Prescription Drug Recalls on Florida's Medicaid Preferred Drug List

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Abstract
Prescription drug use is rising among Americans in all age groups. In general, utilization of prescription medications increases with age due to chronic health conditions that require pharmaceutical interventions. Because Medicaid is the single largest payer of prescription medications in Florida, this study's objectives were to: (1) examine Medicaid spending on recalled drugs for the 2001-02 fiscal year, (2) assess Medicaid expenditures for comparison drugs on the Medicaid preferred drug list for the same time period, and (3) contrast the drugs that received fast track approval with those undergoing standard approval. In this study, Medicaid spending for recalled drugs was much lower than comparison drugs on the preferred drug list, in part because of a fewer number of claims and associated dispensing fees. On the other hand, a higher percentage of recalled drugs had received fast track review than comparison drugs which were more likely to utilize the standard approval process. Given the widespread use of prescription drugs, it is essential to assure the efficacy and safety of new medications prior to consumption by the general public, particularly because of their higher cost and impact on health expenditures.
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Introduction

In 2002, national drug expenditures totaled over $160 billion, a four-fold increase compared to approximately $40 billion a decade earlier (Centers for Medicare and Medicaid Services, 2004). The escalation in prescription drug expenditures and consumption is due to a number of factors including: (1) greater availability — more rapid approvals of new drugs that replace existing lower cost drugs, (2) promotion of utilization — marketing to doctors and direct advertising to consumers, (3) payment mechanisms — growth of third party insurance coverage by private and public payers, and (4) clinical guidelines — recommending use of medications for treatment of chronic conditions (Bernt, 2001; General Accounting Office, 2004 October). Ten percent of U.S. health expenditures go toward prescription medications and prescription drug spending is rising faster than any other health care category (Centers for Medicare and Medicaid Services, 2004).

Ensuring Consumer Drug Safety

According to the Centers for Disease Control and Prevention (CDC), approximately 45% of Americans take at least one prescription drug and one in six take at least three (CDC, 2004). Given the widespread use of prescription drugs, it is essential to assure the efficacy and safety of medications prior to consumption by the general public. As a consequence, the standard drug approval process conducted by the Food and Drug Administration (FDA) may take anywhere from 20 months to 15 years and involve multiple stages (Meadows, 2002).

In the first step, *Stage 1*, an investigational new drug (IND) application is submitted to the FDA. The manufacturer presents pre-clinical study data obtained from laboratory and animal tests. Next, in *Stage 2*, clinical trials observe the new drug's effects on the human body, including side effects and metabolic reactions. Finally, in *Stage 3*, submission of a new drug application (NDA) requests the FDA to consider approving a new drug for marketing and distribution. The NDA contains data collected from the clinical trials. In reviewing the NDA, scientists evaluate the efficacy and safety of the potential drug, as well as its risk/benefit ratio to determine approval or disapproval. After the drug has been approved for general public consumption, post-market studies continue to assess long-term effects and explore new therapeutic uses.

Drug Safety Recalls and Withdrawals

Post-market studies analyze the information collected from a larger and more diverse patient population than pre-approval clinical trials. If a product has proven to be unsafe or ineffective at the prescribed dosages, it may be necessary for the FDA to initiate recall and/or withdrawal of the drug in question. A recall, as defined by the FDA, involves actions to remove a product from the market (FDA, 2002). Recalls may be initiated by the drug manufacturer, by FDA request, or by FDA mandate. Removing a product from the market may be permanent or temporary such that it may be returned to market once the problem has been corrected.

Some drugs may receive an alert if unexpected severe reactions are observed with use by the general public after market release. On the other hand, the FDA recommends a drug for recall or market withdrawal if the risks of side effects and interactions significantly outweigh the drug's

benefits. The FDA classifies pharmaceutical product recalls into the three general categories below (FDA, 2004).

- *Class I***.** Recalls in this class involve dangerous or defective products that may cause serious health conditions or death with continued use or exposure.
- *Class II*. The FDA uses this type of recall to designate products that might cause temporary health problems or have a remote possibility of serious health consequences.
- *Class III***.** These recalls relate to drugs that are unlikely to cause adverse health effects, but that have labeling or manufacturing (e.g., packaging) violations.

Some analysts attribute the recent safety recalls to an act passed by Congress in 1992 that allowed pharmaceutical industry-paid user fees to finance expedited FDA reviews and approvals of new drugs (Carpenter et al., 2003). Most drugs approved by the FDA use standard approval mechanisms or an expedited review that reduces the time frame prior to marketing and release to consumers. Expedited reviews through fast track (i.e., accelerated approval) initiatives generally apply to drugs aimed at serious, life-threatening conditions or address unmet medical needs.

