

Express Scripts

RESEARCH STUDY FINDINGS

2005 Generic Drug Usage Report

Emily Cox, PhD, Andy Behm, PharmD, Doug Mager, MA

Executive Summary

The savings opportunity from increased use of generic medications has never been greater and will continue through 2010 as more than \$50 billion in drug sales are expected to lose patent over the next 5 years. Using data from 2004, Express Scripts reported significant variation in the generic fill rate (GFR) across states in addition to a \$20 billion missed savings potential across six therapy classes from underutilization of generics within the commercially insured market. This study estimates the 2005 savings potential from increased generic usage nationally, by state and across the same six therapy class. These savings are extrapolated to a commercially insured population.

Key Findings

- The overall generic fill rate in 2005 varied from a low of 45 percent in New Jersey to a high of 60 percent in New Mexico.
- Massachusetts had the highest GFR for three of the six therapy classes (antihypertensives, antidepressants, and NSAIDs) and New Jersey with the lowest GFR for three of the six therapy classes evaluated (anti-hypertensives, anti-depressants, and lipid lowering).
- The estimated annual savings opportunity among commercially insured members across the 48 states and six therapy classes evaluated was over \$21.7 billion.
- The two therapy classes with the greatest savings opportunity comes from increased use of generics in the anti-hyperlipidemic and gastrointestinal therapy classes, where reaching generic targets would save employers, state governments and members \$6.8 and \$6.5 billion annually respectively.
- The state with the greatest savings opportunity per capita was Kentucky where savings of over \$163 per commercially insured member could be realized.

Implications

The savings opportunity for employers, state governments, unions, and members from achieving higher generic fill rates is unprecedented. Reaching these generic targets calls for:

- A recognition that using more generic drugs will free up resources to meet other pressing health care needs and help preserve the pharmacy benefit as we know it – without impacting quality.
- Increased awareness of generic alternatives to brand drugs by patients and physicians.
- Adoption of pharmacy benefit plan designs that encourage greater use of generic drugs, for example by using a program called step therapy where a generic drug is tried first, before a brand.
- Enactment of state laws and regulations that promote the use of chemically equivalent generic alternatives to brand drugs.

2005 Generic Drug Usage Report

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The savings opportunity from increased use of generic medications has never been greater and will continue through 2010 as more than \$50 billion in drug sales are expected to lose patent over the next 4 years. Despite the growing availability of tools to encourage greater generic use, adoption varies. Evidence of this can be seen in the variation in generic fill rate (GFR) across states reported by Express Scripts in 2004.¹ In that study, commercially insured residents of New Jersey had the lowest GFR of 41.0 percent compared to a GFR of 56.1 percent among commercially insured residents of Oregon.

Failure to capture the generic opportunity results in significant missed savings for businesses, state government and patients. On average, a generic drug costs approximately \$67 less than a brand name drug and for each 1 percentage point increase in generic fill rate, plan sponsors' pharmacy spend is estimated to decrease by 1 percent. These savings are typically shared by both patients and plan sponsors since patients benefit by paying a lower copayment for generic medications.

This study re-estimates the generic opportunity or targets from therapeutic and chemically equivalent generic substitution across six therapy classes in 2005. Further, we estimate the potential savings nationally, by state and therapy class for a commercially insured population. We also project savings for the top therapy classes in 2006 based upon projected GFRs across these same therapy classes.

Methods

Express Scripts' clinical pharmacists estimated the therapy class generic targets for 2005 by evaluating the clinical efficacy and market dynamics of branded and generic medications across six of the top therapy classes. The description of the products included in each therapy category and the clinical rationale for determining generic targets is included in Appendix C. These six therapy classes represent 40 percent of all commercially insured drug spending according to the 2005 Express Scripts Drug Trend Report.²

Table 1: Actual Generic Fill Rate, Generic Targets and Total Estimated Savings in 2005 if Targets Were Reached

Therapy Class	Actual 2005 GFR	Generic Targets	Gap	Potential Savings if Generic Usage Targets Reached
Gastrointestinals	32%	95%	63%	\$6.5 billion
Anti-hyperlipidemics	7%	70%	63%	\$6.8 billion
Calcium Channel Blockers	44%	95%	51%	\$0.7 billion
Anti-hypertensives*	54%	75%	21%	\$2.1 billion
NSAIDs	68%	95%	37%	\$1.8 billion
Anti-depressants	50%	80%	30%	\$3.8 billion
Total Savings				\$21.7 billion

*Includes ACE inhibitors, ARBs, antiadrenergics (e.g., alpha blockers), vasodilators (e.g., hydralazine), and certain combination products

Actual GFRs for each therapy class and for each state were estimated using a database containing ambulatory administrative pharmacy claims and eligibility information for a random sample of

¹ Geographic variation in generic fill rate. Available at: <http://www.express-scripts.com/ourcompany/news/outcomesresearch/onlinepublications/>.

² Miller S, Parker A, Peterson C, et al. Therapy Class Review. In: *2005 Express Scripts Drug Trend Report*. St Louis, MO: Express Scripts, Inc; 2006:70-71.

approximately 3 million commercially insured Express Scripts members in 2005. Eligibility data were used to identify the state of residence for each member in addition to their date of birth and gender. The health plan sponsors for these beneficiaries included private and public sector employer groups, managed care organizations, third-party administrators, and unions. The GFR was calculated as the total number of generic prescription claims divided by total prescription claims. This percentage was age and gender adjusted using a generalized linear model. Claims were adjusted to 30-day equivalent prescriptions; for example a prescription claim with a 90-day supply was converted to three prescription claims, each with a 30-day supply.

