

Perspectives on the “Generic Cliff”—Pushing and Falling

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Wall Street health sector analyst Tim Anderson, MD, now at BernsteinResearch, called it the “generic cliff” in early 2007.¹ From the perspective of brand-name pharmaceutical manufacturers and investors, the generic cliff is indeed formidable and often foreboding. What was a relatively gentle slope in erosion of the brand share of days of drug therapy when generic ranitidine entered the market in 1997, became steeper in August 2001 with generic fluoxetine (Prozac), and steeper yet with generic citalopram (Celexa) in November 2004 and generic simvastatin (Zocor) in July 2006 (Figure). For managed care organizations (MCOs), the generic cliff is a gold mine with a huge opportunity to increase the generic dispensing ratio (GDR) for individual drugs and for therapeutic classes through therapeutic selection.

MCOs have used physician and member financial incentives to increase GDRs, and thereby reduce the drug cost per therapeutic outcome. Low generic copayments and multiple-tier copayment designs are common tools to encourage health plan beneficiaries to use generic drugs. Fairman recently (2008) summarized nicely the literature on the controversial subject of member cost-share for pharmacy benefits, including the relationship of drug manufacturer sponsorship of the research and the study findings.² While much of the research sponsored by pharmaceutical manufacturers concludes that higher member cost-share is associated with reduced medication adherence, Shrank et al. (2006) showed the flip side, that patients initiating therapy with lower-cost generic drugs had higher rates of medication adherence.³ Research in commercial populations has generally demonstrated consumer price insensitivity in response to copayment change.² And, Klepser et al. (2007) dispelled the myth that making health plan members more aware of the true cost of drugs via a coinsurance design is associated with reduction in drug utilization.⁴

For physicians, MCOs have exercised many methods to encourage prescribing of generic drugs, including an innovative method of generic sampling to physicians as recently reported in *JMCP* (2007).⁵ The success of some recent MCO interventions with physicians to increase generic prescribing is evident in the push-back from brand-name pharmaceutical manufacturers, including lobbying medical societies to prevent the spread of physician-incentive programs for generic prescribing.⁶ For example, Blue Care Network (BCN), a division of BlueCross BlueShield of Michigan, conducted its Blue Reward\$ program in 2007 that targeted prescribers of fluvastatin (Lescol) or atorvastatin (Lipitor), paying its participating physicians \$100 for each patient converted to a generic statin from either Lescol or Lipitor.⁶ The Blue Reward\$ program reportedly spent \$2 million in incentive payments to physicians, saving \$5 million in annual drug cost for

BCN and \$1 million in lower (generic) copayments for members. Other health plans such as Excellus BCBS in upstate New York use physician-incentive programs to achieve increases in GDRs, and the GDR is evolving as a fundamental measure in physician pay for performance (P4P).⁶

MCOs and employers have also found success in step-therapy programs and pharmacy benefit designs that impose maximum allowable costs by therapeutic indication. For heartburn for example, a therapeutic maximum allowable cost (TMAC) per day of drug therapy was found to produce savings per day of more than 80% and net savings per member per month (PMPM) of more than 90% for the drug plan sponsor.⁷ Admittedly, TMAC is limited to therapeutic classes such as drugs for heartburn, where there is little if any controversy about the interchangeability of therapeutic alternatives to obtain the same clinical outcome (relief of heartburn with comparable safety).⁸

Yokoyama et al. found that a step-therapy intervention, which required first-line use of a (generic) angiotensin-converting enzyme (ACE) inhibitor prior to use of an angiotensin II receptor blocker (ARB), was associated with 13% in drug cost savings in the antihypertensive drug class, or approximately \$368,000 in savings in 1 year or \$0.03 PMPM across the 1 million health plan members.⁹ Since Yokoyama et al. evaluated outcomes for only 6 months of the intervention, the annual drug cost savings could have been twice as much, \$0.06 PMPM or more than \$700,000.¹⁰ Gleason estimated drug cost savings of \$0.11 PMPM from a similar step-therapy intervention for ACE inhibitors as first-line therapy before ARBs.¹¹ Dunn et al. found 9.0% drug cost savings for the entire class of antidepressants associated with a step-therapy intervention that required first-line use of a generic antidepressant, excluding tricyclics, in a 440,000-member health maintenance organization.¹² The step-therapy intervention for antidepressants produced impressive drug cost savings of \$0.36 PMPM or almost \$1.9 million in 2005 dollars with only a 1.5% decrease in utilization of antidepressants, less than the decrease in utilization of antidepressants (-5.0%) in the comparison group.