Florida Analysis

Prescription drug use is rising among all Americans and use increases with age due to chronic health conditions that require pharmaceutical medications for treatment (CDC, 2004). The sizeable segment of Florida's population over age 65 contributes to the state's high demand and consumption of pharmaceutical products. In 2003, Florida ranked fourth in the nation in retail prescription drug sales with a total of $10.57 billion spent, a 9.9% increase over the previous year (Kaiser Family Foundation, 2005).

Moreover, prescription drug coverage is one of the benefits for Florida's Medicaid recipients and Medicaid is the single largest payer for prescription medications in the state (Agency for Health Care Administration, 2004). In the 2001-02 fiscal year, Florida spent a total of $1.65 billion for prescription drug coverage among Medicaid participants representing 10% of all prescriptions in the state (Agency for Health Care Administration, 2002). The federal government passed Medicare reform legislation in 2003 that established prescription drug coverage for seniors starting January 1, 2006 (Centers for Medicare and Medicaid Services, 2003).

Methods

The study's objective was to investigate Medicaid spending on recalled drugs for fiscal year 2001-02. Medicaid expenditures for the comparison drugs on the Medicaid preferred drug list for the same time period also were examined. Another component of the study contrasted the drugs that received fast track approval with those that underwent standard approval. The Medicaid allowable cost (MAC) given to pharmacies that submit cost reimbursement claims for Medicaid clients was determined by adding the dispensing fee to the Medicaid ingredient cost (MIC). The dispensing fee in fiscal year 2001-02 was $4.23 per claim for each drug dispensed.

Thirty prescription drugs were selected for comparison, of which 15 were recalled and 15 were comparison drugs. The recalled drugs were permanently withdrawn from the U.S. market after adverse health consequences were observed (Figure 1). *Vioxx* was not included in the analysis because it was a voluntary manufacturer recall, not an FDA mandated recall.

Comparison drugs were obtained from Florida's Preferred Drug List (PDL) that was instituted in 2001 as a cost containment mechanism for the rapidly rising costs of prescription medications for Medicaid patients. The Florida Medicaid Preferred Drug List contains "prescription products selected by the Pharmaceutical and Therapeutics Committee as efficacious, safe and cost effective choices when prescribing for Medicaid Patients" (Agency for Health Care Administration, 2004). Comparison drugs were matched to the recalled drugs by therapeutic classification and drug function as shown in Figure 2.

Results

Of the recalled drugs on the Medicaid preferred drug listing, 53% were drugs that were approved through the fast track mechanism, whereas 47% of recalled drugs underwent standard approval. On the other hand, two out of three PDL comparison drugs that were not recalled were approved through the standard, albeit longer, review process. Figure 3 shows a graph and listing of recalled drugs and PDL comparison drugs by approval type.

Figure 1. Drug Recalls

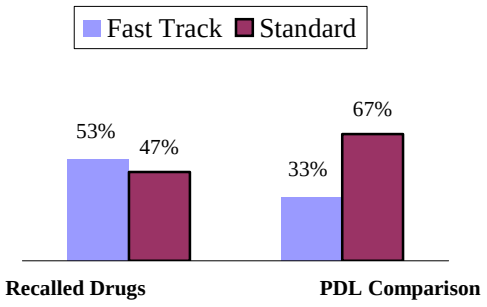
Recall Date	Brand Name	Recall Reason	Approval Date	Post Market Time
9/15/1997	**Redux**®	Abnormal Heart Valves	4/29/1996	1.5 years
2/27/1998	**Seldane**®	Drug Interactions	5/08/1985	13 years
6/08/1998	**Posicor**®	Sudden Deaths	6/20/1997	1 year
6/22/1998	**Duract**®	Liver Failure	7/15/1997	1year
6/18/1999	**Hismanal**®	Adverse Reaction Data	12/19/1998	6 months
10/15/1999	**Rotashield**®	Intussusception	8/31/1998	1 year
11/01/1999	**Raxar**®	Ventricular Arrhythmias	11/06/1997	2 years
3/21/2000	**Rezulin**®	Liver Failure	1/29/1997	3 years
7/14/2000	**Propulsid**®	Cardiac Arrhythmias	7/29/1993	7 years
7/26/2000	**Norplant**® **System I**	Removal Problems	12/10/1990	9.5 years
11/28/2000	**Lotronex**®	Constipation Problems	2/09/2000	9 months
3/27/2001	**Raplon**®	Bronchospasm	8/18/1999	1.5 years
8/08/2001	**Baycol**®	Rhabdomyolysis	6/26/1997	4 years
3/01/2002	**Versed**®	Potency, Crystallization	3/18/1997	5 years
2/28/2003	**Trovan**®	Liver Toxicity	12/18/1997	5 years

Figure 2. Recalled Drugs and Comparison Drugs on the Medicaid Preferred Drug Listing

