Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

August 19, 2010

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

Drug Utilization Review Board

Frank Wade, M.D.
Family Medical Clinic
376A Simpson Highway 149
Magee, MS 39111
Term Expires: June 30, 2011

Alvin Dixon, R.Ph.
182 Cherry Street
Clarksdale, MS 38614
Term expires: June 30, 2011

Jason Strong, Pharm.D.
Canton Discount
726 East Peace Street
Canton, MS 39046
Term Expires: June 30, 2011

William Bastian, M.D.
Bastian Center of Pediatric Endocrinology
1860 Chadwick Drive, Suite 206
Jackson, MS 39204
Term Expires: June 30, 2011

Laura Gray, M.D.
905 Garfield Street
Tupelo, MS 38801
Term Expires: June 30, 2012

Gera Bynum, R.Ph.
Scott Regional Hospital
371 Highway 13S
Morton, MS 39117
Term Expires: June 30, 2012

Paul Read, Pharm.D.
CVS Pharmacy #5744
3910 Hardy Street
Hattiesburg, MS 36402
Term Expires: June 30, 2012

Jason Dees, D.O.
New Albany Medical Group
620 West Longview Drive
New Albany, MS 38652
Term Expires: June 30, 2012

Lee Merritt, R.Ph.
Medfusion
2211 5th Street North
Columbus, MS 39705
Term expires: June 30, 2013

Edgar Donahoe, M.D.
Indianola Family Medical Group
122 Baker Street
Indianola, MS 38751
Term expires: June 30, 2013

Mark Reed, M.D.
University of Mississippi Medical Center
2500 North State Street, Trailer 16
Jackson, MS 39216
Term Expires: June 30, 2013

Vickie Veazey, R.Ph.
MS State Hospital at Whitfield
Building #50
Whitfield, MS 39193
Term expires: June 30, 2013

Upcoming Mississippi DUR Board Meeting Dates

November 18, 2010
May 19, 2011

February 17, 2011
August 18, 2011

DIVISION OF MEDICAID
OFFICE OF THE GOVERNOR
DRUG UTILIZATION REVIEW BOARD
AGENDA

August 19, 2010

Welcome

Old Business

Approval of Meeting Minutes

Cost Management Analysis — **Ashleigh Holeman, Pharm.D.**

Pharmacy Program Update — **Judy Clark, R.Ph.**

New Business — **Ashleigh Holeman, Pharm.D.**

Addendum: Long-Acting Injectable Antipsychotic Use in Long-Term Care Settings

Evaluating Ondansetron Quantity Limits

Low-Dose Seroquel Utilization

Appropriate Duration of Therapy with Proton Pump Inhibitors

Other Criteria Recommendations

Next Meeting Information

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the May 20, 2010 Meeting

Members Attending: William Bastian, M.D.; Gera Bynum, R.Ph; Alvin Dixon, R.Ph; Edgar Donahoe, M.D.; Lee Merritt, R.Ph; Mark Reed, M.D.; Paul Read, Pharm D; Jason Strong, Pharm D; Frank Wade, M.D.
Members Absent: Jason, Dees, D.O.; Laura Gray, M.D.; Vickie Veazey, R. Ph

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, Pharm D., DOM DUR Coordinator; Terri Kirby, R.Ph., DOM Clinical Pharmacist;
HID Staff: Ashleigh Holeman, Pharm D., Project Manager; Leslie Leon, Pharm D., Clinical Pharmacist; Kathleen Burns, R.N., Call Center Manager

Call to Order: Dr. Mark Reed, Chairman of the Board, called the meeting to order at 2:03 p.m. Dr. Reed asked for a motion to accept the minutes from the meeting of February 18, 2010. Dr. Paul Read made a motion to accept the minutes with a second from Dr. Bastian. All voted in favor of the motion.

Dr. Reed continued the meeting by moving into the cost management analysis under the direction of Dr. Holeman.

Cost Management Analysis:
Dr. Holeman began the presentation with the Top 15 Therapeutic Classes by total cost of claims dating December 2009 thru February 2010. This report remains constant with Antipsychotic Agents leading the top therapeutic classes. The Top 25 Drugs based on the number of claims for these same dates remains consistent with hydrocodone-acetaminophen, azithromycin and amoxicillin as the highest utilized medications through the Mississippi Medicaid pharmacy benefit. The Top 25 Drugs based on total claims costs report varied slightly with Singulair®, Abilify® and Synagis® in the top three positions for the time period analyzed.