The savings opportunity for each state was then estimated for each therapy class as the difference in actual total costs given each state's 2005 GFR and what costs could be if the state were able to reach the generic targets for that therapy class. Total costs were estimated as a function of the prevalence of prescription use within the respective therapy class, the average number of refills per utilizer per year, the total state population with employer sponsored insurance, and the costs per prescription for generic and brand name drugs. For example, the total cost for therapy class *i* and state *j* was calculated using the formula below:

$$\text{Total Cost}_{ij} = \text{Prevalence}_{ij} * \text{Population commercially insured}_i * \text{number of Rxs PUPY}_{ij} * (\text{ave cost} * \text{GFR}_{ij} + \text{ave cost} * (1 - \text{GFR}_{ij}))$$

generic_i
brand_i

where PUPY = per utilizer per year. For each state, the prevalence of prescription use was measured as the percent of continuously enrolled commercially insured members with at least one prescription for the respective therapy class divided by the total number of continuously enrolled members. The average number of refills by state was calculated as the total number of 30-day equivalent prescription claims for the respective therapy class divided by the total number of members continuously eligible with at least one claim in that therapy class. Estimates of the state population with employer-sponsored health care coverage were obtained from Henry J Kaiser Family Foundation.³ The average cost per 30-day equivalent prescription for brands and generics was estimated using the discounted ingredient cost. Therefore, the savings opportunity represents the savings both to plan sponsors (i.e., employers and state governments) and members.

Savings projections for 2006 were estimated for each therapy class using the actual GFR from 1st quarter 2006 and projecting out through 2006. The GFR opportunity and overall savings for 2006 was estimated using a similar method as described above.

Results

The overall generic fill rate in 2005 varied from a low of 45 percent in New Jersey to a high of 60 percent in New Mexico. (Appendix A) States with the highest GFR included New Mexico, Massachusetts and Oregon with GFRs at or approaching 60%. Those states with the highest GFR in 2005 saw an increase of from 3 to 4.5 percentage points from their 2004 values. Although New Jersey was again an outlier with a GFR of 45%, they did increase their GFR in 2005 by a similar 4 percentage points.¹

Evaluation of states at the therapy class level show significant gaps in the GFR across states. (Table 2) The greatest difference in GFR between states was in the antihypertensive therapy class where a 36 percentage point difference was observed between Massachusetts at 74% and New Jersey at 38%. Several reasons may explain this discrepancy including variations in prescribing patterns and differences in adoption of drug benefit designs and programs that encourage greater use of generics in this therapy class. Similar gaps were

³ The Kaiser Family Foundation, statehealthfacts.org. Data Source: Urban Institute and Kaiser Commission on Medicaid and the Uninsured estimates based on pooled March 2003 and 2004 Current Population Surveys.

seen in the gastrointestinal (31 percentage point gap) and Calcium channel blocker therapy classes (29 percentage point gap).

Table 2: States with the Highest and Lowest Generic Fill Rate by Therapy Class

Therapy Class	Highest GFR	Lowest GFR
Gastrointestinals	Rhode Island (49%)	Utah (18%)
Calcium Channel Blockers	Vermont (57%)	Wyoming (28%)
Antihypertensives	Massachusetts (74%)	New Jersey (38%)
Antidepressants	Massachusetts (65%)	New Jersey (38%)
Antihyperlipidemics	New Mexico (18%)	New Jersey (3%)
NSAIDs	Massachusetts (80%)	Louisiana (52%)

Given the discrepancies between actual GFR and the GFR targets, the estimated annual savings opportunity in 2005 among commercially insured members across the 48 states and six therapy classes evaluated was over \$21.7 billion. (Appendix A and Table 1) This represents an approximate increase in savings of \$1.7 billion from the 2004 estimates. The greatest savings opportunity comes from increased use of generics in the gastrointestinal and anti-hyperlipidemics therapy classes, where reaching generic targets would save employers, state governments and members over \$6.5 billion annually. This is driven by a combination of factors including the gap between actual and generic opportunity, the difference in the average cost of brands and generics, and the prevalence and utilization within the respective therapy classes. For example, in the antihyperlipidemic and gastrointestinal therapy classes the gap between actual and potential GFR is around 63 percentage points. And while the difference in cost between brands and generics is much greater for gastrointestinals than antihyperlipidemics (\$83 compared to \$50), the higher prevalence and number of prescriptions used by those with a prescription claim in the antihyperlipidemic therapy class, produce a slightly greater savings opportunity for lipid lowering compared to gastrointestinals.

The states with the largest savings opportunity include California, Texas, Florida, New York, Pennsylvania, Ohio, and Illinois, each with the potential to save over \$1 billion annually in prescription drug costs for employers, government agencies and state residents. (Appendix B)

2006 Savings Projections

Table 3 presents the savings projections for 2006 based upon actual GFR for the first quarter of 2006, projected through year end. Several key factors change in 2006 that influence not only the actual GFR but also GFR targets. For example, the actual GFR for the antihyperlipidemic class is expected to increase from 7% in 2005 to 19% in 2006. Contributing toward this rise is the patent expiration of Zocor on June 23, 2006, the second most utilized drug in this therapy class. As a result, the generic target for 2006 also increased as did the potential savings. In total, savings of approximately \$25 billion would be expected if these targets were reached with the greatest area of savings being in the antihyperlipidemic therapy class where savings of over \$10 billion could be achieved if clients were able to achieve a GFR of 85%.

Table 3: 2006 Projected Generic Fill Rate, 2006 Generic Targets and Total Estimated Savings in 2006 if Targets Were Reached

Therapy Class	Projected 2006 GFR	Generic Targets	Gap	Potential Savings if Generic Usage Targets Reached
Gastrointestinals	35%	95%	60%	\$6.8 billion
Anti-hyperlipidemics	19%	85%	66%	\$10.3 billion
Calcium Channel Blockers	49%	95%	46%	\$0.9 billion
Anti-hypertensives*	58%	75%	17%	\$2.1 billion
NSAIDs	77%	97%	20%	\$1.2 billion
Anti-depressants	57%	85%	28%	\$3.4 billion
Total Savings				\$24.7 billion

*Includes ACE inhibitors, ARBs, antiadrenergics (e.g., alpha blockers), vasodilators (e.g., hydralazine), and certain combination products

Limitations

Projected savings may be over or underestimated to the extent that the prescription prevalence, utilization and costs within Express Scripts' commercially insured sample does not reflect the state's entire commercially insured population. That said, we believe these estimates may underestimate total savings for many states, given that Express Scripts has one of the highest generic fill rates among the leading PBMs.

