



Overall Drug Trend

2

Express Scripts 2006 Drug Trend Report

Overall Drug Trend

For 2006, trends have been measured in terms of per member per year (PMPY) ingredient costs for Express Scripts group members with funded, integrated benefits. This year marks the first time that trends for both nonspecialty and specialty medications are reported from the same data samples.

Overall trends were low from 2005 to 2006, rising only 7.2%. Nonspecialty medication PMPY costs rose only 5.9%, while specialty medication PMPY costs rose a significant 20.9%.

As in past editions of the *Drug Trend Report*, the 2005 to 2006 PMPY ingredient-cost trend was analyzed in terms of the following major dimensions:

- Changes in the ingredient cost per prescription of common drugs (medications that were dispensed in both 2005 and 2006)
- Changes in the utilization of common medications
- Introduction of new products (prescription medications dispensed in 2006 but not in 2005)

Of the 5.9% nonspecialty increase:

- 58.9% was due to an increase in the cost per prescription of common prescription drugs
- 38.5% was due to increases in the utilization of common prescription drugs
- 2.6% was due to the introduction of new medications in 2006

Of the 20.9% specialty increase:

- 42.9% was due to an increase in the cost per prescription of common prescription drugs
- 40.2% was due to increases in the utilization of common prescription drugs
- 16.9% was due to the introduction of new medications in 2006

NONSPECIALTY DRUG TREND

Exhibit 3

Components of PMPY Nonspecialty Cost Trend 2002 to 2006*

	AWP Less Discount	AWP Less Discount	AWP Less Discount	Ingredient Cost
	2002 v 2003 Nonspecialty	2003 v 2004 Nonspecialty	2004 v 2005 Nonspecialty	2005 v 2006 Nonspecialty
Price	6.6%	6.0%	5.3%	4.3%
X Units per Prescription	0.3%	0.2%	0.1%	0.4%
X Brand/Generic Mix	-2.6%	-2.6%	-2.7%	-2.9%
X Therapeutic Mix	2.6%	3.7%	0.8%	1.7%
= Cost per Prescription	6.8%	7.2%	3.3%	3.5%
X Utilization	6.8%	2.9%	4.0%	2.2%
= Common Drugs	14.0%	10.4%	7.5%	5.8%
+ New Drugs	0.5%	0.3%	0.4%	0.2%
= All Drugs	14.5%	10.6%	7.9%	5.9%

* The percentage contribution of each factor does not total to the All Drug 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). The resulting total is then multiplied by the percentage contributed by the second factor (number of units dispensed), and so on for each Common Drug factor. The percentage contribution of the New Drugs is then added to the total Common Drug percentage to yield an All Drug percentage increase. Final results may differ due to rounding.

Trends for nonspecialty medications are further broken down into utilization, cost per prescription and new drugs.

Utilization of common medications was further divided into two components:

1. Prevalence — the proportion of members who fill one or more prescriptions from one year to the next (i.e., users)
2. Intensity — the number of prescriptions filled by users from one year to the next

Per-prescription costs were separated into the relative effects of four factors:

1. Price
2. Therapeutic Mix
3. Brand/Generic Mix
4. Units per Prescription

The remainder of this section presents general information for the 25 nonspecialty therapy classes with the highest PMPY cost according to each of the trend components: utilization, price, therapeutic mix, brand/generic mix, units per prescription and new drugs. A brief discussion of specialty trends is also included. Detailed reviews for selected top therapy classes — both nonspecialty and specialty — are in the Therapy Class Review section.

UTILIZATION

Across the Express Scripts book of business, utilization of common nonspecialty prescription drugs grew by 2.2% from 2005 to 2006. Prevalence, the measure of new users, increased by 1%; and intensity, the measure of treatment duration, increased by 1.2% — compared with changes of 2.1% and 1.9%, respectively, in 2005.

Growth slowed in several classes that had previous double-digit increases. Some classes even had negative growth. This reversal contributed to the decline from a 4% growth rate seen between 2004 and 2005. A mild cold and flu season in 2006 reduced the use of two antibiotic classes, macrolides and quinolones — the 24th and 25th nonspecialty classes in 2005. With utilization changes of -2% and 2.4, respectively, both dropped out of the top 25. Similarly, utilization of antivirals, often used for flu, grew only 4.1% in 2006 versus 16.5% in 2005.