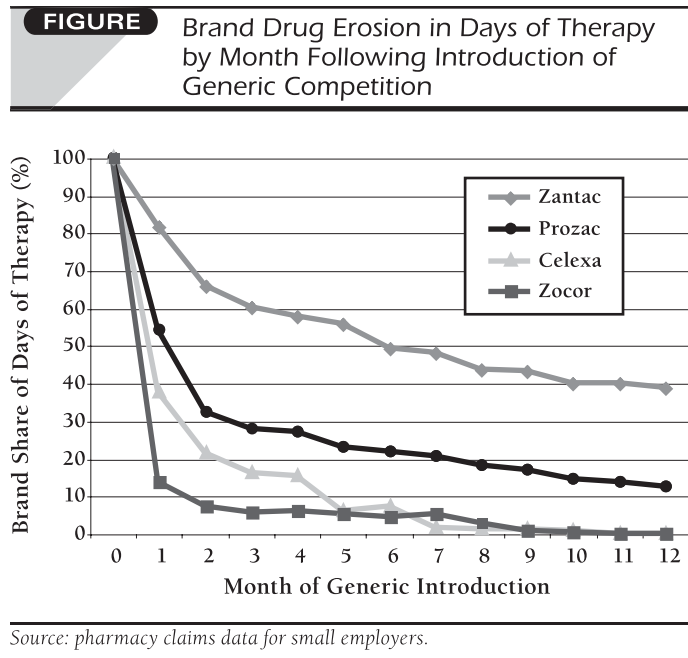
The generic cliff is made higher and the gold mine deeper by widespread uptake of generic drugs. Data from IMS Health show that generic drugs accounted for 63% of all prescriptions dispensed in the first 6 months of 2007, up 10 percentage points (relative 19%) in just 30 months, from 53% in 2004.¹³ This increase in the nationwide GDR translates into a relative 33% increase in the proportion of total U.S. drug spending accounted for by generic drugs, from 12% in 2003 and 2004 to 16% in the first 6 months of 2007. A separate report in March 2008 from IMS data put the nationwide GDR even higher at 67% for the full year 2007, with a 20% ratio for generic drugs of total prescription drug spending.¹⁴

The gold mine could be even richer for MCOs. Pharmacy benefit manager Express Scripts, in a non-peer reviewed analysis, estimated \$17.1 billion in savings to health plan members and sponsors in 2006 for increased GDR in just 2 drug classes: \$10.3 billion for anti-cholesterol drugs if the GDR increased to 85% from 18.8% in 2006 and \$6.8 billion from an increase in GDR for the gastrointestinal drugs to 95% from 35.4%.¹⁵ A total of \$24.7 billion in savings could be achieved from increased GDR for these 2 drug classes plus 4 other drug classes, \$3.4 billion from a GDR increase to 85% from 57% for antidepressants, \$2.1 billion from a GDR increase to 75% from 58.3% for antihypertensives, \$1.2 billion for a GDR increase to 97% from 77.0% for nonsteroidal anti-inflammatory drugs, and \$0.9 billion for an increase in GDR to 95% from 49.4% for calcium channel blockers. For 2005, the estimate of health plan savings from simply increasing the GDR in these 6 drug classes was \$21.7 billion.⁶

The generic cliff looms disproportionately for pharmaceutical manufacturers. According to the analysis performed in late 2007 by Anderson, Das, Kowalski, and Chou at BernsteinResearch, the average lost revenue at the generic cliff for the 10 largest pharmaceutical manufacturers for the period from 2007 through 2012 is 24.7%, meaning that these 10 companies have to replace an average of one quarter of their total annual revenue with increased sales of either existing patent-protected products or new products.¹⁶ However, the generic cliff looms largest for Pfizer, which between 2007 and 2012 will lose patent protection on atorvastatin (Lipitor), amlodipine (Norvasc), and cetirizine (Zyrtec), accounting for 36.9% of Pfizer's total revenue in 2007. The generic cliff through 2012 looms large also for Bristol-Myers Squibb, which has to replace the 31.3% of annual revenue accounted for by aripiprazole (Abilify), irbesartan (Avapro), and clopidogrel (Plavix). Two other companies with above average exposure are sanofi-aventis, with 27.8% of revenue in zolpidem (Ambien), enoxaparin (Lovenox), and docetaxel (Taxotere), and Wyeth with 26.1% of total revenue in venlafaxine (Effexor), pantoprazole (Protonix), and piperacillin/tazobactam (Zosyn).

To make the situation more perilous for brand-name pharmaceutical manufacturers, the generic cliff jumpers are being pushed. Some generic drug companies became more aggressive in 2007 in launching first-time generics "at risk" after the automatic 30-month stay that is granted at the beginning of litigation but prior to resolution of the litigation. There were 8 generic at-risk launches in 2007 compared with 2 in 2006.¹⁷ At-risk generic launches are indeed risky since triple damages are available to the brand-name pharmaceutical manufacturer, but the absolute financial risk may be less since triple damages have never been awarded to a brand-name pharmaceutical company that sued a generic manufacturer.