Implications

The savings opportunity for employers, state governments, unions and members from achieving higher generic fill rates continues to be strong. Active management of the pharmacy benefit is key to taking advantage of these savings. Proven tactics are available to encourage greater use of generic medications including tiered copays, generic policies, formularies, and step therapy. However, plan design alone may not be enough to reach the goal. Optimal generic fill rates will be achieved only through a concerted effort by all those involved in the prescribing process including physicians, pharmacists and patients. Health care providers and the public are rarely provided information on the clinical appropriateness and cost-effectiveness of generics compared to newer branded medications. This information in the form of guidelines and cost-effectiveness studies are available, yet less well disseminated compared to the information on the newer branded medications.

In summary, reaching generic targets calls for:

- A recognition that using more generic drugs will free up resources to meet other pressing health care needs and help preserve the pharmacy benefit as we know it – without impacting quality.
- Increased awareness of generic alternatives to brand drugs by patients and physicians.
- Adoption of pharmacy benefit plan designs that encourage greater use of generic drugs, for example by using a program called step therapy where a generic drug is tried first, before a brand.
- Enactment of state laws and regulations that promote the use of chemically equivalent generic alternatives to brand drugs.

Appendix A: State Age-Gender Adjusted Generic Fill Rate Overall and By Therapy Class and Total Potential Savings From Reaching GFR Opportunity: 2005

State	Total ESI Sample	Overall Age-Gender Adjusted GFR	Age-Gender Adjusted Generic Fill Rate						Total Potential Savings From 6 Therapy Classes
			NSAIDS	Antihypertensives	Antidepressants	GI	Calcium Channel Blockers	Lipid Lowering	
AL	22,411	54.4%	55.8%	48.1%	45.3%	27.1%	48.7%	6.9%	\$392,023,999
AR	18,712	53.9%	57.3%	44.8%	45.5%	27.9%	49.8%	6.7%	\$207,717,947
AZ	31,302	56.2%	70.2%	60.9%	51.4%	38.0%	50.1%	11.5%	\$339,184,151
CA	103,034	53.8%	71.8%	57.2%	49.6%	28.8%	50.0%	12.1%	\$1,733,579,948
CO	21,198	54.1%	64.2%	65.1%	49.0%	35.8%	48.3%	10.4%	\$301,564,560
CT	59,386	51.5%	70.2%	56.8%	46.0%	24.3%	39.1%	6.4%	\$284,321,932
DE	28,680	51.8%	74.9%	59.9%	47.2%	37.8%	46.2%	5.0%	\$71,926,345
FL	104,628	49.0%	60.5%	46.5%	43.0%	28.4%	41.7%	6.1%	\$1,353,788,594
GA	55,515	51.0%	67.1%	47.5%	42.6%	26.3%	43.4%	5.3%	\$795,041,184
IA	16,893	54.9%	66.7%	57.8%	48.3%	33.2%	46.7%	10.4%	\$228,024,989
ID	7,842	54.0%	63.1%	53.2%	51.0%	35.4%	42.9%	13.6%	\$94,510,103
IL	79,472	50.9%	65.4%	53.8%	48.1%	28.1%	47.1%	6.1%	\$1,026,899,768
IN	64,743	51.1%	64.3%	49.0%	49.1%	24.8%	41.4%	5.9%	\$596,215,748
KS	37,446	52.8%	57.9%	50.7%	52.6%	31.5%	50.4%	6.4%	\$230,397,844
KY	27,618	53.1%	65.0%	55.1%	48.1%	31.3%	42.9%	5.4%	\$381,762,534
LA	87,394	48.7%	51.9%	41.1%	40.7%	22.6%	45.1%	5.6%	\$375,260,431
MA	290,819	59.3%	79.5%	73.6%	65.1%	46.4%	49.0%	6.1%	\$400,053,259
MD	149,830	49.5%	69.4%	48.7%	44.1%	19.6%	40.6%	4.3%	\$520,606,756
ME	6,141	56.7%	74.1%	70.8%	55.3%	39.1%	44.0%	10.1%	\$83,275,900
MI	84,477	52.7%	70.3%	58.2%	48.9%	34.5%	46.0%	7.8%	\$992,490,076
MN	44,335	54.9%	67.7%	69.7%	55.0%	39.2%	41.6%	8.7%	\$346,984,394
MO	68,925	55.4%	65.6%	60.4%	51.6%	34.4%	49.8%	10.9%	\$457,612,677
MS	18,007	51.9%	58.4%	42.7%	42.6%	24.7%	41.9%	5.9%	\$235,604,734
MT	8,376	55.6%	65.0%	63.0%	51.3%	27.4%	45.2%	8.5%	\$44,963,524
NC	53,167	51.8%	66.5%	52.7%	45.5%	27.9%	44.4%	7.7%	\$714,741,792
ND	1,368	57.4%	66.3%	62.2%	55.0%	32.6%	44.2%	8.5%	\$34,399,390
NE	14,301	51.1%	57.9%	52.2%	42.4%	30.5%	45.8%	5.2%	\$146,096,387
NH	20,511	56.2%	76.5%	69.4%	57.7%	39.0%	43.2%	6.7%	\$109,627,424
NJ	88,464	44.8%	61.5%	38.2%	38.1%	21.0%	33.2%	3.2%	\$768,352,130
NM	34,516	60.1%	78.3%	67.2%	58.4%	41.2%	47.7%	18.1%	\$71,645,929
NV	21,603	55.3%	69.8%	52.5%	55.4%	24.9%	41.9%	10.9%	\$153,031,678
NY	388,123	48.8%	69.6%	47.5%	45.0%	31.4%	39.7%	6.0%	\$1,199,709,687
OH	101,960	52.2%	65.0%	54.4%	46.0%	24.9%	41.8%	5.9%	\$1,051,976,435
OK	19,194	53.3%	57.7%	50.2%	46.1%	30.4%	44.4%	9.1%	\$287,165,718
OR	11,362	59.0%	70.9%	62.7%	54.1%	31.1%	50.1%	13.3%	\$207,866,941
PA	252,459	51.9%	66.6%	51.5%	45.6%	33.1%	44.4%	5.1%	\$1,077,223,346
RI	9,183	57.4%	77.8%	69.4%	60.3%	48.7%	39.3%	7.0%	\$57,809,450
SC	38,890	51.8%	63.4%	46.8%	48.7%	28.6%	39.6%	4.8%	\$324,703,698
SD	7,422	53.8%	62.8%	60.0%	48.7%	35.1%	37.8%	8.1%	\$45,099,265
TN	48,337	53.5%	63.8%	48.4%	45.5%	32.6%	47.9%	8.1%	\$513,113,601
TX	123,386	49.8%	58.3%	47.5%	42.1%	25.6%	44.8%	7.1%	\$1,644,882,869
UT	41,015	56.3%	72.8%	56.0%	55.8%	17.9%	46.2%	7.3%	\$211,025,511
VA	86,749	50.5%	72.8%	51.4%	45.2%	24.4%	41.6%	5.4%	\$623,200,018
VT	6,696	55.3%	71.4%	59.8%	54.5%	32.2%	57.1%	8.3%	\$49,814,585
WA	45,525	56.1%	71.7%	61.2%	55.0%	35.0%	46.0%	12.2%	\$413,153,801
WI	54,996	57.2%	70.8%	65.6%	57.4%	35.8%	49.3%	12.0%	\$348,579,287
WV	51,257	54.7%	75.8%	57.3%	49.3%	47.0%	42.6%	6.3%	\$129,467,612
WY	3,004	56.0%	62.7%	58.5%	43.2%	21.3%	27.6%	6.6%	\$37,615,107
Total	2,960,672		68.1%	53.7%	49.6%	31.8%	43.8%	6.7%	\$21,714,108,870

