



IMPACT OF RISING PRESCRIPTION DRUG COSTS

*Left unchecked, prescription drug costs
will hinder reduction of America's
health care spend*

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LEFT UNCHECKED, PRESCRIPTION DRUG COSTS WILL HINDER REDUCTION OF AMERICA'S HEALTH CARE SPEND



The U.S. is working to curb health care costs on many fronts. The Patient Protection and Affordable Care Act (PPACA) became law in 2010 with the promise of slowing the rate of health care spending over a 10-year period. Collectively, all payers for health care – public and private – are taking measures to pay for quality and outcomes versus volume in the provision of care by physicians and health care facilities. In this context, prescription drug costs deserve more attention to realize needed progress on reducing total health care costs.

This paper is intended to explore some of the issues in drug pricing and offer some recommendations for addressing the problem.

Costs keep rising, despite increased use of generics

In 2009, Americans spent \$411.3 billion on prescription drugs, up 9.3% over 2008. That was for 4 billion prescriptions, which was 2.7% higher than 2008. The cost per prescription was \$103.75, up 6.5%.¹ Costs rose another 8% in 2010, according to the annual Milliman Medical Index.² Although utilization has slowed somewhat, the cost of prescription drugs continues to escalate at roughly three times the rate of general inflation.

These increases in unit price have come despite the continuing increased use of generic drugs, which are generally cheaper than their brand name equivalents. In 2006, generics accounted for 63% of all prescriptions; in 2010, 78%.³ By six months after the patent expires on a drug, the generic version is taking an average of 80% of the market, as opposed to 55% in 2006.⁴ This switch has been supported by a big push from the health plan industry toward three-tier formularies and by public information campaigns.

The “good news” for us in Tennessee is that where it had been No. 1 in the nation for many years in total prescriptions per capita, in 2009 the state dropped to No. 3, behind West Virginia and Kentucky.⁵ In a previous white paper, specific issues that elevate the use of prescription drugs in Tennessee were discussed.⁶ Those factors (older median age, greater disease burden, lower education level and physician-patient dynamic) remain largely unchanged. What has changed is that TennCare now has a limit on covered prescriptions, where it did not before, and that has lowered the overall utilization of drugs in the state. This paper focuses on pricing, or unit cost. That is a problem for all Americans, not just Tennessee. The paper does not address the disparity in drug cost among the OECD (Organization for Economic Cooperation and Development) countries. It is well known and documented that we in the U.S. pay from 30-100% more for the same drugs as Canadians and Europeans.

¹ Pharmacy Benefit Report, Novartis, 2010-11, p 43

² 2011 Milliman Medical Index, May, 2011, p. 3

³ IMS Institute for Healthcare Informatics, The Use of Medicines in the United States: Review of 2010, p.22

⁴ *ibid.* p. 21

⁵ *op. cit.*, Novartis, p. 47

⁶ Coulter, S., “Rx for Pharmacy Costs in Tennessee,” 2001.

Let us examine drug prices from five different perspectives:

- **Quality Adjusted Life Years. (QALY)** This is a measure of the effectiveness of any treatment. In simple terms, it means how much longer you are going to live and enjoy your life as a result of the treatment. Let us take the case of one recently introduced drug, sipuleucel-T (Provenge, made by Dendreon Corporation) which was approved by the FDA for treatment of asymptomatic (without symptoms) or minimally symptomatic, metastatic (spread throughout the body) castration-resistant (not responsive to female hormone administration) prostate cancer.

Compared to placebo, there was an increase in median survival of 4.1 months.⁷ So far, so good. This drug was priced at \$31,000 per dose, with an average treatment course of three doses.⁸ Thus, the cost of the drug alone was \$93,000 to extend life by one-third of a year. This converts to \$279,000 per QALY.

There are no official or even widely accepted standards as to what constitutes “cost-effective” care. However, suffice it to say that this figure is in the high range for drug therapies. So much so, that it prompted not only a review by the FDA, which evaluates “safety and efficacy” of drugs, but also by CMS (Centers for Medicare and Medicaid Services), which reviews treatments from a standard of “reasonable and necessary.”⁹ Lacking any standards by which to reject this drug, it was approved by both agencies. As an aside, there is a less expensive alternative treatment with docetaxel, but Provenge has not been tested head-to-head with it, only against placebo, since that is all that is required for FDA approval. If this seems to be an isolated example, consider the fact that in 2011, there are 460 specialty drugs in the pipeline, over one-third of which are oncologic agents.

