

UNIVERSITY OF ARKANSAS
FOR MEDICAL SCIENCES
COLLEGE OF PHARMACY

ARKANSAS MEDICAID EVIDENCE-BASED PRESCRIPTION DRUG PROGRAM (EBR_x)

QUARTERLY REPORT – THIRD QUARTER 2007



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INTRODUCTION

OVERVIEW OF THE EVIDENCE-BASED PRESCRIPTION DRUG PROGRAM

The Evidence-Based Prescription Drug Program (EBRx) came into existence in November 2004. The program is a collaboration between the University of Arkansas for Medical Sciences (UAMS) College of Pharmacy and the Arkansas Department of Health and Human Services (DHHS) Medicaid Program, with the support and input of the Arkansas Medical Society and the Arkansas Pharmacist's Association. The primary role of EBRx for DHHS is to facilitate development of an Evidence-based Preferred Drug List and provide related Prior Authorization review services for Medicaid and ARKids recipients.

Medicaid is an entitlement program for individuals and families with low-income or disabilities. Prior to January 1, 2006, the Medicaid program provided prescription benefits for qualifying elderly patients whose primary insurance was through the Federal Medicare program. With the availability of Medicare Part D prescription drug coverage, the Arkansas Medicaid enrollee population is now predominantly children. In fact Arkansas' Medicaid and ARKids programs are estimated to provide healthcare coverage to approximately half of all Arkansas children.

In the years before development of the Evidence-based Preferred Drug List, medication cost growth was a major contributor to increased costs of the Arkansas Medicaid program. In the nine years before EBRx began, Medicaid prescription drug spending grew at a compound annual growth rate exceeding 16 percent. This growth was due to increases in the costs of medications as well as increases in the numbers of enrollees. The largest contributor to the increase in total medication expenditures was increases in average medication costs. The rate of medication cost growth far exceeds state revenue growth, and jeopardizes continuation of the optional Medicaid drug benefit, or other benefits at current levels.

The goals of the EBRx program are to: identify differences between medication options; recommend inclusion on the PDL of superior medications, if they exist; enhance predictability and reduce costs of medications whenever possible; and to provide access to medications not on the PDL through Prior Authorization Call Center activities. These efforts are hoped to ensure the continued ability of the state to provide appropriate medical coverage for Arkansas' Medicaid and ARKids recipients.

Preferred Drug List Summary

PDL CATEGORIES, SELECTIONS, RATIONALE, AND SPECIAL CONSIDERATIONS

Medication Class	Medicaid Preferred Agents (Brand Name Agents in Bold)	Drug Review Committee Recommendation Summary	Special Considerations
Less Sedating Antihistamines	Loratadine	No difference in patient total symptom scores	Patients under age 2 years
Proton Pump Inhibitors	Prevacid capsules Nexium capsules Prevacid Solutabs	No difference in outcomes with equipotent dosing	Patients under age 7 years, Patients with feeding tubes
HMG-CoA Reductase Inhibitors (statins)	Zocor (generic products are now also available)	Three agents superior to others based on prevention of heart attacks	Need for more potent agent
Calcium Channel Blockers	Diltiazem ER capsules (equiv to Dilacor XR) Dynacirc CR Norvasc (removed after PDL contract expired) Nifedipine ER tablets Verapamil SR tablets	At least 1 product from each of the three sub-classes of calcium channel blockers should be available, no significant difference in outcomes with equipotent dosing.	Dosage strengths of extended release diltiazem
Beta Blockers	Atenolol Metoprolol tartrate Propranolol IR Bisoprolol (only for CHF) Toprol XL (only for CHF)	3 agents superior for treatment of congestive heart failure, few advantages for one agent over another for all other uses.	Diagnosis of symptomatic Congestive Heart Failure
Long-Acting Opioids	Methadone Morphine sulfate ER tablets	No clinical advantage for one agent over another for treatment of chronic pain.	Terminal cancer diagnosis. Patients with long-term care coverage Patients unable to swallow
Angiotensin-Converting Enzyme (ACE) Inhibitors	Altace Captopril	No significant differences among the agents for most indications although there are differences in approved indications and data supporting use of specific products in specific conditions.	Patients under age 18 years
Serotonin 5-HT ₁ Receptor Agonists (triptans)	Maxalt Maxalt MLT	No significant difference among 5 of the 7 agents that any one agent is clinically superior to another agent.	Nasal spray and injectable formulations
Angiotensin II Receptor Blockers	Cozaar, Hyzaar Diovan, Diovan HCT	No significant advantage or disadvantage among the agents.	Congestive Heart Failure

