billed through medical benefits — an increase from 51% in 2005. The transition of spending to the medical benefit is likely due to the need for physician monitoring of some therapies, as well as to safety concerns for other treatments. Our findings show that conditions including immune deficiencies, blood cell deficiencies and hemophilia had significant movement of spending out of pharmacy benefits and into medical benefits. Administering specialty drugs is an important source of revenue for some physicians which may explain some of the transition. However, many products can be managed appropriately and safely through specialty pharmacies that use drug-utilization monitoring specifically designed for hard-to-manage conditions. Given the significant savings under pharmacy benefits, plan sponsors should ensure that appropriate drugs are covered only under pharmacy benefits. They can also implement utilization management programs under medical benefits for patients most appropriately managed by physicians.

## Methods

The CuraScript 2008 *Specialty Drug Trend Report* was produced based on research and analysis provided by CuraScript's parent company, Express Scripts.

In Express Scripts' 2008 *Drug Trend Report*, prescription-drug use was analyzed for two independent samples of approximately 3 million individual members each. The plan sponsors providing pharmacy benefits to the sampled members paid at least some portion of the cost for prescriptions dispensed to its members in both 2007 and 2008 and they had stable membership (50% or less of the membership changed in 2007 and 2008). Plan sponsors used Express Scripts for both retail and home-delivery pharmacy services. Prescription counts have been converted to equivalent quantities that would have been dispensed through retail pharmacies to allow for varying benefit structures and adjust for differential home-delivery usage rates.

Non-prescription medications (except for diabetic supplies, which were included for the first time) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings were not included in this analysis. Calculations also excluded claims for Medicaid recipients and Medicare beneficiaries receiving prescription-drug benefits through Medicare Part D plans or Managed Medicare Prescription Drug Plans (PDPs).

For the first time, plan sponsor rebates were included to provide a more accurate representation of actual costs.

Utilization was determined on a per member per year (PMPY) basis. It was calculated by dividing the total number of 30-day adjusted prescriptions by the total number of member-years for all members. A member-year is the total number of months of eligibility for all members in the sample divided by 12. Prevalence of use for each drug class was calculated as the number of members taking medications in the class divided by the total number of members (both utilizers and non-utilizers) in the sample. The average number of prescriptions per user per year (# Rx/User/Year) is the total number of 30-day adjusted prescriptions divided by the total number of user-years. A user-year is determined by adding the number of months of eligibility for all sample members who had at least one claim for a given drug class and then dividing the total by 12.

# THERAPY CLASS REVIEW

2008 SPECIALTY  
DRUG TREND REPORT

CuraScript ®

## SPECIALTY

Following are detailed analyses of the three top specialty classes, which accounted for nearly 64% of specialty spend in 2008. Classes to watch include those that had significant impact on 2008 specialty trend. Six of the top eight specialty therapy classes grew at double-digit rates, with PMPY spending for drugs used to treat pulmonary hypertension increasing 59%. Looking closer into the components of these trends will be important as managing specialty drug spending remains a key priority for many clients.

### EXHIBIT 5

#### *Percentages of Total Spend and PMPY Cost Change for Selected Specialty Therapy Classes 2007 to 2008*

<b>Therapy Class</b>	<b>Percentage of Total Spending</b>	<b>Percent Change in PMPY Costs</b>
Inflammatory Conditions	27.5%	17.0%
Multiple Sclerosis	20.2%	18.3%
Cancer	16.0%	18.6%
Growth Deficiency	5.2%	20.3%
Blood Cell Deficiency	4.3%	-11.4%
Respiratory Conditions	3.2%	-0.2%
Hepatitis C	2.9%	-7.3%
Pulmonary Hypertension	2.7%	59.2%
Others	18.0%	16.8%
<b>Total</b>	<b>100.0%</b>	<b>15.4%</b>

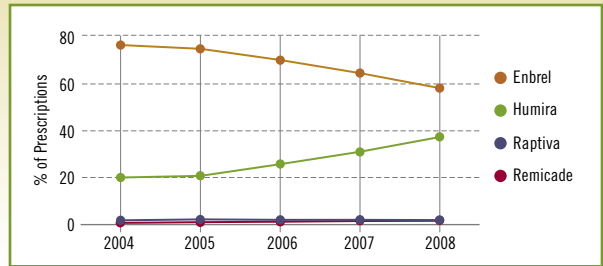
# 1 Specialty Rank

# Inflammatory Conditions

**Overall Trend** 17.0%

<b>Cost/Rx</b>	<b>5.7%</b>
Price	5.9%
Units/Rx	-0.6%
Brand/Generic Mix	0
Therapeutic Mix	0.4%
<b>Utilization</b>	<b>10.5%</b>
Prevalence	9.2%
Intensity	1.2%
<b>New Drugs</b>	<b>0.2%</b>