- **Cost of a new indication for an old drug.** It has been known since 2003 that treatment with 17 alpha-hydroxyprogesterone caproate (17OHP) can help prevent spontaneous pre-term delivery (miscarriage) in women with a previous history of same (who are more likely to have the same problem with subsequent pregnancies) if begun prior to the 21st week of pregnancy in a dose of 250 mg per week.¹⁰ It is not, however, effective at preventing premature delivery of twins.¹¹

For several years, this drug has been provided by compounding pharmacists at a cost of approximately \$15 per dose, or \$300 for an entire treatment course.¹² On Feb. 4, 2011, the FDA approved Makena (made by K-V Pharmaceutical Company). The initial price listed by the manufacturer was \$1,500 per dose, or roughly \$30,000 for a treatment course. This is the same drug, but manufactured rather than individually compounded by a pharmacist. In response to public outrage, the manufacturer reduced the price to \$690.¹³ It should

⁷ Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *NEJM* 2010 363:411-22

⁸ Chambers JD, Neumann PJ, *NEJM* 364:19 1687-9

⁹ *ibid.*

¹⁰ Meis PJ, Klebanoff M, Thom E et. Al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate *NEJM* 2003;348:2379-85

¹¹ *The Medical Letter* 53:1364, May 16, 2011 p.38

¹² Armstrong J, *NEJM* 364:18 May 5, 2011 p 1689ff

¹³ *The Pink Sheet*, April 4, 2011

be noted that taxpayers, through the National Institutes of Health (NIH), funded \$21 million of the research and development costs of Makena, and does not receive royalties or any form of payback in return.¹⁴ By FDA regulation, pharmacists are not supposed to compound medications once they become available from a manufacturer.¹⁵ However, in this case, the FDA has announced that it does not intend to enforce that regulation “at this time and under this unique situation.”¹⁶

- **Off label use of an existing drug.** Wet Macular Degeneration (WMD) is a disease primarily affecting the elderly in which vision gets cloudy in the central area (where you focus to read or watch TV) due to a localized proliferative angiopathy (blood vessels run amok.) It is slowly progressive and can be debilitating. Many ophthalmologists have treated this disease successfully with a drug called Avastin (bevacizumab), made by Genentech, using retrobulbar injections (injections into the eyeball).

Avastin costs about \$50 per dose, but it does not have an official FDA “indication” (approval) for that use, and therefore is not always covered by Medicare, Medicaid or private insurers for that purpose. (It is approved for the treatment of certain cancers.) Lucentis, an identical molecule (also bevacizumab) also made by Genentech, though in different packaging, is specifically approved for WMD, and costs \$2,000 per dose. Just to show how effective this pricing strategy is, in 2008, Medicare spent \$537 million for Lucentis vs. \$20.3 million for Avastin.¹⁷ A recent NIH trial has confirmed that the two drugs are of equivalent efficacy.

- **Price increases for the same drug.** Multiple Sclerosis (MS) is a central nervous system disorder characterized by demyelization (loss of the insulation layer) of the central nervous system. It has fluctuating symptoms and can be progressive and debilitating. Most authorities recommend treatment with a disease-modifying, immuno-modulating drug as early as possible in the course of the disease to help prevent progression.

In 2005, the average annual prescription cost to treat MS was \$16,300; in 2010, \$36,900. Since Jan. 1, 2009, the price of Avonex is up 43%, Betaseron, 31%, Copaxone, 55%, Rebif, 31%.¹⁸ These same drugs have been available for some time. They are not more difficult to manufacture. They have not suddenly become more effective. They are, however, more commonly prescribed as a result of an increasing incidence (or perhaps an increasing degree of diagnosis) of the disease. It is clearly good that MS patients have earlier diagnosis and somewhat effective treatment available. Is it appropriate that the prices go up to this degree? (None of these drugs are curative and must be taken for the rest of a patient’s life, much like insulin for a diabetic which costs about \$20-50 per month.)

