FORECAST

Getting to Zero Waste

2008 DRUG TREND REPORT

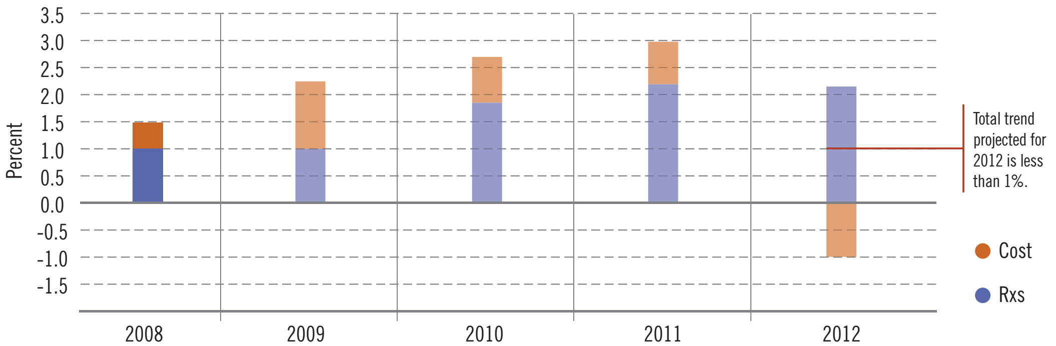
EXPRESS SCRIPTS®

TRADITIONAL

Overall trend for traditional prescription drugs is projected to grow less than 1% annually through 2011, and then drop to just over 1% in 2012 when many first-time generics drive cost-per-prescription (cost/Rx) growth into negative values.

EXHIBIT 15

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



From 2009 through 2012, overall utilization is projected to increase between 1% and 2.1% each year. Factors that contribute to utilization include the conversion of previously prescription-only drugs to over-the-counter (OTC) versions and the use of combination products, which reduce the number of prescriptions required. Prescription drug use for the annual influenza season is much more difficult to predict. Depending on the severity of the season, utilization in the antiviral and antibacterial classes can vary significantly, changing overall utilization, as well.

As more specialty drugs are approved, utilization in some classes will transition from predominantly traditional pharmacy into the specialty market. For instance, the bone-condition category currently is dominated by oral bisphosphonate drugs. In 2008, the introduction of the first generic bisphosphonate, alendronate, resulted in cost savings for plan sponsors. Looking forward, however, use of the once-a-year infusion, Reclast,® and probable approval of a new injectable product, denosumab (D-mab), will move utilization in the class from traditional-drug spend into specialty-drug spend.

The introduction of generics for several top-selling brands in highly used drug classes will keep the cost impact of new brand drugs and inflation to less than 1% of overall cost trend for the next three years. Products facing direct generic competition in 2011 include Actos,® Levaquin,® Lipitor® and Zyprexa.® Following in 2012 are Avandia,® Diovan,® Plavix,® Seroquel® and Singular.® We expect that the introduction of so many new generics will drop cost trend to -1% in 2012. Even if new brands are approved in the affected classes, brand manufacturers will struggle to replace sales due to the time needed to accumulate market share after the launch of a new drug.