## Market-Share Trend



### Top Brand Drugs

Enbrel®  
Humira®  
Raptiva®  
Remicade®

### Top Generic Drugs

None

## Year in Review

- Expanded indications and earlier use of tumor necrosis factor (TNF) inhibitors (Enbrel, Humira and Remicade) to treat rheumatoid arthritis (RA) continue to drive trend growth.
- Due in part to its 2007 approval for Crohn's disease, Humira continued to make market-share gains on Enbrel, the market leader in the class.
- Cimzia,® a long-acting TNF inhibitor that is administered as a once-monthly subcutaneous (SQ) injection, was approved for Crohn's disease in April 2008.

## A Closer Look

- Utilization growth among drugs to treat inflammatory conditions is being driven by both better channel management — moving reimbursement from the medical benefit to the pharmacy benefit — and expanded indications for many of the agents in the class.
- CuraScript works with clients to manage out waste in this high-use class. For instance, clinical guidelines help physicians determine appropriate dosages for anti-inflammatory agents. After implementing guidelines, one CuraScript client realized significant savings from an 11% reduction in inappropriate utilization.

## What's Ahead

- Cimzia is expected to gain market share in 2009 due to increased use for Crohn's disease and probable approval of an expanded indication for RA.
- In 2009, Simponi™ (golimumab), another long-acting TNF inhibitor, is expected to be approved by the FDA for RA, ankylosing spondylitis and psoriatic arthritis. Like Cimzia, Simponi is a monthly SQ injection that will be more convenient than Enbrel and Humira, which require more frequent dosing.
- In late 2009, Stelara™ (ustekinumab), a novel biologic drug that works by inhibiting interleukins 12 and 23, may be approved in the U.S. to treat psoriasis.
- Several drugs, including LymphoStat-B® (belimumab), which are in development for the treatment of lupus, may be approved by the end of the decade.

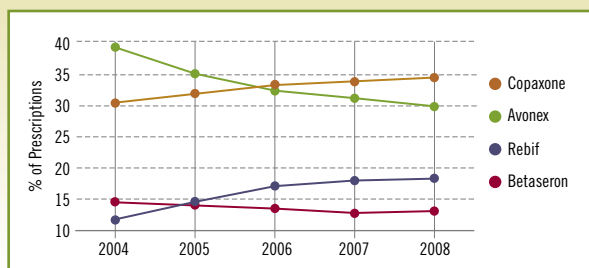
# Key Facts

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
<b>\$27.17</b>	<b>0.02</b>	<b>0.18%</b>	<b>\$1,633.01</b>	<b>8.3</b>

**Overall Trend** 18.3%

<b>Cost/Rx</b>	<b>21.9%</b>
Price	23.5%
Units/Rx	-0.2%
Brand/Generic Mix	0
Therapeutic Mix	-1.1%
<b>Utilization</b>	<b>-2.9%</b>
Prevalence	-1.0%
Intensity	-1.9%
<b>New Drugs</b>	<b>0</b>

## Market-Share Trend



### Top Brand Drugs

Copaxone®  
Avonex®

### Top Generic Drugs

None

## Year in Review

- Although utilization decreased slightly in 2008, cost/Rx growth continues to be a major driver of trend for drugs to treat multiple sclerosis (MS). Double-digit price inflation was seen for six of the seven MS drugs, driving the class to 24% price inflation.
- Copaxone, a daily non-interferon, was the market leader. Primarily taking market share from Avonex, an interferon that is used weekly, Copaxone is associated with fewer flu-like symptoms than Avonex and other interferons such as Rebif and Betaseron.

## A Closer Look

- While price inflation for MS drugs increased 24%, copayments per prescription went up by only 45 cents. Member share of total costs in the class actually decreased from 2.4% to 2%.
- Utilization decreased by nearly 3%, partly due to side effects from the drugs. Because MS drugs delay disease progression rather than improve function, patient perceptions of treatment effectiveness also affect utilization. In a study presented at the 2009 American Academy of Neurology annual meeting, Express Scripts researchers found that only 22% of patients believed that the benefits received from taking MS medication were worth the costs.