Pharmacy Program Update:
Ms. Clark began by noting several upcoming changes with the DOM pharmacy program. The newest PDL will be introduced on July 1, 2010 with several changes. It was noted that on the alphabetical hand-out to the Board that the preferred Brands were listed with notations of highlighted additions and deletions from the preferred list. This was made available to providers throughout the state by DOM to alert them of the upcoming pharmacy program changes. Ms. Clark also noted several generics that would no longer be preferred which might cause some confusion for providers. These changes were carefully scrutinized by DOM to manage the costs to the program without compromising the care of the beneficiary. She continued that there would not be “grandfathering” for the PPI therapeutic class or the short-acting beta-agonist inhalers. Dr. Reed questioned the reason for Prevacid® Solutabs as preferred products as opposed to the Prevacid® capsules or the generic equilivent product. Ms. Clark reminded the Board that the

majority of the Medicaid beneficiaries are now under the age of 21. Prevacid® Solutabs met the needs of this age group. In the therapeutic class of growth hormones, Ms. Clark stated that there would be a consideration for stable therapy. If the beneficiary has been non- compliant with the non-preferred agent, they will be required to restart treatment with a preferred agent. The antiemetic agent ondansetron will be open for all beneficiaries, with the oral tablets being the preferred formulation. The only carve-out would be for beneficiaries under age 11, for whom the ondansetron ODT will be approved. This medication will still have the set quantity limits of 12 tablets/units per 30 days. Once again, Ms Clark reminded the Board that DOM does cover the acne products for beneficiaries under age 21. The confusion at the pharmacy point of sale is that not all generics are covered. This then causes more confusion to the physician when he receives a call from the pharmacist to submit a prior authorization. Ms.Clark referred the Board to the PDL where they could find the preferred agents in this therapeutic class.

New Business:

Duplicate Atypical Antipsychotic Therapy in Pediatric Beneficiaries:
At the February meeting the DUR Board asked HID to present data regarding duplicate therapy with multiple agents in this therapeutic class. Dr. Holeman presented a table noting the duration of duplicate therapy with more than one atypical antipsychotic for beneficiaries < 21 years old with the beneficiary count and percentage. A total of 7,308 beneficiaries < 21 years old received an atypical antipsychotic in 2009. Of these, 3.6% (262) were on duplicate therapy for 30 days, 2.3 %(165) were on duplicate therapy for 60 days, 1.4 %(105) received duplicate therapy for 90 days and 1% (74) were on duplicate therapy with two or more atypical antipsychotics for 120 days. The overall incidence of duplicate therapy appears to be minimal, based on these results. However, when considering the potential metabolic and extra pyramidal effects, in conjunction with expert opinions, the implementation of duplicate therapy edits may need to be considered.
Recommendation: HID recommended establishing edits at the point of sale that prohibit duplicate therapy with two or more atypical antipsychotics in pediatric beneficiaries. The edit would cause claims at the point of sale to deny when beneficiaries less than 18 years old receive more than one atypical antipsychotic within a specified time frame and can be overridden with a prior authorization request providing medical justification for requested therapy.
Dr. Donahoe questioned the support for duplicate therapy. Dr. Holeman stated that there was no support found for this duplication of therapy. It was the consensus of the Board to have HID present data at the next meeting on the usage of low-dose therapy of atypical antipsychotics. Dr. Donahoe motioned that duplicate therapy be denied at point of sale with the option of a prior authorization when medically justified by the prescriber. This motion was seconded by Dr. Strong. All voted in favor of the motion.
Attention Deficit Hyperactivity Disorder: A Medicaid Prescribing Update
The Board had requested that HID develop a Medicaid Prescribing Update that would outline recommendations from clinical guidelines regarding the proper evaluation and diagnosis of children for ADHD. The rationale provided for the development of such a document was to provide prescribers with a concise and accurate reference that could be used when evaluating children for possible ADHD, particularly those providers with little

or no formal training or education in the disorder. This update was presented to the Board for discussion and review. Dr. Donahoe suggested adding the Vanderbilt questionnaire to the back of this to facilitate the physician's review. HID will inquire about needed permission to add this document to the Medicaid Prescribing Update prior to the distribution by the Academic Detailers to the medical community. Dr. Holeman also noted that beginning 7/15/2010, Medicaid will implement quantity limits for the ADHD therapeutic class. This will require a physician to request an override through HID when prescribing more than the allowable quantity by Medicaid.