Recalled Drug	**Comparison Drug**	
Brand *(Generic)* Name	**Brand *(Generic)* Name**	**Function**
Baycol® *(Cerivastatin)*	Zocor® *(Simvastatin)*	Cholesterol Lowering
Duract® *(Bromfenac)*	Celebrex® *(Celecoxib)*	Arthritis
Hismanal® *(Astemizole)*	Zyrtec® *(Cetirizine hydrochloride)*	Antihistamine
Lotronex® *(Alosetron)*	Asacol® *(Mesalamine)*	Bowel Disease (Crohn's)
Norplant® System I *(Levonorgestrel)*	Norplant® System II *(Levonorgestrel)*	Contraceptive
Posicor® *(Mibefradil)*	Norvasc® *(Amlodipine Besylate)*	High Blood Pressure
Propulsid® *(Cisapride)*	Reglan® *(Metoclopramide hydrochloride)*	Heartburn
Raplon® *(Rapacuronium bromide)*	Lioresal® *(Baclofen)*	Muscle Relaxant
Raxar® *(Grepafloxacin)*	Cipro® *(Ciprofloxacin hydrochloride)*	Antibiotic
Redux® *(Dexfenfluramine)*	Meridia® *(Sibutramine monohydrate hydrochloride)*	Weight Loss
Rezulin® *(Troglitazone)*	Avandia® *(Pioglitazone hydrochloride)*	Type 2 Diabetes
Rotashield® *(Rotavirus vaccine)*	Infanrix® *(Rotavirus vaccine)*	DPT Vaccine
Seldane® *(Terfenadine)*	Allegra® *(Fexofenadine hydrocloride)*	Antihistamine
Trovan® *(Trovafloxacin)*	Tequin® *(Gatifloxacin)*	Antibiotic
Versed® *(Midazolam hydrochloride)*	Ativan® *(Lorazepam)*	Anxiety, Insomnia

[Insert Figure 3 about here]

Figure 3. Drug Approval Type for Recalled vs. PDL Comparison Drugs



Drugs	Approval Type	REMOVED
Baycol®	Standard	Yes
Duract®	Standard	Yes
Redux®	Fast track	Yes
Hismanal®	Standard	Yes
Lotronex®	Fast track	Yes
Norplant® System I	Fast track	Yes
Posicor®	Standard	Yes
Propulsid®	Standard	Yes
Raplon®	Fast track	Yes
Raxar®	Standard	Yes
Rezulin®	Fast track	Yes
Trovan®	Fast track	Yes
Rotashield®	Fast track	Yes
Seldane®	Standard	Yes
Versed®	Fast track	Yes
Allegra®	Standard	No
Asacol®	Fast track	No
Ativan®	Standard	No
Avandia®	Fast track	No
Celebrex®	Fast track	No
Cipro®	Fast track	No
Infanrix®	Standard	No
Lioresal®	Fast track	No
Meridia®	Standard	No
Norplant® System II	Standard	No
Norvasc®	Standard	No
Reglan®	Standard	No
Tequin®	Standard	No
Zocor®	Standard	No
Zyrtec®	Standard	No

Recalled drugs comprised a total of $6,551.06 of Medicaid drug expenditures as measured by the Medicaid allowable cost (determined by the sum of Medicaid ingredient costs and dispensing fees of $4.23 per claim). In contrast, the state spent $2,664,214.92 for the comparison drugs in fiscal year 2001-02. Relative to the amount spent for comparison drugs, the amount spent on recalled prescription drugs was miniscule – 0.25% of comparison drugs (Figure 4 and Figure 5).

Discussion

The introduction and use of more expensive drugs in the same therapeutic category leads to increases in the average prescription drug price paid by consumers and institutional payers. In Florida, utilization of new expensive drugs fueled the significant upsurge in Medicaid drug expenditures. Over the six-year period spanning fiscal years 1995-96 through 2000-01, the average reimbursement for a Medicaid prescription rose by 84% from $34.40 to $63.23 (Agency for Health Care Administration, 2001). To stem the growth in prescription drug costs, a number of cost containment measures were instituted. One of the pharmacy reforms enacted by the Florida legislature in 2001 was the development of the Medicaid preferred drug list. This study found that Medicaid spending for recalled drugs was much lower than for comparison drugs on the preferred drug list, in part, because of fewer claims and associated dispensing fees. By far the greatest number of claims among the recalled drugs was for the cholesterol-lowering medication, *Baycol*, a drug that was on the market for four years before removal in 2001.

When looking at the Medicaid preferred drug list, it is clear that there are numerous drugs for each type of symptom and for many disease states. A limitation of the study is that there is more than one drug for a given type of symptom or condition. It is difficult to assign an exact substitute for every drug removed from the market. This study's selection of PDL drugs matched the removed drugs by therapeutic classification and drug function for comparisons of approval types.