## What's Ahead

- Current MS therapies are injected, but several oral drugs for MS, including fingolimod, Panaclar™ and teriflunomide, are in late-phase development.
- Cladribine tablets may be the first disease-modifying oral drug to receive FDA approval for MS.
- Another oral drug, Fampridine SR, may be approved in late 2009 for treatment of symptomatic MS, despite an FDA request for more information from the manufacturer.
- Some oral therapies may be used in combination with currently available injectable drugs, and they also may be used earlier in the course of MS.

# Key Facts

Cost PMPY  
**\$20.00**

# Rx PMPY  
**0.01**

Prevalence of Use  
**0.10%**

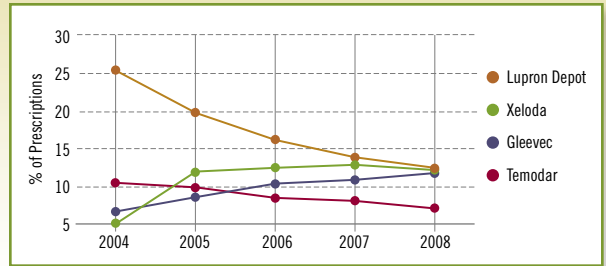
Average Cost/Rx  
**\$2,006.43**

# Rx/User/Year  
**9.5**

**Overall Trend** 18.6%

<b>Cost/Rx</b>	<b>15.7%</b>
Price	10.6%
Units/Rx	-0.7%
Brand/Generic Mix	0
Therapeutic Mix	5.3%
<b>Utilization</b>	<b>2.0%</b>
Prevalence	0.9%
Intensity	1.0%
<b>New Drugs</b>	<b>0.7%</b>

**Market-Share Trend**



**Top Brand Drugs**

Lupron Depot®  
Xeloda®

Gleevec®  
Temodar®

**Top Generic Drugs**

methotrexate injection  
leuprolide

**Year in Review**

- Cost/Rx was the primary influence on cancer trend growth in 2008.
- Utilization continues a shift to new brands, driving up cost for cancer treatment.
- After contributing 2.8% to trend in 2007, however, new drugs had a much smaller effect on cancer trend in 2008. No new blockbuster medications for cancer were approved in 2008.

**A Closer Look**

To address adherence, complexity and cost issues associated with oral specialty medications for cancer, CuraScript piloted an oral oncology specialty care management program with two large Blue Cross Blue Shield plans in 2008. Focused on preventing disease progression, the program provides clinical care counseling, side-effect management and proactive monitoring for patients using oral anticancer therapy.

**What's Ahead**

- The cancer pipeline is extensive, accounting for approximately half of all specialty drugs in development.
- Even the vast cancer-drug pipeline has significant hurdles to market entrance. The FDA often requires data on improved overall survival before approving new cancer medications.
- While many current cancer drugs and most in the pipeline are administered by intravenous (IV) infusion, one-fourth of investigational cancer drugs are oral. Prescription-drug benefits are affected more by oral drugs than by IV drugs, which usually fall into medical benefits.
- Oral cancer drugs in late-phase development include Afinitor® (everolimus) for kidney cancer, deforolimus for bone and soft tissue sarcomas, phenoxodiol for ovarian cancer and abiraterone for prostate cancer.
- Therapeutic vaccines such as BiovaxID™ for non-Hodgkin's lymphoma and Provenge® for prostate cancer may enter the market within the next couple of years.
- Targeted therapies, such as the oral tyrosine kinase inhibitor Zactima™ (vandetanib) and the IV monoclonal antibodies Arzerra™ (ofatumumab) and HuMax-EGFr™ (zalutumumab), are expected to play an increasingly important role in the treatment of various cancer types.

**Key Facts**

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
<b>\$15.78</b>	<b>0.01</b>	<b>0.16%</b>	<b>\$2,097.03</b>	<b>4.3</b>

# Specialty Classes to Watch

## Growth Deficiency

Specialty Rank 4

Overall Trend	20.3%	Top Drugs	
Cost/Rx	6.5%	Humatrope®	Genotropin®
Utilization	12.9%	Nutropin AQ®	Norditropin NordiFlex®
New Drugs	0		

### Year in Review

- A new, easier-to-administer pen cartridge of the follow-on biologic growth hormone Omnitrope® was approved in September 2008.
- Accretropin™ is a recombinant human growth hormone that was approved in early 2008, but not yet launched on the U.S. market.
- Clients with prior authorization (PA) in place to manage age-appropriate utilization found that only 21% of utilization was for patients over the age of 25 compared to 32% for clients without PA in place.