Long-Acting Injectable Antipsychotic Use in Long-Term Care Settings

Injectable antipsychotic formulations are divided into two groups: short-acting and long-acting. LTC beneficiaries are not required to have a prior authorization for the long-acting injectable antipsychotics, which is in contrast to the prior authorization requirement for these agents for all other beneficiaries. Dr. Holeman presented an analysis noting that there were 248 pharmacy claims for LTC residents totaling $132,926.91 for long-acting injectable antipsychotics. Long –acting injectable antipsychotic injections typically have been reserved for the most difficult patients where non-adherence to oral medication has been identified as a primary obstacle. Concerns have been raised over the need for long acting injectable antipsychotic medications in a LTC setting when beneficiaries live in a controlled environment where medication administration is supervised. The Board requested a cost comparison of oral antipsychotic therapy versus long-acting injectable antipsychotic therapy, to determine if shifting therapy to the oral agents would be a cost-efficient endeavor for Medicaid. The Board also requested a report identifying those beneficiaries receiving concurrent therapy with oral and long-acting injectable antipsychotic therapy, as well as the LTC facilities where the long-acting injectable antipsychotics are being used. These reports will be presented at the August meeting for further Board review before a decision is made to require prior authorizations for the long- acting injectable antipsychotics in LTC beneficiaries.

The Role of Lipotropics in the Treatment of Cardiovascular Disease

During the March 2010 Pharmacy and Therapeutics (P&T) meeting, there were discussions about non-statin lipotropics. Although the non-statin lipotropics have not been proven to reduce morbidity and mortality related to cardiovascular disease, prescribers often times use these agents based on data illustrating their LDL-lowering effects without regard to the lack of data for risk reduction of cardiovascular events. There seems to be a false sense of protection of the patient's wellbeing for both the prescriber and the patient. Based on this concern, the P&T Committee and DOM requested that the DUR Board review the utilization of this class to determine if the non-statin lipotropics are being used appropriately. The Committee also requested that the DUR Board determine what steps may be necessary to encourage appropriate use and improve outcomes for the Medicaid beneficiaries. The P&T Committee outlined two particular areas that should be addressed:

1. Are beneficiaries being given a trial of a statin prior to attempting treatment with a non-statin lipotropic?

The ATPIII Final Report from the National Heart lung and Blood Institute supports the use of statins as first-line therapy for LDL-reduction based on results from 5 large clinical trials. These trials showed a documented decrease in cardiovascular disease and

total mortality as well as reductions in myocardial infarctions, revascularization procedures, stroke and peripheral vascular disease across all genders and ages with statin therapy. The P&T Committee agrees that statins should be the first line of treatment for beneficiaries with elevated cholesterol. Of the 1609 beneficiaries receiving non-statin lipotropics from 07/01/2009 – 12/31/2009, 518 (32%) received a statin in the prior 6 months. This indicates that a majority of beneficiaries were not given a trial of a statin prior to initiating therapy with the other lipotropics.

2. Of those beneficiaries being treated with a non-statin lipotropic, how many have a hypertriglyceridemia diagnosis?

According to the ATPIII Final Report, statins should be used as first-line treatment for LDL reduction in patients with hypertriglyceridemia, with the addition of nicotinic acid or fibrates for triglyceride reduction. In the absence of elevated LDL, the ATPIII Final Report does recommend the use of fibrates or nicotinic acid as first-line therapy to lower triglyceride levels. HID analyzed the data of the non-statin lipotropics to determine what percentage of utilization could be credited to a hypertriglyceridemia diagnosis. Only 35% of the beneficiaries receiving a non-statin lipotropic had a documented diagnosis of elevated triglycerides in the six-month period reviewed. Based on this data, it appears that the P&T Committee concerns are appropriate that the utilization of these agents cannot be attributed to a hypertriglyceridemia diagnosis.

After Board discussion on the HID analysis the following recommendation was presented:

Dr. Donahoe recommended a point of sale denial for a non-statin lipotropic if pharmacy claims fail to indicate a trial of a statin in the last 6 months. This motion also included the allowance of approval for non-statin lipotropics in the presence of a hypertriglyceridemia diagnosis. Dr. Donahoe continued that this motion should exclude bile acid sequestrants which are commonly and appropriately used for other indications. This motion was seconded by Dr. Frank Wade and all voted in favor of the motion.

ACEIs vs. ARBS: Appropriate Place in Treatment of Cardiovascular Disease

At the April Pharmacy and Therapeutics Committee meeting, questions were raised regarding the relative efficacy of ACEIs and ARBs. Specifically, it was noted that current literature does not indicate that the more expensive ARBs are more beneficial than the cheaper ACEI in the treatment of hypertension and heart disease. Additionally, treatment guidelines such as the JNC7 report and the ACC/AHA Heart Failure guidelines both recommend ACEI as the primary therapy over ARBs. DOM asked HID to review the utilization data for these agents to determine what percentage of Medicaid beneficiaries received an ACEI before starting treatment with an ARB.