EXHIBIT 16

Forecast for Selected Traditional Therapy Classes 2009 to 2012

Therapy Class	Trend 2009	2010	2011	2012	Comments
High Blood Cholesterol	-5.1%	-0.6%	3.0%	-9.1%	Market share will continue to shift away from Vytorin® in 2009, but it will stabilize in later years. In 2010, new guidelines will raise awareness, slightly increasing utilization in 2011. Cost/Rx for brand products will drop in 2010 as manufacturers attempt to gain formulary status in advance of generics to Lipitor,® now expected in late 2011. Significant cost savings will result in 2012.
High Blood Pressure/ Heart Disease	2.0%	-2.0%	0	2.0%	The large class of cardiovascular medications is dominated by generic products. Inflation for both generics and brands will continue to impact cost trend. However, the economy affects utilization in this category. Generics to Cozaar,® the first ARB to face patent expiration, could enter the market in 2010.
Diabetes	8.1%	10.2%	7.1%	5.0%	Utilization growth is expected to continue as the population ages and obesity is more prevalent. Cost will continue to increase as more patients use newer brand products. New generic opportunities are limited; the next significant patent expiration is for Actos,® in July 2011.
Depression	0.9%	-2.2%	-3.1%	-7.1%	Utilization of antidepressants may increase in 2009 and 2010. Looking forward, generics to Effexor XR,® expected in 2010, will be the first for an SNRI. Generics for Lexapro® will reach the market in 2012.
Ulcer Disease	0.4%	-10.0%	-9.8%	-6.9%	Generics to Prevacid® in late 2009 will decrease cost/Rx in 2010. In 2011, additional generics to Protonix® are expected, continuing negative cost trend. Possible OTC availability of additional PPIs, such as Prevacid and Zegerid,® will reduce prescription utilization, even though both will retain prescription status, as well.
Asthma	6.7%	10.2%	7.1%	7.1%	HFA inhalers completely replaced CFC albuterol products at the end of 2008, transitioning the market to brand-only products. Brand asthma drugs will continue to increase cost/Rx trend due to inflation. The brand asthma drugs will continue to hold the major part of market share until Singulair® becomes generic in August 2012.

Therapy Class	Trend 2009	2010	2011	2012	Comments
Seizures	-14.4%	1.7%	9.1%	9.1%	The 2008 availability of generics to Depakote,® Keppra® and Lamictal® will continue to reduce the cost/Rx in 2009. In addition, new generics to Depakote® ER and Topamax® will decrease cost in 2009 and 2010. Continued expansion of current agents into the pain market will increase utilization going forward. The market will rebound to 9% growth in 2011 and beyond.
Pain	12.2%	16.6%	13.4%	13.4%	The pain category is dominated by generics. In the near future, use of brand drugs, such as Celebrex® and Flector® patches, will increase cost/Rx slightly. Other brands, such as Pennsaid® topical lotion, which could be approved in late 2009, will affect this market by increasing cost/Rx.
Mental/Neurological Disorders	9.7%	14.5%	11.3%	8.2%	Generics to Risperdal,® Razadyne® and Razadyne® ER, released in 2008, will result in cost/Rx savings in 2009. Three new antipsychotics — Fanapta,™ Serdolect® and Saphris® — are currently under review by the FDA. If approved, they will have minor impact in 2009, but they will gain market share and drive up trend in 2010. Generics for Aricept® and Zyprexa,® expected late in 2010, will moderate 2011 cost trend. Seroquel® and Geodon® could go generic in Q1 2012 and Q3 2012, respectively, further mitigating overall trend in the class.
Attention Disorders	10.3%	4.9%	12.3%	12.3%	The first generics to Adderall XR™ became available in April 2009. Generics to Concerta® continue to be delayed due to litigation and its complex drug-release properties. Nuvigil,™ a brand alternative to Provigil,® is due in the second half of 2009.
Migraine Headaches	-21.6%	-10.0%	9.6%	9.6%	Generic Imitrex® (sumatriptan) will decrease cost trends in 2009 as additional supplies become available. In 2010, telcagepant, the first in a new class of drugs for migraines, could be approved, beginning to take market share away from the triptans. The patent expiration of Amerge® in mid-2010 will moderate cost/Rx growth in 2011.
Bone Conditions	-9.8%	-8.0%	-3.1%	-9.8%	Alendronate (generic Fosamax®) continues to take market share away from brand bisphosphonates. Utilization will continue to decrease as more patients use specialty medications, such as injectable Reclast.®
Total	**2.2%**	**2.8%**	**3.1%**	**1.1%**	

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 17.

EXHIBIT 17

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,® 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® 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,® Epogen® and Procrit,® 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™ and Promacta,® 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 18 on the next page details our 2009 to 2012 projections for trend in leading specialty categories.

EXHIBIT 18

Forecast for Selected Specialty Therapy Classes 2009 to 2012

Therapy Class	Trend 2009	2010	2011	2012	Comments
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.
Total	**15.2%**	**17.7%**	**19.4%**	**21.2%**	

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