### What's Ahead

- While market share of Omnitrope has been minimal since its launch in early 2007, it will continue to grow with the availability of the new pen formulation.
- Tesamorelin, a growth hormone-releasing factor analog, may be approved in 2009 for HIV-related lipodystrophy.
- ALTU-238, a long-acting human growth hormone that is administered once monthly, is not expected to be approved until 2012.

## Key Facts

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
\$5.16	Less than 0.01	0.02%	\$2,646.61	7.9

## Specialty Classes to Watch

## Blood Cell Deficiency

Specialty Rank 6

Overall Trend	-11.4%	Top Drugs	
Cost/Rx	7.1%	Procrit®	Neupogen®
Utilization	-17.3%	Aranesp®	Neulasta®
New Drugs	0.1%		

### Year in Review

- Safety concerns associated with erythropoiesis-stimulating agents (ESAs) — Aranesp, Epogen® and Procrit — resulted in decreased utilization for these anemia medications and possibly shifting reimbursement through medical benefits.
- Nplate™ and Promacta® are new medications for idiopathic thrombocytopenic purpura (ITP), a bleeding disorder related to low platelet counts.
- Mozobil,™ a drug used in combination with Neupogen to mobilize stem cells for transplantation, was approved in December 2008.

### What's Ahead

- Following their approvals in the second half of 2008, Nplate and Promacta are expected to have a greater effect on cost in 2009 than in 2008.
- Approval of Hematide,™ a synthetic peptide-based ESA for anemia, is expected in 2010.
- Two additional oral medications for ITP (AKR-501 and fostamatinib) may be approved in the next few years.

### Key Facts

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
\$4.21	Less than 0.01	0.05%	\$1,745.08	4.5

# Specialty Classes to Watch

## Respiratory Conditions

Specialty Rank 8

Overall Trend	-0.2%	Top Drugs
Cost/Rx	8.8%	Xolair®
Utilization	-8.2%	Pulmozyme®
New Drugs	0	TOBI®

### Year in Review

- One reason that the use of medications for respiratory conditions decreased in 2008 is that fewer patients are taking Xolair, an injected biologic medication used to treat allergic asthma.
- While price inflation increased over 23%, clients absorbed the extra costs since copayments per prescription only increased by 45 cents. Member share of total costs in this category actually decreased from 2.4% to 2.0%.

### What's Ahead

- In 2009, pirfenidone may be the first medication approved to treat idiopathic pulmonary fibrosis (IPF), a rare condition characterized by scarring of the lungs. IPF can lead to death as early as two years from the time of diagnosis. Pirfenidone is a biologic drug that is administered orally.
- Among several drugs that may be approved within the next couple of years for cystic fibrosis (CF) are denufosal and VX-770, which both improve mucus clearance for CF patients.
- If approved by the FDA, Cayston™ (aztreonam lysinate for inhalation) will compete with TOBI, another inhaled medication, for treating CF lung infections.

## Key Facts

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
\$3.14	Less than 0.01	0.02%	\$2,354.33	7.2

## Specialty Classes to Watch

## Hepatitis C

Specialty Rank 9

Overall Trend	-7.3%	Top Drugs	
Cost/Rx	4.6%	Pegasys®	ribavirin
Utilization	-11.4%	PegIntron® Redipen®	ribapak
New Drugs	0		

### Year in Review

- Declining use of hepatitis C medications may be due to the growing population of non-responders to currently available treatment options.

### What's Ahead

- At least initially, many of the oral drugs that are in development for the treatment of hepatitis C will be used in combination with ribavirin and pegylated interferon.
- Oral protease inhibitors such as telaprevir and boceprevir are among the most promising drugs in the hepatitis C pipeline. Approval of these agents is not expected until 2011, however.
- Albuferon® and Locteron® are long-acting interferons that may be administered once every two weeks or once-monthly compared to weekly dosing with currently available interferons. Albuferon may be approved in 2010 while approval of Locteron is not expected until 2012.

Key Facts	Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
	\$2.86	Less than 0.01	0.02%	\$1,171.00	10.1

## Specialty Classes to Watch

## Pulmonary Hypertension

Specialty Rank 10

Overall Trend	59.2%	Top Drugs
Cost/Rx	17.0%	Revatio®
Utilization	36.1%	Tracleer®
New Drugs	0	Letairis®

### Year in Review

- At almost 60%, drug trend for pulmonary hypertension (PH) was the third highest for all specialty therapy classes. Large increases in both cost/Rx and utilization contributed to the rise.
- In 2008, Tracleer — an endothelin receptor antagonist (ERA) — lost market share to a similar agent, Letairis. Approved in mid-2007, Letairis may be associated with less liver toxicity and fewer drug interactions than Tracleer. It is also indicated for use earlier in the disease.
- Revatio (sildenafil, the same drug as Viagra®) is a phosphodiesterase type-5 (PDE5) inhibitor that relaxes muscles in the lungs. FDA-approved in June 2005, Revatio represented over 50% of PH prescriptions in 2008.