NSAIDs = Non-steroidal anti-inflammatory drugs, GFR = Generic Fill Rate, GI = Gastrointestinals

Appendix B: State Age-Gender Adjusted Generic Fill Rate Overall and By Therapy Class and Total Potential Savings From Reaching GFR Opportunity, Sorted by Total Potential Savings: 2005

State	Total ESI Sample	Overall Age-Gender Adjusted GFR	Age-Gender Adjusted Generic Fill Rate							Total Potential Savings From 6 Therapy Classes
			NSAIDs	Antihypertensives	Antidepressants	GI	Calcium Channel Blockers	Lipid Lowering		
CA	103,034	53.8%	71.8%	57.2%	49.6%	28.8%	50.0%	12.1%	\$1,733,579,948	
TX	123,386	49.8%	58.3%	47.5%	42.1%	25.6%	44.8%	7.1%	\$1,644,882,869	
FL	104,628	49.0%	60.5%	46.5%	43.0%	28.4%	41.7%	6.1%	\$1,353,788,594	
NY	388,123	48.8%	69.6%	47.5%	45.0%	31.4%	39.7%	6.0%	\$1,199,709,687	
PA	252,459	51.9%	66.6%	51.5%	45.6%	33.1%	44.4%	5.1%	\$1,077,223,346	
OH	101,960	52.2%	65.0%	54.4%	46.0%	24.9%	41.8%	5.9%	\$1,051,976,435	
IL	79,472	50.9%	65.4%	53.8%	48.1%	28.1%	47.1%	6.1%	\$1,026,899,768	
MI	84,477	52.7%	70.3%	58.2%	48.9%	34.5%	46.0%	7.8%	\$992,490,076	
GA	55,515	51.0%	67.1%	47.5%	42.6%	26.3%	43.4%	5.3%	\$795,041,184	
NJ	88,464	44.8%	61.5%	38.2%	38.1%	21.0%	33.2%	3.2%	\$768,352,130	
NC	53,167	51.8%	66.5%	52.7%	45.5%	27.9%	44.4%	7.7%	\$714,741,792	
VA	86,749	50.5%	72.8%	51.4%	45.2%	24.4%	41.6%	5.4%	\$623,200,018	
IN	64,743	51.1%	64.3%	49.0%	49.1%	24.8%	41.4%	5.9%	\$596,215,748	
MD	149,830	49.5%	69.4%	48.7%	44.1%	19.6%	40.6%	4.3%	\$520,606,756	
TN	48,337	53.5%	63.8%	48.4%	45.5%	32.6%	47.9%	8.1%	\$513,113,601	
MO	68,925	55.4%	65.6%	60.4%	51.6%	34.4%	49.8%	10.9%	\$457,612,677	
WA	45,525	56.1%	71.7%	61.2%	55.0%	35.0%	46.0%	12.2%	\$413,153,801	
MA	290,819	59.3%	79.5%	73.6%	65.1%	46.4%	49.0%	6.1%	\$400,053,259	
AL	22,411	54.4%	55.8%	48.1%	45.3%	27.1%	48.7%	6.9%	\$392,023,999	
KY	27,618	53.1%	65.0%	55.1%	48.1%	31.3%	42.9%	5.4%	\$381,762,534	
LA	87,394	48.7%	51.9%	41.1%	40.7%	22.6%	45.1%	5.6%	\$375,260,431	
WI	54,996	57.2%	70.8%	65.6%	57.4%	35.8%	49.3%	12.0%	\$348,579,287	
MN	44,335	54.9%	67.7%	69.7%	55.0%	39.2%	41.6%	8.7%	\$346,984,394	
AZ	31,302	56.2%	70.2%	60.9%	51.4%	38.0%	50.1%	11.5%	\$339,184,151	
SC	38,890	51.8%	63.4%	46.8%	48.7%	28.6%	39.6%	4.8%	\$324,703,698	
CO	21,198	54.1%	64.2%	65.1%	49.0%	35.8%	48.3%	10.4%	\$301,564,560	
OK	19,194	53.3%	57.7%	50.2%	46.1%	30.4%	44.4%	9.1%	\$287,165,718	
CT	59,386	51.5%	70.2%	56.8%	46.0%	24.3%	39.1%	6.4%	\$284,321,932	
MS	18,007	51.9%	58.4%	42.7%	42.6%	24.7%	41.9%	5.9%	\$235,604,734	
KS	37,446	52.8%	57.9%	50.7%	52.6%	31.5%	50.4%	6.4%	\$230,397,844	
IA	16,893	54.9%	66.7%	57.8%	48.3%	33.2%	46.7%	10.4%	\$228,024,989	
UT	41,015	56.3%	72.8%	56.0%	55.8%	17.9%	46.2%	7.3%	\$211,025,511	
OR	11,362	59.0%	70.9%	62.7%	54.1%	31.1%	50.1%	13.3%	\$207,866,941	
AR	18,712	53.9%	57.3%	44.8%	45.5%	27.9%	49.8%	6.7%	\$207,717,947	
NV	21,603	55.3%	69.8%	52.5%	55.4%	24.9%	41.9%	10.9%	\$153,031,678	
NE	14,301	51.1%	57.9%	52.2%	42.4%	30.5%	45.8%	5.2%	\$146,096,387	
WV	51,257	54.7%	75.8%	57.3%	49.3%	47.0%	42.6%	6.3%	\$129,467,612	
NH	20,511	56.2%	76.5%	69.4%	57.7%	39.0%	43.2%	6.7%	\$109,627,424	
ID	7,842	54.0%	63.1%	53.2%	51.0%	35.4%	42.9%	13.6%	\$94,510,103	
ME	6,141	56.7%	74.1%	70.8%	55.3%	39.1%	44.0%	10.1%	\$83,275,900	
DE	28,680	51.8%	74.9%	59.9%	47.2%	37.8%	46.2%	5.0%	\$71,926,345	
NM	34,516	60.1%	78.3%	67.2%	58.4%	41.2%	47.7%	18.1%	\$71,645,929	
RI	9,183	57.4%	77.8%	69.4%	60.3%	48.7%	39.3%	7.0%	\$57,809,450	
VT	6,696	55.3%	71.4%	59.8%	54.5%	32.2%	57.1%	8.3%	\$49,814,585	
SD	7,422	53.8%	62.8%	60.0%	48.7%	35.1%	37.8%	8.1%	\$45,099,265	
MT	8,376	55.6%	65.0%	63.0%	51.3%	27.4%	45.2%	8.5%	\$44,963,524	
WY	3,004	56.0%	62.7%	58.5%	43.2%	21.3%	27.6%	6.6%	\$37,615,107	
ND	1,368	57.4%	66.3%	62.2%	55.0%	32.6%	44.2%	8.5%	\$34,399,390	
Total	2,960,672		68.1%	53.7%	49.6%	31.8%	43.8%	6.7%	\$21,714,108,870	