Medication Class	Medicaid Preferred Agents (Brand Name Agents in Bold)	Drug Review Committee Recommendation Summary	Special Considerations
Skeletal Muscle Relaxants	Chlorzoxazone Cyclobenzaprine 10mg Methocarbamol Baclofen (spasticity only) Tizanidine (spasticity only)	Muscle spasms and spasticity disorders have different preferred agents, no advantage of one product over another.	None
Systemic Estrogens	Estradiol 0.5mg, 1mg, 2mg Estropipate	No difference in the products at equipotent doses. At least one oral and one topical product should be available	None
Non-Benzodiazepine Sedative Hypnotics	Ambien CR Rozerem Sonata	No significant differences among the agents.	None
Targeted Immune Modulators	Enbrel Humira	No differences found, but generally lacking comparative data for analysis.	Subject to previous DUR clinical edits
Inhaled Corticosteroids	Asmanex Azmacort (removed after contract terminated) Flovent (only to age 12)	No significant differences among the products at equipotent doses	Patients under age of 12 years
Anticholinergics for Overactive Bladder	Detrol LA Oxybutinin syrup, 5mg tablet Vesicare	No significant differences among the products at equipotent doses. None particularly effective	Patients under age of 18 years with spina bifida diagnosis
Antiemetics 5-HT3 and NK1 Receptor Antagonists	ondansetron	No significant differences among the products at equipotent doses.	None
Antidiabetics-meglitinides	Starlix	At least one agent from each of the sub-classes of antidiabetics should be included. No significant differences in efficacy among the agents.	None
Antidiabetics-First Generation Sulfonylureas	Chlorpropamide Tolazamide		
Antidiabetics-Second Generation Sulfonylureas	Glimepiride Glipizide Glyburide Glyburide micronized Metformin Metformin/glipizide Metformin/glyburide		
Antidiabetics-Thiazoladinediones	Actos 30mg, 45mg Actosplus Met Avandamet Avandaryl Avandia		
Nasal Corticosteroids	Nasacort AQ Nasonex		

Antidepressants	Bupropion regular release Citalopram Fluoxetine 10mg,20mg caps, 20mg/5ml solution Lexapro 10mg,20mg Mirtazapine 15mg,30mg,45mg Paroxetine Pexeva Sertraline Venlafaxine regular release Wellbutrin XL	No significant differences in efficacy among the agents but at least 3 should be available due to high initial failure rates. Fluoxetine should be available to those<18yo	Patients stable and compliant on non-preferred agents.
Beta ₂ Agonists	<u>Short Acting</u> Albuterol 90mcg inhaler Albuterol 5mg/ml solution Albuterol 0.83mg/ml solution Maxair Autohaler Proair HFA Ventolin HFA <u>Long Acting</u> Serevent Diskus	No significant differences among the agents in regards to efficacy or safety.	Long acting agents still subject to previous DUR clinical criteria edits.
NSAIDs	Ibuprofen suspension and doses above 200mg Indomethacin 25mg Ketoprofen 50mg,75mg Ketorolac Meloxicam 7.5,15mg Naproxen 250mg,375mg,500mg Naproxen sodium 275mg,550mg Naproxen 375mg, 550mg enteric coated tablets Piroxicam Salsalate	No significant differences exist among the agents in regards to safety or efficacy. At least 3 agents should be available.	None.
ADD/ADHD	Amphetamine salts Adderall XR Focalin Focalin XR Concerta Daytrana Methylphenidate tablets	At least 1 IR and SR methylphenidate and amphetamine preparation should be available. Absent some co-morbidities, methylphenidate and amphetamines are more likely to be appropriate initial choices than atomoxetine.	Patients compliant on non-preferred agents.

FINANCIAL IMPACT OF PDL SELECTIONS

COST SAVINGS TO THE STATE RESULTING FROM THE PDL

METHOD OF ESTIMATING COSTS AVOIDED/SAVINGS

Products placed on the Preferred Drug List (PDL) represent therapies with proven advantages over other alternatives, or cost-effective selections in categories where no important differences between products can be found. Even though the foundation of the PDL is clinical, it has impacted the net medication costs for Arkansas Medicaid. Estimates of the cost impact of PDL selections are presented in this section. The costs for a medication category could be either increased or decreased as a consequence of the PDL.

Several factors make it likely that medication costs in a drug category will decrease after preferred agents are selected. First, manufacturers of patent-protected, single source products offer supplemental rebates to Arkansas Medicaid in consideration of inclusion on the Preferred Drug List. Selection as a preferred agent has significant impact on product sales and market share, and manufacturers often generate higher sales from Arkansas Medicaid if their products are selected as preferred agents. These supplemental rebate offers ensure Arkansas Medicaid lower net costs than without the PDL. Second, there are situations where no important clinical differences exist among the medications in a category. In many cases there are less expensive, equally effective generic medications available at lower costs than single source agents in a drug category. Where there is the opportunity to gain all important clinical benefits offered by a group of drugs, while using a lower cost agent, these agents are selected for the PDL.

These estimates of medication costs avoided are calculated with estimates of the Medicaid net cost per prescription. Two estimates of net costs are made. One value is based on the weighted average net cost per prescription in a drug category immediately prior to the preferred drug selection. This average net cost per prescription represents the expected Medicaid net cost which would have been incurred without the PDL. It is important to remember that the estimated expected Medicaid net cost is not adjusted for price increases imposed after the PDL effective date for the category. Multiplying the expected net cost per prescription by the total number of prescriptions dispensed in the current period yields the Estimated Expected Costs. The second estimate is based on current Medicaid net costs for preferred agents. These costs are multiplied by the prescription volumes for each preferred drug. The total net costs estimated for each of the non-preferred drugs currently used is added to this result. This estimate is called the Post-PDL Net Cost Estimate. The difference between the Estimated Expected Costs and the Post-PDL Net Cost Estimate is our estimate of costs avoided (or incurred) as a consequence of the PDL.