### What's Ahead

- Tyvaso, an inhaled form of treprostinil, is likely to be approved for PH in April 2009. For use in combination with other oral PH drugs, Tyvaso requires four inhalations per day compared to as many as nine inhalations per day for its already-approved competitor, Ventavis®.
- Approval of a second PDE5 inhibitor Adcirca® (tadalafil, the same drug as Cialis®) for PH is expected in May 2009. Adcirca may capture market share from Revatio because it requires less frequent administration (once-daily versus three times daily).
- Thelin®, a third ERA, may also be approved in 2009.

### Key Facts

Cost PMPY	# Rx PMPY	Prevalence of Use	Average Cost/Rx	# Rx/User/Year
\$2.68	Less than 0.01	0.01%	\$2,846.36	9.3



# FORECAST

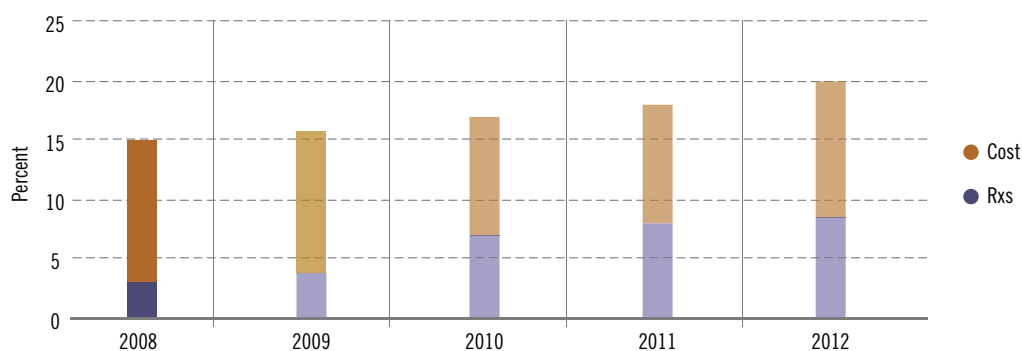
2008 SPECIALTY  
DRUG TREND REPORT

## SPECIALTY

Although specialty drug trend was slightly higher in 2008 than in 2007, it was still significantly less than the trend observed in 2006. The economy played a part in moderating the growth of specialty medications. While total drug trend in 2009 is expected to be flat, Express Scripts projects that by 2012 overall drug trend for specialty prescription drugs will rebound to around 20%, largely due to growth in cost/Rx. Our specialty predictions are presented in Exhibit 6.

### EXHIBIT 6

**Changes in PMPY Specialty Ingredient Cost for Express Scripts Commercial Business 2008 (Actual) and 2009 to 2012 (Projected)**



Because a high percentage of specialty drugs are still covered by medical benefits that are not available in our analysis, our trend reflects only the portion of specialty spend covered by pharmacy benefits. In the next few years, the possible introduction of follow-on biologics may affect some specialty classes, even though a pathway for approving them has yet to be decided by the FDA. Additionally, many unique new drugs, including some for previously untreated conditions, are in development.

Cost/Rx growth continues to have a significant impact on specialty trend, primarily due to inflation. Over the next four years, movement toward new, more expensive products will be the primary driver of cost/Rx growth in most specialty categories. However, increased utilization is the key factor in trend for the leading specialty therapy class, inflammatory conditions. In addition, significant growth rates for therapy classes such as pulmonary hypertension and osteoporosis are expected as blockbuster medications in these classes gain approval. Watch for denosumab (D-mab), a biologic drug administered as a twice-yearly subcutaneous injection to affect trend in the osteoporosis category.

Drugs to treat inflammatory conditions, such as rheumatoid arthritis (RA), psoriasis and Crohn's disease, will continue to be key leaders of specialty trend. The introduction of new medications including Simponi™ and Stelara™ for inflammatory conditions in 2009 will impact trend in 2010. In addition, new specialty drugs to treat lupus will begin playing an important role in the class over the next several years.