NSAIDs = Non-steroidal anti-inflammatory drugs, GFR = Generic Fill Rate, GI = Gastrointestinals

Appendix C: 2005 Generic Targets Across 6 Therapy Classes

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The following is an update to “Use of Generic Therapeutic Substitution Can Save Billions in Drug Costs”, an article that defined generic fill rate (GFR) and savings opportunities for some of the most highly utilized therapy classes in 2004.¹

This article provides the clinical rationale used to define generic fill rate GFR opportunities for GI medications, antihyperlipidemics, calcium channel blockers, antihypertensives, NSAIDs, and antidepressants. All therapy classes are defined in a manner consistent with the Express Scripts’ *2005 Drug Trend Report* and frequently include multiple drug groups.² The GFRs for each therapy class, 2005 actual and generic ceiling values, take into account all available medications within each therapy class. The 2005 average GFRs cited here may vary slightly from the geographic averages presented in the companion study, as they are representative of not only commercially insured pharmacy benefit plans but claims data from MCOs, third-party administrators, and federal and state government programs. The GFR ceiling values represent the peak clinical potential and may not be attainable in practice without strict protocols and aggressive trend-management strategies.

The reported GFR ceiling values for these therapy classes are based on a combination of factors, of which treatment guidelines and primary literature serve as the foundation. Layered on top of the clinical information are specific market dynamics of 2005, including the withdrawal of some medications from the market, generic availability, and the introduction of new brand-name products. The GFR ceiling values do not take into account pharmaceutical marketing, direct-to-consumer advertising, financial considerations, or patient and health care practitioner brand loyalty. The proposed GFR ceiling values are calculated based on information available in 2005 and apply solely to that year. In addition, the GFR ceiling values consider the entire year and are not based on simply one point in time.

Gastrointestinals

The Gastrointestinal (GI) therapeutic category includes histamine₂ (H₂) receptor blockers (eg, ranitidine [Zantac]); proton pump inhibitors (PPIs) (eg, omeprazole [Prilosec]); and miscellaneous GI products, including Carafate (sucralfate), Levsin (hyoscyamine), and Librax (chlordiazepoxide and clidinium).