Hypnotics saw explosive growth, primarily due to increased use of three relatively new products: Ambien CR™, Lunesta® and Rozerem™. The class of diagnostic products, which includes blood-sugar test strips, is new to the top 25 this year. It also showed double-digit growth due to increased prevalence of diabetes.

Exhibit 4

Utilization of Common Drugs for the Top 25 Nonspecialty Therapy Classes 2005 to 2006

Ranked by Total Percent Change

Therapy Class	Rxs PMPY		% Change		
	2005	2006	Prevalence	Intensity	Total
1. Hypnotics	0.14	0.16	10.6%	5.3%	16.5%
2. Diagnostic Products	0.08	0.09	9.8%	0.2%	10.0%
3. Anticonvulsants	0.23	0.25	9.2%	-1.2%	7.9%
4. Stimulants/Anti-Obesity	0.14	0.15	6.1%	0.6%	6.7%
5. Misc. GI Agents	0.06	0.06	9.3%	-2.3%	6.7%
6. Antidiabetics	0.57	0.60	5.4%	0.7%	6.2%
7. Decongestants	0.18	0.19	7.0%	-1.2%	5.7%
8. Antidepressants	0.86	0.90	4.2%	1.3%	5.5%
9. Antihyperlipidemics	0.99	1.04	3.9%	1.3%	5.3%
10. Narcotic Analgesics	0.56	0.59	4.7%	0.6%	5.3%
11. Migraine Products	0.07	0.07	4.9%	0.1%	5.0%
12. Gastrointestinals	0.55	0.58	2.8%	2.1%	4.9%
13. Antivirals	0.08	0.09	-0.1%	4.2%	4.1%
14. Antiasthmatics	0.45	0.46	0.7%	1.6%	2.2%
15. Antihypertensives	1.10	1.12	2.7%	-0.6%	2.1%
16. Antihistamines	0.28	0.29	1.3%	0.8%	2.1%
17. Beta Blockers	0.57	0.58	1.4%	0.4%	1.8%
18. Contraceptives	0.48	0.49	1.9%	-0.9%	1.1%
19. Misc. Hematologicals	0.10	0.10	-0.8%	1.9%	1.1%
20. Ophthalmic Products	0.18	0.18	4.1%	-4.0%	-0.1%
21. Antipsychotics	0.08	0.08	1.0%	-1.8%	-0.9%
22. Dermatologicals	0.31	0.30	1.4%	-2.6%	-1.3%
23. NSAIDs	0.33	0.32	0.3%	-2.6%	-2.4%
24. Misc. Endocrines	0.22	0.21	-3.0%	-2.8%	-5.7%
25. Calcium Blockers	0.34	0.31	-7.1%	-0.3%	-7.4%
Top 25	8.92	9.20	-0.1%	3.2%	3.1%
Other	4.14	4.15	-0.8%	1.2%	0.3%
Total	13.06	13.34	1.0%	1.2%	2.2%

PRICE

Price represents the cost-per-prescription impact of manufacturers' unit price changes (inflation) and changes in contractual rates negotiated with Express Scripts clients. These rates may be influenced by client mix, channel mix or market dynamics. Price does not include retrospective manufacturer rebates, but it does reflect the value of discounted rates. Not surprisingly, the 4.3% overall nonspecialty price increase in 2006 was lower than inflation-only measures reported in previous years. The overall price rate included 6.9% for common brands and -5.7% for common generics. Common drugs were available in both years.

The brand increase was driven by price changes in classes with consistently above-average cost increases. For example, major brand-name hypnotics and stimulants/anti-obesity drugs are nearing patent expirations. Historically, anticipated generic introductions have signaled high inflation.

In several nonspecialty classes, market dynamics changed generics more than brands. As additional manufacturers begin selling the same generic, the price declines, and the lower price is passed on to clients. The price impact from multiple generics is evident in gastrointestinals and anticonvulsants.