The reported savings or costs avoided do not consider the impact of PDL decisions on total care costs. There may be either increases or decreases in others categories of Medicaid spending as a result of the PDL. There may also be shifts to or from particular drug categories as a consequence of the PDL recommendations. Along with the EBRx staff, UAMS' College of Pharmacy, Pharmaceutical Evaluation and Policy Division conducts ongoing analyses and reviews of the impact of the PDL on total Medicaid costs.

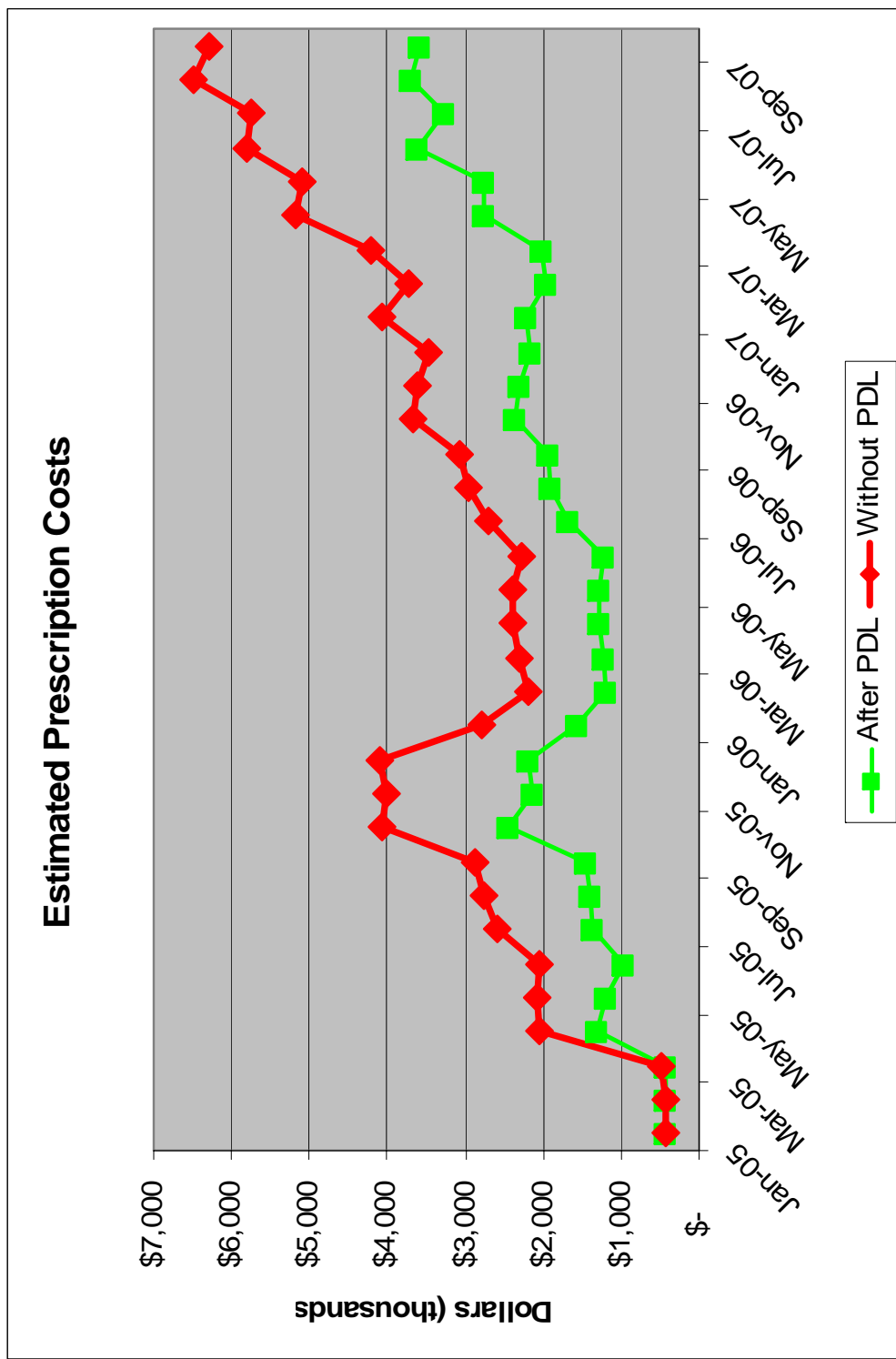
OVERALL RESULTS

The first PDL selection became effective March 25, 2005. By the end of September, 2007 preferred drugs had been selected and implemented in twenty two drug classes. Since the first PDL selection, EBRx estimates that the PDL process has yielded potential savings/excess costs avoided of at least \$46.5 million. Table 1 shows implementation dates, and costs avoided or incurred for each category reviewed.