¹⁴ The Pink Sheet, May 16, 2011 p. 27

¹⁵ Food and Drug Administration compliance policy guide, Section 460.200 pharmacy compounding

¹⁶ The Pink Sheet, April 4, 2011

¹⁷ The Pink Sheet, May 9, 2011

¹⁸ Internal BlueCross BlueShield of Tennessee data

- **Price increases prior to patent expiration.** Many drug manufacturers significantly increase the price of drugs in the year or two prior to patent expiration. A few examples:
 - Ambien CR, made by Sanofi Aventis, had price increases of 20% in the year prior to coming off patent in December of 2010
 - Concerta, made by Johnson and Johnson, 22% increase prior to coming off patent in May of 2011
 - Flomax, by Boehrler Ingelheim, 28% increase prior to its March 2010 patent expiration
 - Lipitor, by Pfizer, 22% increase in the last four quarters, coming off patent in November of 2011

Why is this such a seemingly widespread practice within the industry? When patents expire on a brand-name drug, it is typical for the generic equivalent to capture about 80% of the market for that drug within six months. This is because the generic usually sells for 30-80% less than the brand equivalent. That still leaves, however, 20% of the market for the original brand drug.

Drug companies typically spend about 50% on manufacturing and make about a 20% profit margin. If a company is making a drug that sells \$1 billion per year, that means they are spending \$500 million and making \$200 million in profit. (The rest goes for SG&A which stands for sales, general and administrative expenses, such as sales commissions, accounting and the like.) If volume is cut by 80%, they will spend \$100 million manufacturing the drug, and have a profit of \$40 million. However, if the price is increased by 20% one year prior to coming off patent, the revenue goes to \$1.2 billion, though the cost of manufacturing does not increase. So, for that year, there is an extra \$200 million profit. Furthermore, when the 80% loss of market share comes from the move off patent, the cost of making the drugs drops to \$100 million, and the profit is now \$80 million per year. Therefore, this one simple maneuver of raising prices at the right time nets the company \$200 million – plus an ongoing, extra \$40 million per year.

Table 1.
Drug X in Final Year of Patent

Calculations based on not changing price	
Revenue	1,000,000
Cost of Goods Sold	(500,000)
SG&A	(300,000)
Profit	200,000

Table 2.
Drug X in Final Year of Patent

Calculations based on increasing price 20%	
Revenue	1,200,000
Cost of Goods Sold	(500,000)
SG&A	(300,000)
Profit	400,000

NOTES: All of the above figures are reported in thousands. The calculations for Costs of Goods Sold and SG&A are based on approximate industry averages, not a specific drug.

Table 3.
Drug X One Year After Patent Expired and Every Year Following

Calculations based on not changing price	
Revenue	200,000
Cost of Goods Sold	(100,000)
SG&A	(60,000)
Profit	40,000

Table 4.
Drug X One Year After Patent Expired and Every Year Following

Calculations based on increasing price 20%	
Revenue	240,000
Cost of Goods Sold	(100,000)
SG&A	(60,000)
Profit	80,000

NOTES: All of the above figures are reported in thousands. The calculations for Costs of Goods Sold and SG&A are based on approximate industry averages, not a specific drug.

Specialty pharmaceuticals: Prescription drug cost impact from influx of new, high-priced therapies

Specialty drug spend continues to increase at an alarming rate of percent of total drug spend, now at 20% and expected to be 40% by 2014. While these drugs represent break-through therapies for under- or untreated diseases and can be life saving or life prolonging, they are very costly, sometimes prohibitively expensive.

- **The technology.** Personalized medicine is aimed to specifically treat characteristics of individual patients using genetic information to determine if the individual is susceptible to a particular disease or responsive to a specific treatment. There is great promise in using this technology to prevent progression of diseases, reduce adverse events and improve overall health outcomes. However, the technology comes at a price. Molecular diagnostics and biomarkers are tools used to determine which specialty drug should be used to treat a specific condition, such as cancer and HIV. Today, the tests are costly and add to the total drug cost burden of treatment. Presently, surveys from the EMD Serono Specialty Digest, 7th Edition, have demonstrated that most payers are reluctant to require molecular diagnostics before approving the use of a specialty drug to treat the targeted disease state due to lack of evidence. The tests run anywhere from \$300 to \$2,500 per test. Payers are considering other utilization management techniques such as prior authorization to manage the high cost of molecular diagnostics tests and specialty drugs.
- **The pipeline.** According to a 2011 report, there are 460 drugs in the pipeline for rare diseases. One-third of these drugs under development are going to be used to treat rare cancers, including solid tumors of the liver, thyroid, cancer of the blood and melanoma. Rare diseases are defined by the Orphan Drug Act of 1983 as affecting less than 200,000 patients. Of the nearly 7,000 rare diseases, the NIH reports that they affect 25-30 million Americans. In 2010, as an example, BlueCross BlueShield of Tennessee spent over \$344 million on specialty drugs and conservatively estimates that it will rise to over \$1.25 billion in the next three years.