Exhibit 5**Price Changes for the Top 25 Nonspecialty Therapy Classes 2005 to 2006**

Ranked by Total Percent Change

Rank	Therapy Class	Price % Change		
		Brand	Generic	Total
1.	Hypnotics	14.2%	-2.7%	13.8%
2.	Stimulants/Anti-Obesity	11.9%	-2.5%	10.5%
3.	Antiasthmatics	8.1%	10.0%	8.2%
4.	Antipsychotics	7.5%	0.2%	7.2%
5.	Decongestants	6.9%	-7.2%	6.7%
6.	Antihistamines	8.2%	-4.0%	6.7%
7.	Misc. GI Agents	7.8%	-3.3%	6.5%
8.	Migraine Products	6.4%	-3.3%	6.3%
9.	Antivirals	6.3%	-1.7%	5.9%
10.	Antihyperlipidemics	5.9%	-6.0%	5.5%
11.	Antidiabetics	7.9%	-5.7%	5.2%
12.	Ophthalmic Products	6.1%	-4.0%	5.1%
13.	Contraceptives	11.0%	-0.9%	5.0%
14.	Misc. Endocrines	5.1%	0.1%	5.0%
15.	Dermatologicals	9.7%	-4.5%	5.0%
16.	NSAIDs	7.4%	-2.2%	4.7%
17.	Diagnostic Products	4.3%	26.5%	4.3%
18.	Antihypertensives	6.4%	-4.5%	3.6%
19.	Calcium Blockers	4.8%	0.1%	3.3%
20.	Misc. Hematologicals	3.6%	-16.5%	2.7%
21.	Beta Blockers	4.9%	-4.2%	2.5%
22.	Antidepressants	5.5%	-8.8%	1.9%
23.	Gastrointestinals	4.1%	-12.1%	1.8%
24.	Narcotic Analgesics	14.5%	-7.2%	1.3%
25.	Anticonvulsants	9.2%	-22.0%	0.6%
	Top 25	6.8%	-6.3%	4.6%
	Other	7.1%	-4.4%	3.3%
	Total	6.9%	-5.7%	4.3%

THERAPEUTIC MIX

Therapeutic mix reflects changes in market shares within therapy classes, new strengths of existing medications, and changes in overall market shares for each class. In 2006, therapeutic mix rose to 1.7% after bottoming out in 2005 at 0.8%.

Across the top 25 nonspecialty classes, 16 classes experienced increases in cost due to therapeutic mix. The nonspecialty classes with the biggest increases were anticonvulsants, miscellaneous GI agents and antivirals. In each case, increases were due to new, more expensive brands. New to the top 25, the miscellaneous GI class includes several different types of drugs. Safety issues caused one of them, Zelnorm®, to be withdrawn in March 2007.

New dosages had significant effects on antivirals and contraceptives. Atripla™, a new, once-daily combination medication for HIV, impacted antivirals; and a new contraceptive, Yaz®, accounted for most new dosage impact in its class.

One class had no appreciable change, but eight decreased due to therapeutic mix. NSAIDs continued to slide after the market withdrawal of Bextra® in 2005. Dermatologicals fell due to safety concerns with acne and eczema products.

Exhibit 6

Price Changes Due to Therapeutic Mix for the Top 25 Nonspecialty Therapy Classes 2005 to 2006

Ranked by Overall Percent Change

Therapy Class	% Change		
	General Therapeutic Mix	New Dosages	Overall Therapeutic Mix
1. Anticonvulsants	6.8%	0.1%	6.9%
2. Misc. GI Agents	4.1%	0.6%	4.7%
3. Antivirals	1.8%	2.5%	4.3%
4. Beta Blockers	3.3%	0	3.3%
5. Hypnotics	3.1%	0	3.1%
6. Antidiabetics	2.9%	0.1%	2.9%
7. Antipsychotics	0	1.9%	1.9%
8. Ophthalmic Products	1.3%	0.6%	1.9%
9. Antidepressants	1.7%	0	1.7%
10. Narcotic Analgesics	0.2%	1.3%	1.5%
11. Misc. Endocrines	1.3%	0	1.3%
12. Misc. Hematologicals	1.2%	0	1.2%
13. Antiasthmatics	0.8%	0	0.8%
14. Contraceptives	-1.4%	2.2%	0.8%
15. Stimulants/Anti-Obesity	-0.5%	0.9%	0.3%
16. Migraine Products	0.2%	0.1%	0.3%
17. Diagnostic Products	0	0	0
18. Decongestants	-0.1%	0	-0.1%
19. Antihypertensives	-1.0%	0.6%	-0.4%
20. Antihyperlipidemics	-1.1%	0	-1.1%
21. Antihistamines	-1.2%	0	-1.2%
22. Gastrointestinals	-1.4%	0.2%	-1.3%
23. Calcium Blockers	-2.0%	0	-2.0%
24. Dermatologicals	-2.6%	0.2%	-2.4%
25. NSAIDs	-4.6%	0	-4.6%
Top 25	0.8%	0.3%	1.2%
Other	2.0%	0.4%	2.4%
Total	1.4%	0.4%	1.7%