TABLE 1 – Summary of Estimated Prescription Costs Avoided to Date by Category

Drug Category	PDL Effective Date	Costs Avoided/Potential Savings or Costs Incurred Estimates		
		State Fiscal Year 06	State Fiscal Year 07	State Fiscal Year 08(to date)
Less Sedating Antihistamines	3/25/05	\$ 2,340,000	\$ 2,400,000	\$ 550,000
Proton Pump Inhibitors	5/18/05	\$ 8,540,000	\$ 6,560,000	\$ 1,720,000
“Statin” Cholesterol Agents	6/8/05	\$ 1,940,000	\$ 40,000	\$ 510,000
Calcium Channel Blockers	7/12/05	\$ 580,000	\$ 490,000	\$ 90,000
Beta Blockers	10/5/05	\$ 650,000	\$ 510,000	\$ 120,000
Long-Acting Opioids	10/26/05	\$ 1,240,000	\$ 1,520,000	\$ 400,000
ACE Inhibitors	11/16/05	\$ 290,000	\$ 250,000	\$ 60,000
“Triptan” Antimigraine Agents	2/7/06	\$ 120,000	\$ 280,000	\$ 70,000
Angiotensin Receptor Blockers	2/21/06	\$ 140,000	\$ 300,000	\$ 80,000
Skeletal Muscle Relaxers	3/20/06	\$ 100,000	\$ 370,000	\$ 90,000
Estrogens	4/17/06	\$ 20,000	\$ 100,000	\$ 20,000
Sedative Hypnotics (Sleep Aids)	5/9/06	\$ 100,000	\$ 3,220,000	\$ 1,390,000
Targeted Immune Modulators	6/13/06	\$ (20,000)	\$ 90,000	\$ 70,000
Inhaled Corticosteroids	7/11/06	\$ -	\$ 1,810,000	\$ 490,000
Overactive Bladder Agents	8/15/06	\$ -	\$ 180,000	\$ 50,000
Newer Antiemetics	10/10/06	\$ -	\$ (130,000)	\$ (50,000)
Oral Diabetes Agents	11/28/06	\$ -	\$ 300,000	\$ 90,000
Nasal Steroids	11/28/06	\$ -	\$ 890,000	\$ 320,000
Antidepressants	4/10/07	\$-	\$ 700,000	\$ 740,000
Beta ₂ Agonists	5/29/07	\$-	\$ 120,000	\$ 220,000
NSAIDs	6/18/07	\$-	\$ 5,000	\$ 90,000
ADD/ADHD	7/10/07	\$-	\$-	\$ 840,000
Grand Total		\$ 16,030,000	\$ 20,000,000	\$ 7,960,000

Graph 1



MARKET SHARE IMPACT OF PDL RECOMMENDATIONS

The success of the PDL depends in large part on participation by prescribers with the recommendations of the Drug Review and Drug Utilization and Cost Committees. Prescribing compliance with the Preferred Drug List is monitored by EBRx. The following table presents data on the percentage of prescriptions that were filled for preferred product(s) in each of the therapeutic categories reviewed and implemented to date. This percentage is commonly called market share in the pharmaceutical industry. Outcomes and cost savings are maximized as market share approaches 100 percent compliance with the Preferred Drug List recommendations. However, it should be noted that complete compliance with the Preferred Drug List is unlikely as there remains individual variation in response to any medicine.

Percent Market Share of PDL Preferred Agents by Drug Class and Month

	Oct 06	Nov 06	Dec 06	Jan 07	Feb 07	March 07	April 07	May 07	June 07	July 07	Aug 07	Sept 07
Less Sedating Antihistamines	84	84	83	84	84	84	84	84	84	81	83	84
Proton Pump Inhibitors	100	100	100	99	100	100	100	100	99	99	100	100
Statins	98	98	99	98	98	98	98	98	98	98	98	98
Calcium Channel Blockers	80	80	80	82	85	88	88	88	88	94	94	94
Beta Blockers	91	91	92	91	91	91	91	91	90	91	91	91
Long-acting Opioids	83	83	81	80	80	77	77	76	76	77	77	76
ACE Inhibitors	78	78	79	77	77	76	76	76	76	76	76	76
Triptans	87	88	88	87	85	89	88	88	88	88	89	90
ARBs	100	100	100	100	100	100	100	100	100	100	100	100
Skeletal Muscle Relaxers	99	99	99	99	99	99	99	99	99	99	99	99
Estrogens	92	91	93	91	92	91	90	89	90	91	90	90
Newer Sleep Aids	99	100	100	99	100	99	100	100	100	100	100	100
Targeted Immune Modulators	82	77	88	82	76	75	84	81	87	84	87	82
Inhaled Corticosteroids	68	67	67	65	65	67	67	68	65	66	68	70
Overactive Bladder Agents	89	89	93	88	89	90	90	90	90	89	90	89
Newer Antiemetics	93	96	98	96	95	98	97	97	97	97	97	98
Oral Diabetes Agents	66	67	66	67	65	64	64	64	62	61	60	59
Nasal Steroids	46	53	100	100	100	100	100	100	100	100	100	100
Antidepressants				74	74	74	82	88	89	90	91	91
Beta₂ Agonists				80	79	79	83	85	97	97	97	97
NSAIDs							84	83	88	99	99	99
ADD/ADHD							77	77	77	81	86	87

Data in bold highlight the month PDL recommendations for the drug class became effective.