Teva Pharmaceuticals has been active in pushing brand-name drugs off the generic cliff. In December 2007, Teva launched generic pantoprazole (Protonix) at risk in the United States.¹⁸ This bold move by Teva upended the anticipated strategy by



Wyeth to launch an authorized generic to capture a large part of the generic sales of pantoprazole. Instead, the amount of generic pantoprazole that was shipped by Teva in December 2007 was sufficient to cause the projected earnings per share for Wyeth for 2008 to be downgraded by 13% in late January 2008.¹⁸ One month later in the week ended January 25, 2008, generic pantoprazole from Teva had captured 60.3% of the total prescriptions for pantoprazole.

Teva had used this strategy previously with the at-risk launch of generic Lotrel in 2007, with enough generic Lotrel shipped to last "well into 2008."¹⁹ Teva had also teamed up with Barr Pharmaceuticals to launch generic Allegra (fexofenadine) at risk, thereby spreading the financial consequences from an unfavorable court ruling, should any occur. Brand-name products threatened with at-risk generic launches in 2008 and 2009 include Allegra D, with an at-risk launch by Barr, and a possible at-risk launch of generic Topamax (topiramate) by Mylan.

Wall Street analysts and patent attorneys have predicted an increase in at-risk generic launches, in part due to 2 recent court cases. One case involving KSR International Co. in the U.S. Supreme Court made it easier to show that obvious ideas or ideas lacking innovation cannot be patented.¹⁷ The second case involved Seagate Technology, in which a federal appellate court decision changed the standard for proving willful disregard for patent rights, thereby making it harder to obtain an award for triple damages.¹⁷

On the horizon are some very large generic cliffs. Among the standouts, Wyeth faces loss of patent protection on Effexor XR

in July 2010. Effexor XR is a top 10 drug by sales in the United States. Effexor XR retail sales in community pharmacies were \$2.25 billion in 2006,²⁰ and the drug was Wyeth's number 1 drug by manufacturer sales last year, accounting for worldwide revenue of \$968 million in the fourth quarter of 2007, 67% from U.S. sales, and \$3.79 billion for the year.²¹

In terms of market financial impact, the most significant generic cliff that may be imminent is esomeprazole (Nexium), with sales of \$5.22 billion in 2007, accounting for 17% of total sales of heartburn drugs.¹⁹ Aside from the attraction of capturing some of the more than \$14 million per day in sales, 2 facts suggest a generic cliff earlier than 2018, when Nexium is expected to officially lose patent protection. Ranbaxy holds "first filer" Abbreviated New Drug Application (ANDA) status for Nexium, and the 30-month stay ends in April 2008. More important perhaps, the 30-month stay for Teva's ANDA for Nexium expires in July 2008. So, while Ranbaxy has no experience itself with at-risk generic launches, it is conceivable that Teva and Ranbaxy could team up to launch generic esomeprazole as early as April 2008.

The nationwide increase in use of generic drugs has contributed to a slowdown in the rate of increase in total prescription drug spending. The 3.8% increase in total prescription drug sales in the United States in 2007 to \$286.5 billion, up from \$274.9 billion in 2006, was the smallest increase since 1961 and down significantly from the more than 8% increase in 2006.¹⁴ IMS Health reported in March 2008 that brand-name drugs, representing \$17 billion in U.S. sales, lost patent protection in 2007, contributing to an increase in the national GDR to 67.3% and generic drugs representing 20.4% of total prescription drug expenditures. Another \$13 billion in brand drugs are expected to lose patent protection in 2008 contributing to estimates of continued smaller growth in total U.S. prescription drug sales, in the range of 3% to 6% per year for 2008 through 2012.

For MCOs, the next 5 years offer the opportunity for no growth in pharmacy benefit costs, even with no increases in member copayments and the anticipated increases in drug utilization as more drugs have lower (generic) cost-share for members. MCOs welcome a larger generic cliff and most have broad generic drug promotion programs that touch employers, members, and physicians. Excellus BCBS, for example, combines physician incentive payments with broad step-therapy interventions with first-line generics in 9 therapeutic categories,²² contributing to reported savings of \$224 million in 2007, 4.5% of about \$5 billion in drug spending as the GDR increased by 3.8 percentage points to 63.9% from 60.1%.²³ The next 5 years pose continued difficult times for most brand-name drug manufacturers but sanguine times for persons responsible for management of pharmacy benefits, certainly a situation much different than just a few years ago.

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