BRAND/GENERIC MIX

Major new generic introductions continued in 2006, resulting in a 2.9% fall in nonspecialty trend due to movement from brands to generics — slightly better than the 2.7% decline seen in 2005.

The antihyperlipidemics class saw the introduction of two major generics in 2006. Although their full impact will not be realized until 2007, they still contributed to a 5.6% drop in brand/generic mix for the class during 2006. As we forecasted last year, the September 2005 introduction of generics to Allegra® resulted in a double-digit brand/generic mix trend for antihistamines, which led all classes in the top 25. However, the macrolides class, which dropped out of the top 25 this year, actually had a huge 28.8% drop in cost caused by the impact of generics for Zithromax®.

In fact, the top seven nonspecialty classes all had significant generic rollouts in 2006. However, two of them — narcotic analgesics and miscellaneous hematologicals — are likely to see a reversal in brand/generic-mix trend because generics for OxyContin® and Plavix® will be forced off the market by ongoing patent disputes.

Exhibit 7

Changes in Brand/Generic Mix for the Top 25 Nonspecialty Therapy Classes 2005 to 2006

Ranked by Percent Change

Rank	Therapy Class	Key Generic Introduction	% Change
1.	Antihistamines	Allegra® (2005)	-11.8%
2.	NSAIDs	Mobic® (2006)	-10.7%
3.	Decongestants	Flonase® (2006)	-10.5%
4.	Narcotic Analgesics	OxyContin® (2005), Duragesic® (2005), Actiq® (2006)	-9.1%
5.	Misc. Hematologicals	Plavix® (2006)	-8.3%
6.	Antihyperlipidemics	Pravachol® (2006), Zocor® (2006)	-5.6%
7.	Antidepressants	Zoloft® (2006)	-2.5%
8.	Misc. Endocrines	DDAVP® (2005)	-2.0%
9.	Antidiabetics	Amaryl® (2005)	-1.8%
10.	Contraceptives	Ortho Tri-Cyclen® (2004)	-1.6%
11.	Anticonvulsants	Zonegran® (2005)	-1.6%
12.	Dermatologicals	Elocon® (2006)	-1.3%
13.	Calcium Blockers	Plendil® (2004)	-0.5%
14.	Beta Blockers	Toprol-XL® (2006)	-0.4%
15.	Antihypertensives	N/A	-0.3%
16.	Stimulants/Anti-Obesity	N/A	-0.3%
17.	Antipsychotics	N/A	-0.2%
18.	Migraine Products	N/A	-0.2%
19.	Antivirals	N/A	-0.2%
20.	Misc. GI Agents	N/A	-0.1%
21.	Gastrointestinals	N/A	-0.1%
22.	Hypnotics	N/A	-0.1%
23.	Ophthalmic Products	N/A	-0.1%
24.	Diagnostic Products	N/A	0
25.	Antiasthmatics	N/A	0
Top 25			-2.8%
Other			-3.4%
Total			-2.9%

UNITS PER PRESCRIPTION

Within the top 25 nonspecialty classes, changes in the number of units per prescription increased overall nonspecialty trend by only 0.4%. However, this change was one of the largest seen in several years.

Leading the way with a 4% change due to units per prescription was the narcotic analgesics class — due mostly to increased dosing of OxyContin® and its generic, oxycodone extended release.