In this analysis, a higher percentage of drugs approved via an accelerated process were recalled compared with those on the Florida Medicaid preferred drug list that received standard FDA approval. Since 1992, speedier FDA reviews have been financed by industry-paid user fees authorized by Congress in the Prescription Drug User Fee Act (PDUFA). Rather than the customary, multi year review, waiting times for drug approval have

Figure 4. Medicaid Spending for Recalled Drugs (Fiscal Year 2001-02)

RECALLED DRUGS	# OF CLAIMS	DISPENSING FEE($)	COST	QUANTITY	Medicaid Ingredient Cost ($)	Medicaid Allowable Cost ($)
Baycol®	1,071	4,530.33	1.41	100	140.75	4,671.08
Duract®	0	0	0.94	100	93.60	93.60
Hismanal®	0	0	1.98	100	198.07	198.07
Lotronex®	18	76.14	5.29	30	158.57	234.71
Norplant® System I	0	0	420.51	1	420.51	420.51
Posicor®	0	0	1.90	100	190.26	190.26
Propulsid®	2	8.46	0.11	450 (mg/mL)	51.14	59.60
Raplon®	0	0	25.14	10 (vials)	251.40	251.40
Raxar®	0	0	2.14	60	128.48	128.48
Redux®	0	0	0.92	30	27.66	27.66
Rezulin®	0	0	1.55	100	154.90	154.90
Rotashield®	0	0	16.59	2.5 (mL)	41.48	41.48
Seldane®	0	0	1.13	30	33.83	33.83
Trovan®	37	156.51	6.93	30	207.83	364.34
Versed®	4	16.92	1.04	100 (mL)	103.86	120.78
TOTAL	**1,132**	**4,656.49**	**487.57**	**1,303.5**	**2,202.35**	**6,551.06**

Figure 5. Medicaid Spending for PDL Comparison Drugs (Fiscal Year 2001-02)

COMPARISON DRUGS	# OF CLAIMS	DISPENSING FEE ($)	COST	QUANTITY	Medicaid Ingredient Cost ($)	Medicaid Allowable Cost ($)
Allegra®	967	4,090.41	1.21	100	121.00	4,211.41
Asacol®	6,649	28,125.27	0.84	100	83.82	28,209.09
Avandia®	31,685	134,027.55	4.39	100	439.41	134,466.96
Celebrex®	237,181	1,003,275.63	2.46	100	246.49	1,003,522.12
Cipro®	17,513	74,079.99	4.12	100	411.86	74,491.85
Infanrix	0	0	19.29	5 (mL)	96.45	96.45
Lioresal®	291	1,230.93	447.63	1 (kit)	447.63	1,678.56
Lorazepam®	5,344	22,605.12	8.04	1 (vial)	8.04	22,613.16
Meridia®	0	0	2.75	100	275.31	275.31
Norplant® System II	2	8.46	434.42	1 (kit)	434.42	442.88
Norvasc®	120,893	511,377.39	1.86	100	186.14	511,563.53
Reglan®	22,790	96,401.70	0.54	100	54.45	96,456.15
Tequinin®	1,504	6,361.92	8.05	30	241.46	6,603.38
Zocor®	79,019	334,250.37	3.58	100	358.49	334,608.86
Zyrtec®	106,148	449,006.04	1.81	100	180.57	49,186.61
TOTAL	**629,986**	**2,664,840.78**	**939.80**	**1,038**	**3,464.55**	**2,664,214.92**

been reduced, sometimes to less than one year. Recent studies have reported that the period for approval of priority drugs has decreased from 20 months to 6 months (GAO, 2002 September; Carpenter, 2004; Olsen, 2004).

Critics allege that the FDA has "systemic problems that contributed to the *Vioxx* catastrophe and to a long line of other drug safety failures in the past 10 years" (Fontanerosa, Drummond, & DeAngelis, 2004; Graham, 2004; Topol, 2004). An early indication was an apparently higher recall rate after Congress enacted the PDUFA. One analysis found that 5.34% of drugs approved between 1997 and 2000 were removed from the market as compared to 1.56% between 1993 and 1996 (GAO, 2002 September). More recently, the number of drugs withdrawn from the market has declined from 10 drugs removed between 1996 and 2001 to 3 product withdrawals between 2001 and 2004 (Kaufman & Masters, 2004). Since 1997, only 16 drugs have been recalled and withdrawn from the

market because of safety concerns (Associated Press, 2004).

The recent criticisms about the drug approval process prompted the FDA to propose measures to bolster the drug safety and approval process (Crawford FDA, 2004). Among the recommendations were: (1) sponsoring an Institute of Medicine study of the drug safety system, (2) appointing a Director for the Office of Drug Safety who would oversee the post-marketing safety for all approved products, and (3) publishing risk management guidance. It is anticipated that the FDA's implementation of measures such as those above will improve the safety of new drugs and lead to better health outcomes for consumers.

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