Prior Authorization Call Center Statistics

P.A. CALL CENTER OPERATIONS AS A RESULT OF THE PDL

“Non-preferred” medications continue to be available to Medicaid recipients, but require prior authorization. Two processes are in place to provide prior authorization. The first is a computer-based system called Smart-PA. If the patient meets predetermined authorization guidelines, Smart-PA can grant an instantaneous prior authorization at the pharmacy counter with no additional effort by the provider or pharmacist. This occurs as a prescription claim is processed at the pharmacy

The second prior authorization process is the PDL Call Center. This center approves or denies prior authorization requests from physicians for products that have been placed in non-preferred status. The approval, denial, and appeal of denials are handled by the clinical pharmacists and medical directors of the EBRx Program. The statistics below represent the Call Center’s activity for SFY 2007 and the most recent quarter, 3Q 2007, which includes July 1st 2007 through September 30, 2007.

PA Call Center Statistics	4Q 2006	1Q 2007	2Q 2007	FY 2007	3Q 2007
Incoming Calls from Healthcare Professionals	2939	3039	5423	14,341	8441
Number of SmartPA Tickets Created	2226	2346	4527	12,027	5766
Total Number of P.A. Requests at the Call Center	1473	1691	2973	7786	5362
Total Number of P.A. Requests Approved at the Call Center	1014	1222	1993	5382	3888
Call Center P.A. Approval Percentage	68%	72%	67%	69%	73%
Point of Sale SmartPA Requests	40,527	42,935	99,637	219,835	161,037
Point of Sale SmartPA Approvals	27,393	26,268	68,858	145,908	126,153
Point of Sale SmartPA Approval Percentage	68%	61%	69%	66%	78%
Average Call Duration	1 min 57 sec	1 min 57 sec	2 min 29 sec	2 min 9 sec	2 min 35 sec

Budget Update

A GENERAL OVERVIEW OF THE PROGRAM BUDGET

The Arkansas Medicaid Evidence-based Prescription Drug Program budget and expenditures to date are presented below. There remain a number of personnel positions initially budgeted but not filled. If needs for additional program personnel arise, the program will work within the existing budget to ensure that service obligations are met. At the end of 3Q 07, the program was approximately \$545,290 under budget for the quarter.

	SFY08 Budget	3Q07 Expenditures
Personnel –(Salary and Fringes, includes DRC stipends)	2,496,381	302,596
Miscellaneous – (Supplies, Travel, etc)	150,750	7,213
Equipment – (computers, phones, furniture, renovation)	13,000	0
Indirect Costs	1,429,451	167,297
TOTAL	4,089,582	477,106

Data Evaluation

TRACKING OUTCOMES OF THE PDL DECISIONS

PEP Division Activities

One of the most important aspects of the EBRx program is the evaluation of Medicaid data to determine what the long term ramifications of the PDL decisions are. Through the College of Pharmacy's Pharmaceutical Evaluation and Policy (PEP) Division, the Medicaid claims database is analyzed to determine impacts to the Medicaid program, beyond potential changes in medication costs.

The PEP division has produced analyses of the impact of four PDL category decisions to estimate the prescription cost impact of the policies of the affected drugs and potential substitute drugs. The categories that have been evaluated are Less Sedating Antihistamines for allergy, Proton Pump Inhibitors for acid reflux, "Statin" cholesterol medicines and Calcium Channel Blocker blood pressure medications. Currently the PEP division is investigating the impact of the PDL on statin adherence/persistence and the impact of the ACE inhibitor PDL on prescription costs. The next analyses will be to assess the impact of the long acting opioid PDL and inhaled corticosteroids. The analyses of the impact of the calcium channel blocker and proton pump inhibitors have been presented at the International Society for Pharmacoeconomics and Outcomes Research annual meeting in May 2007 and the abstracts are presented below.

Graduate student led research activities have included two theses that have utilized the AR Medicaid administrative claims data. The project led by Sudeep Karve, entitled "*Comparing the predictive validity of 8 adherence measures using administrative claims data*", compared several different ways to calculate adherence and offers guidance to persons wishing to calculate adherence with prescription claims data in selecting the ideal measure. The preliminary findings from this research were presented at the ISPOR meeting in May 2007 and the abstract is presented below.

Under the direction of Dr. Donna West, Prathamesh Pathak investigated the off-label uses of atypical antipsychotics in children. He found dramatic increases in antipsychotic utilization from 2001 to 2005 and that 41% of the use was not supported by published evidence. These findings suggest that this class of drugs should be scrutinized and public policy controls should be considered given the potential adverse effects and incumbent costs associated with the use of these agents in children. An abstract of his findings are presented below.

The Impact of a Calcium Channel Blocker Preferred Drug List on Medicaid Prescription Expenditures and Utilization.