At the other end of the spectrum, ophthalmic products dropped by 0.6%, due to fewer units per day for glaucoma treatments Lumigan® and Xalatan®. A 0.6% decline was also seen for miscellaneous GI agents, which are used to treat a number of conditions with symptoms that may fluctuate in severity.

Exhibit 8

Changes in Units per Prescription for the Top 25 Nonspecialty Therapy Classes 2005 to 2006

Ranked by Percent Change

Rank	Therapy Class	% Change
1.	Narcotic Analgesics	4.0%
2.	Dermatologicals	1.8%
3.	Diagnostic Products	1.7%
4.	Migraine Products	1.5%
5.	Gastrointestinals	1.2%
6.	Antidiabetics	1.1%
7.	Misc. Endocrines	0.8%
8.	Antipsychotics	0.7%
9.	Antidepressants	0.3%
10.	Beta Blockers	0.3%
11.	Hypnotics	0.2%
12.	Antihistamines	0.2%
13.	Stimulants/Anti-Obesity	0.2%
14.	Misc. Hematologicals	0.2%
15.	Decongestants	0.1%
16.	Antiasthmatics	0.1%
17.	Contraceptives	0.1%
18.	Antihypertensives	-0.1%
19.	Antihyperlipidemics	-0.1%
20.	Anticonvulsants	-0.3%
21.	Calcium Blockers	-0.3%
22.	Antivirals	-0.4%
23.	NSAIDs	-0.5%
24.	Misc. GI Agents	-0.6%
25.	Ophthalmic Products	-0.6%
	Top 25	0.5%
	Other	0.4%
	Total	0.4%

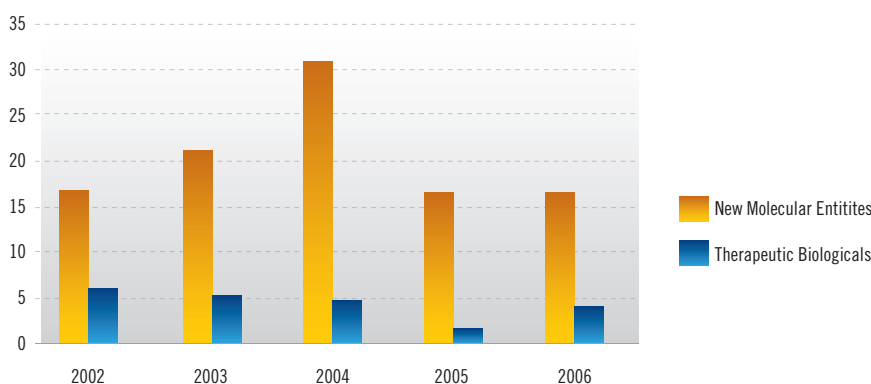
NEW DRUGS

In 2006, new drugs contributed only about 0.2% toward overall nonspecialty trend — one of the lowest new drug impacts in the 11 years that the *Drug Trend Report* has been published. In 2006, the U.S. Food and Drug Administration (FDA) approved 18 new molecular entities (active drugs that are new to the U.S. market) and four new therapeutic biologics.² These low numbers confirm that new brands are not having the largest impact on drug trend.

Despite the generally low new drug trend, antidiabetics has emerged as the one nonspecialty class likely to have a significant impact on future trends. Following the introduction of Byetta® in 2005, four additional new antidiabetics (Apidra®, Avandaryl™, Januvia™ and Levemir®) were approved in 2006.

Exhibit 9

Number of New Drug Approvals by the FDA 2002 to 2006



Adapted from: Owens J. 2006 drug approvals: finding the niche. *Nature Reviews Drug Discovery*. 2007; 6(2): 99-101. Available at <http://www.nature.com/nrd/journal/V6/n2/fohl/nrd2247.html#f1>. Accessed February 7, 2007.