In 2010 and 2011, we expect increased utilization of medications for treating multiple sclerosis (MS) and hepatitis C, as new oral medications are introduced in both classes. Current unmet treatment needs for patients with MS or hepatitis C are likely to mean that the uptake of new therapies in these classes will be rapid and high. Additionally, the role of inflation in driving up trend for MS drugs is expected to continue for the next several years.

Continued movement of spend from medical benefits to pharmacy benefits will impact trend for cancer drugs and anticoagulants, such as Lovenox,<sup>®</sup> through 2012. Increasing use of oral anticancer drugs will also add to trend, because oral drugs are most commonly adjudicated under pharmacy benefits. New oral drugs, such as pirfenidone for respiratory conditions and Tyvaso and Adcirca<sup>®</sup> for pulmonary hypertension, will have a significant impact on cost and utilization in these categories.

Safety concerns with the use of erythropoiesis-stimulating agents (ESAs), Aranesp,<sup>®</sup> Epogen<sup>®</sup> and Procrit,<sup>®</sup> as well as tight control of these drugs by the Centers for Medicare and Medicaid Services (CMS) will result in negative trend in the blood cell deficiency class for one more year. Then we predict that increased use of two new drugs to treat idiopathic thrombocytopenic purpura, Nplate<sup>™</sup> and Promacta,<sup>®</sup> will drive positive growth rates in this class by the end of the decade.

Looking forward, the 111th Congress and the Obama administration share our vision of lowering costs, increasing safety and driving waste out of the healthcare system. Express Scripts continues to advocate for the development of a pathway for generic biologics. With support from Congress and the Administration, the debate around bringing generic competition to the biotech drug market now focuses on *when* instead of *if*.

Exhibit 7 on the next page details our 2009 to 2012 projections for trend in leading specialty categories.

## EXHIBIT 7

**Forecast for Selected Specialty Therapy Classes 2009 to 2012**

Therapy Class	Trend				Comments
	2009	2010	2011	2012	
Inflammatory Conditions	16.1%	18.2%	18.2%	18.7%	In 2010, new products will increase utilization. Drugs for lupus will drive continued utilization increases through 2011. Oral drugs for rheumatoid arthritis may impact the market in 2012.
Multiple Sclerosis	15.0%	15.3%	17.6%	17.6%	New oral brands expected in 2009 and 2010 may increase utilization (due to adjunctive therapy and use earlier in therapy). Continued price hikes for multiple sclerosis medications are anticipated for the next several years.
Cancer	21.0%	24.2%	26.0%	30.5%	Increased use of oral drugs will create a market-share transfer from medical benefits to pharmacy benefits through 2012. The approval of abiraterone, an oral prostate cancer medication in 2011 will increase cost and utilization in 2012.
Growth Deficiency	9.2%	5.1%	9.2%	9.2%	The impact of Omnitrope™ has been minimal since its approval in 2007; however, expect a more significant effect in 2009 due to its new pen formulation. Increased use of this less expensive follow-on biologic will impact mix by mitigating price increases.
Blood Cell Deficiency	-1.9%	1.7%	7.0%	7.1%	Continued negative trend is expected in 2009 due to safety concerns with erythropoiesis-stimulating agents (ESAs). Decreases will be less dramatic than in 2008 due to the full-year impact of Nplate™ and Promacta®, new biologic drugs approved in 2008 for idiopathic thrombocytopenic purpura (ITP). Positive trend is expected in 2010. If a follow-on biologic drug similar to Epogen® is approved in 2012, increased cost per prescription will be mitigated.
Respiratory Conditions	1.2%	23.2%	31.1%	33.4%	Flat trend in 2009 is expected as Xolair® use continues to shift toward the medical benefit. Pirfenidone, which may be the first drug approved for idiopathic pulmonary fibrosis, will increase cost in 2010 and beyond.
Hepatitis C	-5.5%	-3.4%	15.5%	32.0%	Utilization will continue to decline through 2010 as patients who do not respond to existing products wait for the introductions of novel treatments. New oral protease inhibitors that are expected beginning in 2011 are likely to increase utilization dramatically.
Pulmonary Hypertension	43.8%	32.0%	32.0%	38.0%	Significant positive trend in 2009 is expected as physicians continue to use Letairis® earlier in therapy. In addition, the approval of new drugs, Tyvaso and Adcirca® will contribute to trend growth in this class. Double-digit inflation will continue for several years.
<b>Total</b>	<b>15.2%</b>	<b>17.7%</b>	<b>19.4%</b>	<b>21.2%</b>	





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CuraScript is an Express Scripts company