In 2005, the GFR for the GI therapy class was 31%. PPIs dominated this class, accounting for slightly more than 80% of total prescriptions. The remainder consisted of H₂-receptor blockers and miscellaneous GI products, which accounted for 11% and 8% of the market share, respectively. The 2005 GFR of 31% was composed of generic omeprazole (~16%); generic H₂-receptor blockers (10%); and miscellaneous generic GI products (6%).²

The GFR ceiling value for this class could have been 95% in 2004. GI medications are primarily used to manage gastroesophageal reflux disease (GERD) and to manage and prevent ulcers.² PPIs continue to be the mainstay of therapy for these conditions. Although the FDA-approved indications may vary somewhat, all PPIs have comparable effectiveness and safety profiles for acid-related disorders.³⁻¹⁴ Thus, generic omeprazole could be used by most patients; exceptions would be women who are pregnant or breast feeding, persons taking certain drugs that interact with omeprazole, or persons with hypersecretory conditions who need to reduce pill burden.⁹⁻¹⁴ In addition, research evaluating a prior authorization (PA) policy for PPIs found that claims for PPIs decreased 92% in the month immediately following the implementation of the PA policy, while claims for H₂-receptor blockers increased 98%. This study also found that there were no adverse medical consequences of using an H₂-receptor blocker or receiving no therapy.¹⁵

In light of this information, a majority of patients requiring a PPI could have used either generic omeprazole or a generic H₂-receptor blocker. In 2005, generic alternatives were available for all H₂-receptor blockers and all miscellaneous GI medications. In 2004, a GFR ceiling value of 95% was reasonable.¹ Since

there were no major changes in 2005, the GFR ceiling value for the GI therapy class remained the same at 95%.

Calcium Channel Blockers

The calcium channel blocker (CCB) therapy class includes dihydropyridines (eg, amlodipine [Norvasc], felodipine [Plendil], nifedipine ER [Adalat CC/Procardia XL]), and nondihydropyridines (eg, verapamil and diltiazem products). The primary CCB market driver is the dihydropyridine class, which accounts for approximately 62% of the total CCB market share.

Despite the availability of generics, market share for Norvasc continued to dominate and approached 50% in 2005.² The growth of Norvasc outpaced that of generic CCBs, which remained stable with only 44% of the total CCB market in 2005.² The remaining market share (less than 10%) was attributed to other brand-name CCBs that have generic alternatives (eg, Sular [nisoldipine]).

With several generic alternatives available in this class, the GFR ceiling value for the CCBs was 95% in 2005. Many CCBs are approved by the FDA for the management of hypertension and angina.¹⁶⁻³⁸ Guidelines for hypertension and chronic stable angina do not specify the use of one long-acting dihydropyridine over another.^{39,40} Consequently, a brand-name drug may be no more effective than a generic drug for management of hypertension and chronic stable angina.

Outside of FDA-approved indications, Norvasc and felodipine, a generic dihydropyridine that has been available since late 2004, have been studied in patients with heart failure.^{16,41-43} Treatment guidelines for heart failure caution against the use of most CCBs and indicate that only Norvasc does not adversely affect survival.⁴⁴ The use of Norvasc for patients with hypertension or angina without a comorbid diagnosis of heart failure may not be necessary when other cost-effective alternatives are available.

Although there are some circumstances requiring the use of a brand-name CCB, the majority of patients can use a generic version. We previously reported a GFR ceiling of 90% in 2004.¹ The only significant difference in this therapy class during 2005 was felodipine's full year of generic availability, which could have contributed to at least a 5% increase in GFR from 2004. Thus, we think a GFR ceiling value of 95% could have been attained in the CCB therapy class in 2005.

Antihypertensives

The antihypertensive therapy class consists primarily of 2 subclasses: angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors. In fact, just over 85% of the antihypertensive market share in 2005 consisted of ACE inhibitors, ARBs, and combinations of these with hydrochlorothiazide or a CCB.² Antiadrenergic antihypertensives (eg, clonidine and alpha blockers), vasodilators (eg, hydralazine), and combination products (eg, beta blockers plus diuretic) account for the remaining portion of this class. All these medications are commonly used to manage hypertension and may also be used to manage heart failure and other indications, such as renal protection. Although this therapy class is called antihypertensives, it does not encompass the entire range of antihypertensives. Single-entity beta-blockers, CCBs, and diuretics are not included in this therapy class.

Generics accounted for approximately 53% of the antihypertensive market in 2005, with generic ACE inhibitors dominating the class with close to 42% of the market share.² Extensive research and the availability of multiple generic alternatives has contributed to ACE inhibitors dominance in the market. Specifically, ACE inhibitors have benefited from clinical trials showing their positive outcomes on mortality and morbidity; many of the agents studied in these trials are available generically (eg, captopril, enalapril, and lisinopril).⁴⁵⁻⁴⁷ Because of their excellent clinical outcomes data, ACE inhibitors have been deemed by several national treatment guidelines as clinically appropriate first-line options.^{44,48,49}

Considering the abundance of available generic antihypertensives and their safety and effectiveness data, a GFR ceiling of 75% could have been attained in 2005. A major factor in calculating the GFR for this therapy class is the ARB subclass; it is the only subclass in the antihypertensives therapy class for which no generic alternatives are available. ARBs and ACE inhibitors have been studied in similar patient populations

and, in many situations, outcomes associated with ACE inhibitors are similar to or better than those associated with ARBs; despite this, ARBs may be recommended for specific medical needs. For example, ARBs are an alternative therapy for patients who are intolerant of ACE inhibitors. Clinical studies have revealed rates of ACE-inhibitor intolerance from 5% to 33% and discontinuation rates of up to 15%.⁵⁰ Research further indicates that ARBs provide beneficial effects in a subset of hypertensive patients with type 2 diabetes and nephropathy⁴⁸ and may reduce risk of cardiovascular mortality or hospitalization in some patients with heart failure.⁵¹⁻⁵⁵

Given the varying rates of intolerance to ACE inhibitors and the relatively small population requiring benefits from ARBs, the generic ACE inhibitor market share could have been much higher than 42%. In addition, antiadrenergics, vasodilators, and combination products have generic alternatives; any use of these products could contribute to the total GFR. A GFR ceiling of 75% was previously reported in 2004.¹ With no significant new antihypertensives entering the market during 2005, a GFR ceiling of up to 75% was also reasonable in 2005.