Exhibit 10

Top 10 New Nonspecialty Prescription Drugs of 2006

Brand Name	Generic Name	Therapy Class	Cost	
			PMPY	% New Drug
1. Avandaryl™	rosiglitazone and glimepiride	Antidiabetics	\$0.21	20.4%
2. Chantix™	varenicline	Misc. CNS Agents*	\$0.21	20.3%
3. Levemir®	insulin detemir	Antidiabetics	\$0.14	13.9%
4. Januvia™	sitagliptin	Antidiabetics	\$0.07	6.9%
5. Amitiza™	lubiprostone	Misc. GI Agents	\$0.06	6.1%
6. Apidra®	insulin glulisine	Antidiabetics	\$0.04	4.3%
7. Oracea™	doxycycline	Dermatologicals	\$0.04	4.3%
8. Azilect®	rasagiline	Antiparkinsons Agents*	\$0.04	3.4%
9. Ranexa®	ranolazine	Antianginals*	\$0.03	3.3%
10. Prezista™	darunavir	Antivirals	\$0.02	2.0%
Top 10			\$0.88	84.8%
Other			\$0.16	15.2%
Total			\$1.03	100.0%

* Not in the top 25 classes

²Owens J. 2006 drug approvals: finding the niche. *Nature Reviews Drug Discovery*. 2007; 6(2): 99-101. Available at <http://www.nature.com/nrd/journal/V6/n2/fohl/nrd2247.html#f1>. Accessed February 7, 2007.

SPECIALTY DRUG TREND

The 20.9% trend for specialty drugs resulted mainly from just a few drug categories, with the top six accounting for more than 77% of specialty prescriptions filled through the pharmacy benefit. Steady and significant cost increases, especially in the multiple sclerosis (MS) and growth deficiency classes, were responsible for a large part of the trend.

A jump in the use of therapies that treat inflammatory conditions drove an overall increase of nearly 8% in specialty-drug utilization. Additional indications for two previously approved therapies, Enbrel® and Humira®, were primary contributors because 2006 was the first full year that both had expanded indications for psoriatic arthritis. Additionally, Humira was approved as a first-line treatment for moderate-to-severe rheumatoid arthritis (RA) in November 2005 and for ankylosing spondylitis in July 2006.

Exhibit 11

PMPY Cost, Utilization, Cost per Prescription and New Drug Trends for the Top 10 Specialty Categories 2005 to 2006

Ranked by 2006 PMPY Cost

	PMPY			% Change		
	2005	2006	% Change	Utilization	Cost/Rx	New Drugs
1. Inflammatory Conditions	\$15.52	\$19.04	22.7%	15.8%	5.8%	0.1%
2. Multiple Sclerosis	\$11.43	\$13.60	19.0%	3.4%	15.1%	0
3. Cancer	\$ 7.49	\$10.44	39.5%	6.5%	6.2%	26.4%
4. Blood Cell Deficiency	\$ 4.81	\$ 5.01	4.0%	-2.6%	6.8%	0
5. Growth Hormone Deficiency	\$ 3.74	\$ 4.59	22.8%	2.9%	19.1%	0.3%
6. Hepatitis C	\$ 3.76	\$ 3.45	-8.3%	-5.9%	-2.5%	0
7. Anticoagulants	\$ 2.63	\$ 3.34	26.7%	20.6%	5.0%	0
8. Infertility	\$ 2.62	\$ 2.58	-1.6%	-0.2%	-1.4%	0
9. Respiratory Conditions	\$ 2.17	\$ 2.54	17.1%	3.2%	13.5%	0
10. Hemophilia	\$ 1.01	\$ 1.72	69.9%	36.1%	24.8%	0
Top 10 Classes	\$55.19	\$66.31	20.1%	7.0%	8.9%	3.6%
Other	\$ 4.83	\$ 6.27	29.8%	15.8%	10.0%	2.4%
Total	\$60.02	\$72.58	20.9%	7.7%	9.0%	3.5%

Although new drugs made only a minor impact on nonspecialty cost, new specialty therapies accounted for a hefty 16.9% of overall specialty trend. In 2006, most new specialty medicines were introduced to treat various types of cancer, causing an historical impact of over 26% in the class. New cancer drugs that will continue to affect specialty trend include:

- Nexavar® — advanced renal cell carcinoma (RCC)
- Revlimid® — myelodysplastic syndromes and multiple myeloma
- Sutent® — advanced RCC and gastrointestinal stromal tumor (GIST)