- **The trend.** Pharmaceutical companies responsible for developing and manufacturing “traditional” drugs are branching out into the biopharmaceutical field by either buying smaller biotech firms or developing new business units devoted to the biotech field. The pace of developing new and novel drug therapies to treat wide-spread disease states has slowed dramatically over the past three years. Instead, drug companies are focused on extending patents on older drugs and/or developing “Me-Too” drugs that bring no added benefit to the current treatment regimen. Drug companies are placing most of their focus and R&D dollars into producing specialty drugs. In 2011, four drugs to treat cancer have been introduced, topping the six-figures per year mark: Pfizer’s Xalkori at \$115,220; Bristol Meyer Squibb’s Yervoy at \$120,000; Roche/Genetech’s Zelboraf at \$112,800; and Seattle Genetics’ Adcetris at between \$94,000 to \$216,000. Of these four companies, three are “traditional” companies branching out into the biopharmaceutical field. Consider another specialty drug, Revlimid/Celgene. It is used to treat a certain type of myelodysplastic syndrome (a group of conditions in which the bone marrow produces blood cells that are misshapen and does not produce enough healthy blood cells). It is also used along with dexamethasone to treat multiple myeloma (a type of cancer of the bone marrow) in patients who have already been treated with at least one other medication. Revlimid/Celgene has steadily climbed up to the No. 1 spot as BlueCross BlueShield of Tennessee’s most utilized specialty drug in the Medicare D population. It also had an alarming price increase of 30% over the last year.

Increases: Brand vs. Generic

However, we continue to see dramatic increases in the price of brand-name drugs within Tennessee. In the following graphs, you can see that brand drugs have escalated over 25% over the last two years, where generics have “only” increased about 15%. Further, the increase in brand has a disproportionate effect due to the fact that brand drugs in general are vastly more expensive than generics.

Figure 1.
Ingredient costs, brand vs. generic

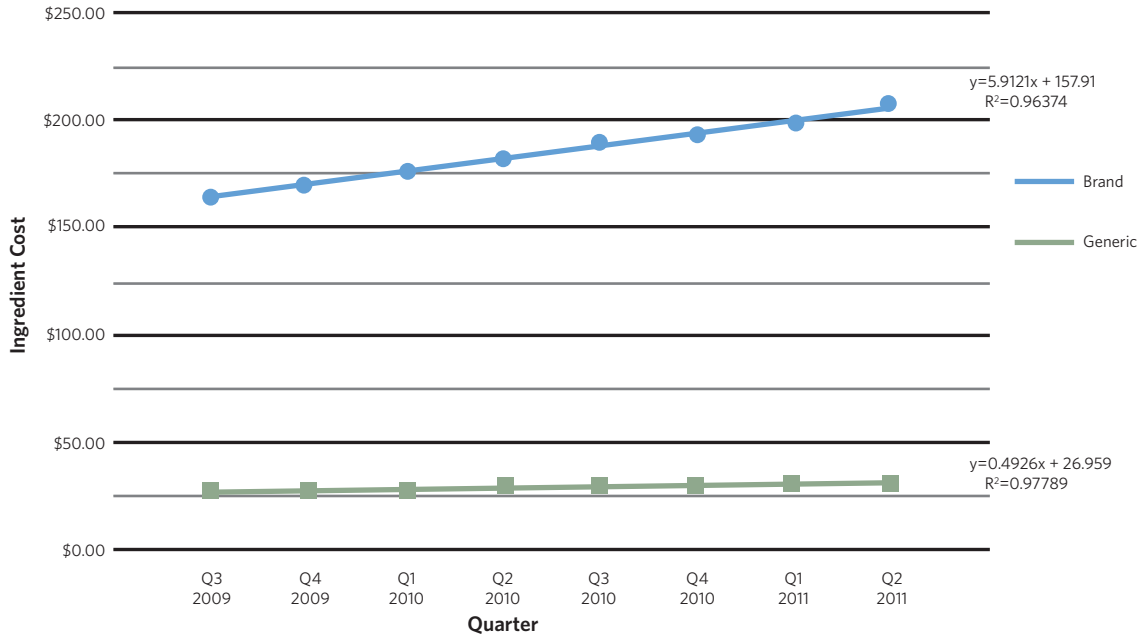
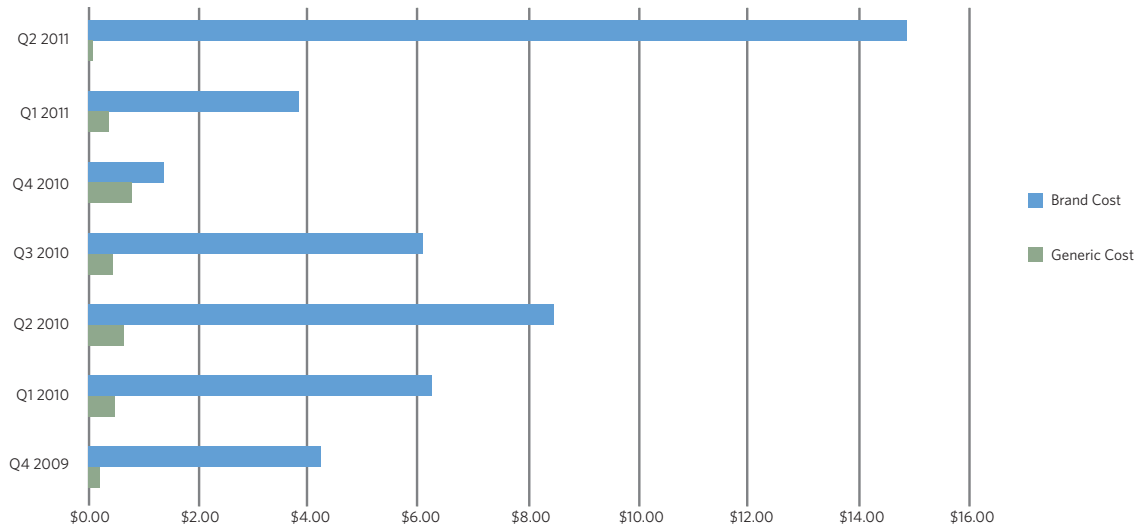