NSAIDs

The NSAID therapy class contains traditional NSAIDs, such as ibuprofen, and the cyclooxygenase-2 (COX-2) inhibitors, which included Celebrex, and Bextra in 2005. Generic market share for this class increased significantly, from 50% in 2004 to 65% in 2005.²

This therapy class underwent dramatic changes in late 2004 and 2005. According to Express Scripts book of business data, COX-2s commanded 55% of the market share in this class during the 1st quarter of 2004. On September 30, 2004, Merck voluntarily withdrew Vioxx from the market because of concerns that the product was associated with increased cardiovascular risk. Questions also arose about the safety of Celebrex and Bextra, culminating in withdrawal of Bextra from the market in early 2005. Following these two events, many patients transitioned from a COX-2 inhibitor to either a generic NSAID or brand name product such as Mobic. As a result, COX-2 inhibitors only comprised 21% of the NSAID market share in 2005. All NSAIDs and COX-2 inhibitors have similar effectiveness at equipotent doses for management of pain and pain-related conditions.^{56,57} Individual response to NSAIDs varies among patients, and no one product can be distinguished from another in terms of effectiveness on a consistent basis. Consequently, patients may need to try more than one product before achieving pain relief.

Although similarities in the efficacy of NSAIDs have been fairly well established, traditional NSAIDs and COX-2 inhibitors are often prescribed based on their GI risk profiles. In comparing the traditional NSAIDs, it is difficult to differentiate them from one another in regard to GI safety. Epidemiologic data exist, but no large head-to-head, double-blind, prospective outcomes trials have been conducted that compare serious GI events. In the absence of prospective clinical trials that evaluate meaningful GI end points—and since NSAIDs are similarly effective—generic alternatives could be selected in most, if not all, cases.

Differences in the risk of serious GI events between COX-2 inhibitors and traditional NSAIDs have been evaluated in 2 large prospective trials.^{58,59} Vioxx was the only COX-2 inhibitor for which a large prospective trial showed a statistically significant reduction in serious GI toxicity compared with a traditional NSAID (naproxen).⁵⁸ A large prospective trial comparing Celebrex with ibuprofen and diclofenac failed to demonstrate a statistically significant difference among these agents in the risk of upper GI tract complications.⁵⁹

Based on these results, patients at high risk for developing a serious GI event—those with advanced age, prior history of an ulcer or an upper GI tract bleed, or serious coexisting conditions, or who use corticosteroids or anticoagulants concomitantly—would have been considered appropriate candidates for Vioxx during much of 2004.⁶⁰ Following Merck's withdrawal of Vioxx from the market and based on the absence of compelling GI safety data for either Celebrex or Bextra compared with traditional NSAIDs, the vast majority of patients could be managed with a generic NSAID. To ensure GI safety in high risk patients,

a medication strategy that combines a generic NSAID with a generic PPI, a high-dose generic H₂-receptor blocker, or generic misoprostil may be appropriate.

While the GFR in the NSAID class increased by 15% between 2004 (50%) and 2005 (65%), we estimate that the generic opportunity was even more significant. In fact, we estimate a generic ceiling of 95% in 2005. How do we account for this difference? First, we believe that nearly all patients receiving a brand name NSAID (11% of market share) or brand name NSAID combination product (4% of market share) could have utilized a generic. Second, based on the lack of compelling GI safety data with the only remaining COX-2 inhibitor, Celebrex, over traditional NSAIDs, we believe that a sizeable portion of COX-2 use (20% of market share) could also be converted to a generic without sacrificing any clinical value. Certainly, some brand name use is still warranted. A brand name product such as Celebrex may be needed for familial adenomatous polyposis. Also, understanding that there is quite a bit of patient variability in response to NSAID therapy, a branded NSAID or Celebrex may be needed after failing multiple generics. After considering these additional situations, we believe that a brand name fill rate of 5% is rather generous. While a GFR of 95% in the NSAID therapy class sounds great, can it be done? GFRs reported by Kaiser Permanente appear to support it. Kaiser Permanente, which partnered with Stanford University, provided its physicians with the Standardized Calculator of Risk for Events (SCORE), a simple automated tool to assess the GI risk of their patients.^{61,62} Once this scoring tool was implemented, Kaiser physicians prescribed COX-2 inhibitors less than 5% of the time when NSAID therapy was considered necessary.⁶³ This approach was utilized prior to the recall of Vioxx and Bextra, which suggests that the generic opportunity may be even greater today.

Antidepressants

This class includes the newer antidepressants, including selective serotonin reuptake inhibitors (SSRIs) (eg, fluoxetine [Prozac], paroxetine [Paxil], sertraline [Zoloft], citalopram [Celexa], escitalopram [Lexapro]); serotonin norepinephrine reuptake inhibitors (SNRIs) (eg, venlafaxine [Effexor/Effexor XR] and duloxetine [Cymbalta]); and the older antidepressants, including bupropion (Wellbutrin) and tricyclic antidepressants (TCAs) (eg, amitriptyline [Elavil]).

In 2005, there were many generic alternatives to brand-name antidepressants. Over the past couple years a number of newly available generic medications significantly expanded the generic market for the antidepressant therapy class. Because of this influx of generic medications, the 2005 GFR for this class was nearly 50%, up almost 20% over the 2004 GFR of 42%.²

Despite the increase in generic drug use, brand-name SSRIs still maintained a significant presence, with 31% of the market share in 2005. This was a decrease from the 40% market share in 2004 with nearly an even split between Zoloft and Lexapro. With no direct generic competition, the SNRIs comprised 13% of the market share in 2005. This was only a slight increase over the 11% market share in 2004. The remainder of the brand market share was accounted for by Wellbutrin XL.^{1,2}

With a full year of generics available for Celexa, Wellbutrin SR, and Remeron SolTab, the 2005 GFR for antidepressants could have been closer to 80% based on the number of available generic alternatives, generic medications covering the majority of FDA-approved indications, and treatment guidelines for depression noting comparable effectiveness for antidepressants.

The antidepressant therapy class already had a number of generic alternatives for older medications, such as the TCAs and Wellbutrin. Then in 2004, all SSRIs had comparable generic alternatives, except for Zoloft.