Bradley C. Martin, Pharm.D., Ph.D., Prathamesh Pathak, B.Pharm., Mark Helm, M.D., Division of Pharmaceutical Evaluation and Policy, University of Arkansas for Medical Sciences, 4301 W. Markham Street, slot#522, Little Rock, AR, 72205, bmartin@uams.edu

Background: On July 12, 2005 the Arkansas Medicaid program implemented a prior approval policy for calcium channel blockers (CCBs) in which Diltiazem ER, Dynacirc CR, Nifedipine ER, XL, CC, CR, Norvasc, and Verapamil SR, SA, were the preferred drugs. Objectives: The objective of this study was to estimate the impact of this policy on CCB expenditures. Methods: This study utilized a time series panel design to evaluate the impact of the policy using Arkansas Medicaid administrative claims data obtained from January 2003 through May 2006. Auto-Regressive Integrated Moving Average (ARIMA) time series

models were specified using monthly prescription expenditures and utilization in the pre-policy period (January 2003 – June 2005) to forecast expenditures and utilization in the post-policy period. The Medicaid payer perspective was used and all prescription costs were calculated based on the amount paid for each claim adjusted for product specific CMS rebates. Results: The average forecast expenditures for CCBs for August 2005 – May 2006 was \$426,706 (95%CI: 410,356-443,055) per month and observed expenditures were \$331,547 indicating that the policy change was associated with a 22% reduction in CCB expenditures or \$95,159 (95%CI: 78,809- 111,508) per month. The average monthly savings were \$114,521 prior to January 2006 and were \$75,796 after Medicare dual eligibles began receiving Part-D benefits. Non-significant reductions in CCB utilization were observed in the initial 4 months following the policy, however by May 2006, 4,065 (95%CI: 3,811-4,319) recipients were expected to be taking CCBs but only 3,046 actually had a CCB prescription filled. Conclusion: This CCB preferred drug list resulted in substantial savings of approximately \$100,000 month. Some of the savings appear to be a result of reduced utilization of CCBs which may indicate that other cardiovascular drugs may have been used in place of CCBs or CCB discontinuation.

Having your Cake and Eating it Too: Results from a Policy Analysis of a Proton Pump Inhibitor Preferred Drug List.

Bradley C. Martin, Pharm.D., Ph.D., Sudeep Karve, B.Pharm., M.B.A., Mark Helm, M.D., Division of Pharmaceutical Evaluation and Policy, University of Arkansas for Medical Sciences, 4301 W. Markham Street, slot#522, Little Rock, AR, 72205, bmartin@uams.edu

Background: On May 18, 2005 the Arkansas Medicaid program implemented an evidence-based Preferred Drug List (PDL) recommendation for Proton Pump Inhibitors (PPIs). Under the PDL program guidelines, esomeprazole and lansoprazole were made available as preferred agents to Medicaid recipients without prior approval. Previously, all PPIs required prior authorization and were not covered unless patients failed on H2 Receptor Antagonist (H2RA) therapy. Objectives: The objective of this study was to estimate the impact of this policy on PPI expenditures and utilization as well as utilization of potential substitute H2RAs. Methods: This study utilized a time series panel design to evaluate the impact of the policy using Arkansas Medicaid administrative claims data obtained from January 2003 through August 2006. Auto-Regressive Integrated Moving Average (ARIMA) time series models were specified using monthly prescription expenditures and utilization in the pre-policy period (January 2003 – April 2005) to forecast expenditures and utilization in the post-policy period. The Medicaid payer perspective was used and all prescription costs were calculated based on the amount paid for each claim adjusted for product specific CMS rebates. Results: The annual forecast expenditures for PPIs and H2RAs collectively for June 2005 – May 2006 was \$9,432,605 (95%CI: 8,747,983- 10,117,226) and observed expenditures were \$4,555,592 indicating that the prior approval policy change was associated with a 52% reduction in GI antisecretory expenditures or \$4,877,013 (95%CI: 4,192,391-5,561,635). Utilization of PPIs increased by 44% (3,001 Rxs/month; 95%CI: 3,695-2,308) which more than offset the 21% (1,660 Rxs/month; 95%CI: 1,199-2,121) decrease in utilization of H2RAs. Conclusions: Replacing step therapy and prior authorization requirements with a preferred drug list selection including supplemental rebates for this Medicaid program significantly lowered expected combined H2RA and PPI prescription expenditures. Since utilization to antisecretory therapy actually increased, increases in non-pharmacy costs or negative outcomes are not anticipated.

THE PREDICTIVE VALIDITY OF DIFFERENT ADHERENCE MEASURES USING ADMINISTRATIVE CLAIMS DATA

Sudeep Karve, B.Pharm. M.B.A., Bradley C. Martin, Pharm.D., Ph.D. Division of Pharmaceutical Evaluation and Policy, University of Arkansas for Medical Sciences, Little Rock, Arkansas

OBJECTIVES: To determine the predictive validity of eight different adherence measures by studying the variability explained between each measure and two outcome measures: hospitalization episodes and total non-pharmacy cost. **METHODS:** This study was a retrospective analysis of the Arkansas Medicaid administrative claims data. Schizophrenia (ICD-9-CM = 295. **) patients were identified in the recruitment period July 2000 through April 2004. Patients had to be >18 years old, have prescription benefits, and continuously eligible for 6 months prior and 24 months after their first antipsychotic prescription. Persons taking two different antipsychotic drug products simultaneously were excluded. MPR, PDC, MPRm, RCR, CR, CMG, DBR, and CSA were computed and modeled to predict hospitalizations and non-pharmacy costs. **RESULTS:** 3,971 patients with a mean age 46.5 years, 54% were female, 55% were white, 38% were black, and females constituted of 54% (n=2,134) and males 46% (n=1837). The one year adherence rates were numerically similar for MPR (0.747 SD= 0.319) and PDC (0.7294, SD=0.299). Other measures such as MPRm (82.21%, SD= 27.27), RCR (97.20 % SD=115.05), CR (81.39% SD = 64.18) DBR (97.20 % SD=115.05) and CSA (0.95 SD=0.8) had higher adherence values. The partial R-squares of the multivariate regression models will be reported. **CONCLUSIONS:** There is considerable variability in rates of adherence among the 8 measures of adherence. MPR and PDC which used the entire study period as the denominator had the most conservative adherence values. In contrast MPRm, PDC, RCR, CR which only consider the time between first and last prescription fill dates estimate higher levels of adherence.