Figure 2.
Ingredient cost change, brand vs. generic



The Role of the Federal Government

An individual state has very little it can do to impact the issues raised in this paper. The primary regulatory responsibility for prescription drugs in the U.S. is the FDA. As mentioned earlier, the FDA is limited to review of “safety and efficacy.” Simplified, this means that a drug must potentially help more people than it hurts, and that it must help more people than a placebo (sugar pill) does. No drug is totally safe, so the judgment as to whether a drug is safe is considerably more complex than this, though this is the basic idea.

As for effectiveness, there is no requirement that a new drug be more effective than ones already on the market. Head-to-head comparisons are not required, nor are they submitted by the drug manufacturers when seeking approval. This function, at present, is left to individual researchers, most of whom are academics. However, most funding of “academic” research currently comes through grants from the pharmaceutical industry, and many researchers receive speaking fees and honorariums from these same drug companies, raising conflict of interest issues.

The role of CMS is different from the FDA. CMS decides whether to cover (pay for) new drugs. To do so they use a standard of “reasonable and necessary.” To meet this standard, a drug must be approved by the FDA, sold in the United States, and approved for use for the specific diagnosis the patient has. There is no financial requirement.

Comparative Effectiveness Research (CER) is the branch of scientific study which actually compares different forms of treatment against each other to see which one is more effective. Under PPACA, there are funds made available for CER. Unfortunately, in that same act, CMS is prevented from using the results of those studies to determine coverage.

The use of CER, as supported by PPACA, should be made available to both the FDA and CMS. To not do so puts the future success of health reform at risk, since if left uncontrolled, the cost of drugs will threaten the long-term financial viability of the legislation.

On an encouraging note, the Institute of Medicine (IOM) released on October 7, 2011 its recommendations regarding the congressionally mandated “Essential Health Benefits” that are the linchpin of coverage under PPACA. The IOM was not asked to make actual recommendations of benefits themselves, but rather to recommend a process for developing such benefits.

The IOM clearly understands that benefits cannot be unlimited, and in its document discusses at length the need for limits and its specific recommendations regarding those limits. Relative to this paper, it is noteworthy they recommend that “benefits be evidence based, specific, and value-improving over time.” Improving value over time in this context is being interpreted by this author and others to mean “cost-effective.”¹⁹

These recommendations are broadly based and do not have the force of law. They apply to all benefits and not just drugs. Yet these are clearly supportive of the standards that are lacking in today’s approval process, as discussed above. Perhaps there is cause for cautious optimism.

¹⁹ Inglehart, NEJM October 7, 2011 (10.1056/NEJMp1109982)

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