Antidepressant medications are approved to manage other medical conditions in addition to depression. Available generic antidepressants cover all FDA-approved indications for medications in this therapy class—except for pain associated with diabetic peripheral neuropathy, an indication unique to the SNRI Cymbalta.⁶⁴⁻⁸³

Published clinical data and treatment guidelines indicate that the effectiveness of antidepressants is comparable between and within classes for managing depression.⁸⁴⁻⁸⁷ Although some patients may require a

trial of an alternative antidepressant because of intolerance to the prescribed drug, or to achieve a better therapeutic response, multiple generic alternatives are now available.⁸⁸ Consequently, generic antidepressant medications can effectively treat a majority of patients.

The previously reported GFR ceiling for antidepressants was 75% for 2004.¹ This GFR target includes only patients newly started on antidepressant therapy (not patients who are stabilized on therapy) and is derived primarily from movement of brand-name SSRIs to generic SSRIs. There may have been a small subset of patients that needed Zoloft (eg, women who are breastfeeding), but the remainder of SSRI use could have been managed with generic medications. With a full year of generics available for Celexa, Wellbutrin SR, and Remeron SolTab, the 2005 GFR for antidepressants was 80%.

Antihyperlipidemics

Antihyperlipidemics contain several unique therapy classes, including 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (eg, lovastatin), fibric acids (eg, gemfibrozil), bile acid sequestrants (eg, cholestyramine), nicotinic acid derivatives (various formulations of niacin), intestinal cholesterol absorption inhibitors (eg, ezetimibe), and combination products. In 2005, HMG-CoA reductase inhibitors, or statins, were the most commonly prescribed antihyperlipidemic, accounting for just over 75% of all prescriptions in this class.

In 2005, the overall percentage of generic antihyperlipidemic prescriptions was 6.5%, consistent with result from 2004.² Lovastatin, the only statin available generically, accounted for 3.5% of the antihyperlipidemic therapy class market share, or almost 5% of all statins prescribed. Other commonly prescribed generic medications included gemfibrozil (2.5% of antihyperlipidemics, 33% of fibric-acid prescriptions) and cholestyramine/cholestyramine light (0.5% of antihyperlipidemics, 33% of bile-acid sequestrant prescriptions).

Antihyperlipidemics are prescribed to manage abnormalities in lipid levels, including high levels of low-density lipoprotein (LDL) cholesterol, high triglyceride levels, and low levels of high-density lipoprotein cholesterol. According to the Third Report of the National Cholesterol Education Program (NCEP III), reduction of LDL cholesterol levels continues to be the primary goal of therapy when managing hypercholesterolemia.^{89,90} Of the available antihyperlipidemics, statins provide the most significant reduction in LDL cholesterol, and their ability to reduce the risk of coronary heart disease has been well documented.

The NCEP III guidelines do not specify a preferred statin, since no unique benefit has been proven for the use of one statin over others at equipotent LDL cholesterol level-reducing doses. Lovastatin, prescribed at daily doses of 40 mg and 80 mg, results in a decline of LDL cholesterol levels of 31% and 42%, respectively.⁸⁹ Using 2004 data representing Express Scripts book of business, over 80% of patients started and stabilized on a brand-name statin could have taken equipotent doses of generic lovastatin and continued to benefit from comparable reductions in LDL cholesterol levels.

The safety profile of statins should always be considered. In terms of side effects, no clear difference among the statins has been documented. In general, the risk of myopathy and persistent increases in serum transaminase levels (greater than 3 times upper limit of normal) appear to be dose-dependent; however, it is difficult to quantify which patients would better tolerate one statin over another.⁸⁹⁻¹⁰⁰ Studies evaluating conversion from various brand-name statins to generic lovastatin have not reported significant differences in side-effect rates and tend to support our assertion that adverse effects will not alter proposed GFR targets.¹⁰¹⁻¹⁰³

Non-single entity statins account for almost 25% of utilization in the antihyperlipidemic class. The majority of use is associated with Zetia, Niaspan, Tricor, and the combination statin, Vytorin. The GFR in this group could be increased in the bile-acidsequestrant and fibric acid classes, and some additional market share could potentially be shifted from Zetia monotherapy (in patients who are not statin intolerant) and the lowest dose of Vytorin to generic lovastatin. This would increase the overall GFR in the antihyperlipidemic therapy class by perhaps 3% to 4% overall.

The generic opportunity in this class is almost exclusively driven by the use of generic lovastatin. Claims data support the possibility that over 80% of brand-name statin prescriptions could have been filled with generic lovastatin. Since statins made up 75% of the market share within the antihyperlipidemic therapy class, it would be expected that statins account for 65% of the entire generic opportunity, while nonstatin classes account for the remaining 5%.

Considering statin and nonstatin opportunities for generic substitution, a GFR ceiling of 70% was estimated for the antihyperlipidemic class in 2005. Although this seems like a large disparity (6% actual vs 70% theoretical), data from Kaiser Permanente support this tremendous opportunity. Kaiser recently disclosed that more than 95% of patients new to statin therapy start taking generic lovastatin, and more than 75% can achieve their cholesterol-lowering goals using the generic.¹⁰⁴ Kaiser found that it could treat 5 patients with lovastatin for the same cost as 1 patient taking brand-name Lipitor.¹⁰⁵ In addition to cost savings, Kaiser noted superior compliance and clinical results with the generic drug. One year after starting a statin regimen, 60% to 70% of patients were still taking their medications (national rate is about 30%) and about 85% of patients had an LDL cholesterol level below 130 mg/dL (national rate, about 45%).⁶³

Kaiser also showed favorable results in patients who were already receiving statin therapy. Between 2002 and 2003, Kaiser actively converted patients using brand-name Zocor to generic lovastatin.¹⁰² Of those patients converted from brand-name Zocor to generic lovastatin, a higher percentage reached target levels of LDL cholesterol using the generic; conversely, no differences were noted in hepatic or muscle enzyme level elevations.¹⁰² During congressional testimony, Kaiser Permanente cited this initiative and noted that heart disease is no longer the leading cause of death among its members in Northern California, although it remains the leading cause of death for non-Kaiser members who reside in the San Francisco area and the nation as a whole.⁶³

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