AN INVESTIGATION OF EVIDENCE-BASED USE OF ATYPICAL ANTIPSYCHOTICS IN ARKANSAS MEDICAID PEDIATRIC POPULATION: 2001 – 2005

Pathak Prathamesh, B.Pharm., MS1, West Donna, RPh., PhD2, Martin Bradley C, Pharm D, PhD2, Helm Mark, MD, MBA3, Hendersen Crystal, Pharm D.2

Context: The rapid increase in the use of atypical antipsychotics in pediatric populations over the past few years has been startling, considering these drugs are mostly unapproved in pediatric populations. Hence, it is imperative to determine the manner in which atypical antipsychotics are being used in children and adolescents. **Objectives:** 1) To identify the trend of new users of atypical antipsychotic drugs in the Arkansas Medicaid population under the age of 18 for years 2001 through 2005, 2) To classify the use of atypical antipsychotic drug for each subject as evidence-based or not depending on the diagnoses for which it was prescribed, and 3) To determine which pediatric patients are more likely to receive an evidence-based atypical antipsychotic prescription. **Design:** Retrospective database analysis. **Setting:** Arkansas Medicaid claims database was used for the period from January 2000 to December 2006. **Participants:** Participants were Medicaid beneficiaries under 18 years of age, with their first atypical antipsychotic prescription claim between 2001 and 2005, with no prior antipsychotic use and having a continuous 2-year Medicaid enrollment. **Main outcome measures:** Main outcome measure was the proportion of study cohort with at least one evidence-based atypical antipsychotic prescription claim. An evidence-based prescription was defined as any use of atypical antipsychotic supported by a clinical study in the literature. **Results:** The trend of new pediatric users of atypical antipsychotic therapy increased significantly from 2001 to 2005. 5989 (51.19%) of the cohort initiated their therapy with risperidone. After identifying 86 clinical studies from the literature and defining the evidence-based use for each atypical antipsychotic, it was found that 41.32% of the cohort did not have an evidence-based prescription. 77.13% of the aripiprazole use was non evidence-based. **Conclusions:** A large proportion of the atypical antipsychotic usage in the Arkansas Medicaid pediatric population is not based on strong clinical evidence.

Other EBRx Activities

With the addition of ADD/ADHD medications to the preferred drug list, the EBRx program saw a dramatic increase in call activity. Much of the increase had been anticipated, and the programming staff under supervision of Dr. Helm identified and extracted recipients who previously used ADHD treatments which were not included on the preferred drug list. These patient's use histories were analyzed, and prior authorizations were entered for all of those patients who were anticipated to qualify prior to an actual request from their physician. This effort was expected to reduce the number of telephone requests made for prior authorizations.

Additionally, work was begun on the grant project funded by the Attorney General Consumer and Prescriber Grant Program. This program was funded from the settlement paid by Pfizer/Pharmacia relating to illegal promotion of Neurontin (gabapentin) for uses not approved by the FDA. UAMS College of Pharmacy was awarded \$370,000 over two years to study approaches to influence prescribers of medications for uses which are not approved by the Food and Drug Administration. This project will focus on "off-label" medication uses in Arkansas' children. Initial work identified several medication classes with significant "off-label" use. In 2006, Arkansas Medicaid spending for "off-label" uses in eleven categories exceeded \$27 million dollars. Many of these uses are known to be ineffective, and potentially dangerous. Others have not been sufficiently studied to determine the risks or benefits they may present.

Drug Review Committee

Activities

Date: July 19, 2007

Subject: DRC Recommendations to DCC and DHS

To: DHS, DCC, Dean's Office

From: Henry F. Simmons, Jr., MD, Ph.D.
Chairman DRC

At its 07/19/07 meeting, the Drug Review Committee considered the potential toxicity and therapeutic roles of selected calcium channel blockers and targeted immune modulators.

PART I

Calcium channel blockers under consideration include the following:

Phenylalkylamine

Verapamil

Benzothiazepine

Diltiazem

Dihydropyridine

Amlodipine

Felodipine

Isradipine

Nicardipine

Nifedipine

Nisoldipine

Indications under consideration in adults

Angina

Systolic dysfunction [LVEF<45%]

Supraventricular dysrhythmias

Essential hypertension [BP \geq 140/90]

Conclusions regarding calcium channel blockers

1. None of the available calcium channel blockers is associated with clinically evident adverse events of sufficient severity or number to exclude it from further consideration.
2. The three classes of calcium channel blockers in use differ pharmacologically to the degree that at least one representative of each should be accessible to prescribers. Accordingly, verapamil, diltiazem and at least one dihydropyridine should be available.
3. When considering use of the dihydropyridines for the captioned indications, the Committee reached the same conclusions as its predecessor in 2005 with the following exception: Amlodipine and at least one other dihydropyridine should be available. The reaffirmed 2005 recommendations follow.

That amlodipine, nicardipine, nifedipine and nisoldipine are considerations for patients with angina

That amlodipine, isradipine, nicardipine, nifedipine and nisoldipine are considerations for patients with hypertension

That amlodipine be available to patients in the following categories:

Patients with both angina and documented left ventricular systolic dysfunction

Patients with hypertension and documented left ventricular systolic dysfunction

Patients with angina, hypertension, and documented left ventricular systolic dysfunction

4. None of the captioned drugs have been proven to differ significantly in either the incidence or nature of clinically evident adverse effects in patients of a particular demographic group.

5. None of the captioned drugs have been proven more efficacious for patients of a particular demographic group.

PART II

Targeted immune modulators under consideration

Abatacept (Orenicia)

Adalimumab (Humira)

Alefacept (Amevive)

Anakinra (Kineret)

Efalizumab (Raptiva)

Etanercept (Enbrel)

Infliximab (Remicade)

Rituximab (Rituxan)

Indications under consideration in adults

Rheumatoid arthritis

Ankylosing spondylitis

Psoriatic arthritis

Crohn's disease

Ulcerative colitis

Plaque psoriasis

Indications under consideration in children

Juvenile rheumatoid arthritis

Conclusions regarding targeted immune modulators

There is insufficient evidence to conclude that one of the available agents differs from the others in terms of safety considerations or frequency of adverse events to the degree that it should be stricken from further consideration.

In the treatment of **rheumatoid arthritis** there is sufficient information to conclude that Orenicia (abatacept), Humira (adalimumab), Kineret (anakinra), Enbrel (etanercept) and Remicade (infliximab) and Rituxan (rituximab) are efficacious for the treatment of rheumatoid arthritis in adults. However, Kineret (anakinra) is not as efficacious as adalimumab (Humira), etanercept (Enbrel) and rituximab (Rituxan). At least two of the FDA approved agents should be available, in particular if Kineret (anakinra) is one of them.

Humira (adalimumab), Enbrel (etanercept) and Remicade (infliximab) efficacious for treatment of **ankylosing spondylitis**. At least two of these FDA approved agents should be available.

For the treatment of **psoriatic arthritis** at least two of the following should be available: Humira (adalimumab), Enbrel (etanercept) and Remicade (infliximab).

For the treatment of **Crohn's disease** either Humira (adalimumab) or Remicade should be available.

Remicade (infliximab) should be available for the treatment of **ulcerative colitis**.

At least two of the following agents should be available for the treatment of **plaque psoriasis**: alefacept (Amevive), efalizumab (Raptiva), etanercept (Enbrel) and infliximab (Remicade).

In the treatment of **juvenile rheumatoid arthritis**, Enbrel (etanercept) should be available.

With respect to use of the aforementioned immune modulators among individuals from different demographic groups there is insufficient data to conclude that one is either more efficacious or more likely to produce adverse events than another.

Henry F. Simmons, Jr.
July 19, 2007

Date: September 20, 2007

Subject: DRC Recommendations to DCC and DHS

To: DHS, DCC, Dean's Office

From: Henry F. Simmons, Jr., MD, Ph.D.
Chairman DRC

At its 09/20/07 meeting, the Drug Review Committee considered the potential toxicity and therapeutic roles of the beta blockers in adults with hypertension, angina, s/p coronary artery bypass graft, heart failure, recent myocardial infarction, atrial arrhythmias, esophageal varices, and migraine.

The Committee reached the following conclusions based upon its perception of the bulk of the best available evidence.

1. There is insufficient data on carteolol, penbutalol and carvedilol phosphate for the Committee to comment on their utility for the aforementioned indications.
2. All of the beta blockers discussed have some efficacy in the treatment of hypertension.
3. Excluding timolol due to lack of sufficient data, all of the remaining drugs have some efficacy in the treatment of angina.
4. Acebutalol, propranolol, timolol, carvedilol and metoprolol tartrate have some efficacy in the treatment of patients with recent myocardial infarction. The Committee does not believe that pindolol should be available for this indication.
5. Bisoprolol, metoprolol succinate and carvedilol have some efficacy in the management of congestive heart failure. At least two of them should be available, one of which should be carvedilol.
6. Atenolol, nadolol, metoprolol succinate, pindolol, bisoprolol and carvedilol have some efficacy in the management of atrial dysrhythmias. There is insufficient data to recommend labetalol for this indication.
7. Atenolol, metoprolol tartrate, propranolol, bisoprolol, and timolol have some efficacy in the treatment of migraine. The Committee does not recommend pindolol for this indication.
8. Atenolol, nadolol, immediate release propranolol, and long acting propranolol all have some efficacy in the management of esophageal varices.
10. There is insufficient data to recommend specific beta blockers to patients simply because they have had coronary bypass grafting.
11. None of the beta blockers has been proven either to be more effective or to have more significant adverse effects on the basis of sex, race, or concomitant use of other medications.
12. There was discussion that carvedilol and labetalol might be beneficial to patients requiring beta blockers who abuse adrenergic stimulants but evidence was felt insufficient to make a formal recommendation. Some members of the group also felt that labetalol should be available for treatment of hypertension in pregnant patients.