From 7/1/2009 thru 12/31/2009, 7,050 beneficiaries received an ARB through the Mississippi Medicaid pharmacy benefit program. Of these beneficiaries, 899 (13%) received an ACEI in the six months prior to this search. From this data, it appears that an overwhelming majority of the beneficiaries being treated with an ARB for hypertension and/or heart disease have not been managed based on current treatment guidelines and medical literature. The P&T Committee members recommended that Mississippi Medicaid require beneficiaries to attempt and fail treatment with an ACEI before starting therapy with an ARB. The P& T Committee asked that the DUR Board determine the necessary measures to promote appropriate use of ARBs in the Mississippi Medicaid

population. Dr. Paul Read made a motion to require a trial of an ACEI before granting approval of an ARB for Mississippi Medicaid beneficiaries. He also included in his motion to allow stable therapy for those beneficiaries currently being treated with an ARB. Dr. Donahoe seconded the motion and all voted in favor of this motion.

Other Criteria Recommendations

Dr. Reed asked for the Board to accept the proposed RDUR criteria recommendations as a block vote. All voted in favor of the motion

FDA Updates:

Dr. Holeman asked if there were any questions in regard to the submitted FDA updates. No questions were raised.

Dr. Reed called for the meeting to be adjourned at 3:35 p.m. The next meeting will be held at 2:00 p.m. on August 19, 2010.

Respectfully Submitted,
Health Information Designs, Inc.

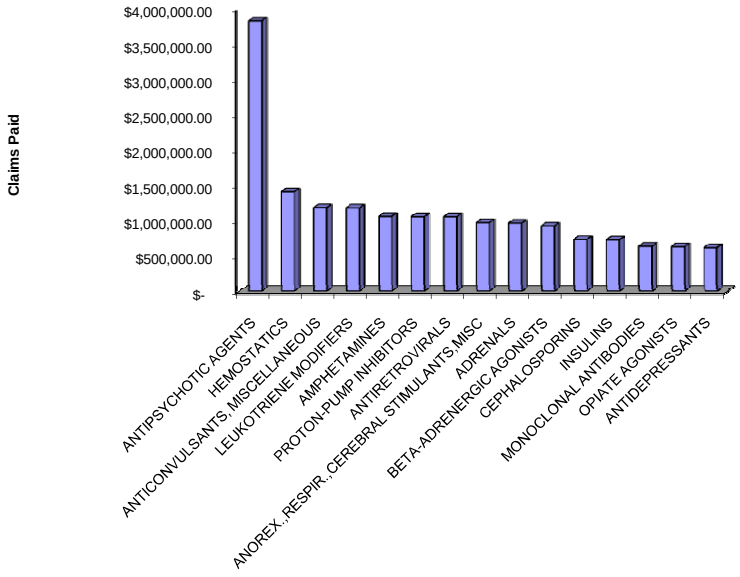
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 03/01/10-03/31/10

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	12,338	$ 3,821,911.29	$ 309.77	2.69%
HEMOSTATICS	64	$ 1,412,227.52	$22,066.06	0.01%
ANTICONVULSANTS, MISCELLANEOUS	13,521	$ 1,186,819.70	$ 87.78	2.95%
LEUKOTRIENE MODIFIERS	9,454	$ 1,182,612.68	$ 125.09	2.06%
AMPHETAMINES	6,920	$ 1,063,374.52	$ 153.67	1.51%
PROTON-PUMP INHIBITORS	8,782	$ 1,059,551.26	$ 120.65	1.91%
ANTIRETROVIRALS	1,286	$ 1,059,456.78	$ 823.84	0.28%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,823	$ 976,351.12	$ 143.10	1.49%
ADRENALS	13,319	$ 970,171.43	$ 72.84	2.90%
BETA-ADRENERGIC AGONISTS	15,152	$ 928,763.13	$ 61.30	3.30%
CEPHALOSPORINS	12,926	$ 739,199.14	$ 57.19	2.82%
INSULINS	4,172	$ 734,985.62	$ 176.17	0.91%
MONOCLONAL ANTIBODIES	409	$ 643,795.03	$ 1,574.07	0.09%
OPIATE AGONISTS	30,133	$ 636,820.90	$ 21.13	6.57%
ANTIDEPRESSANTS	15,725	$ 622,561.73	$ 39.59	3.43%
TOTAL TOP 15	151,024	$ 17,038,601.85	$ 112.82	32.92%

Total Rx Claims	458,824
From 03/01/10-03/31/10	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



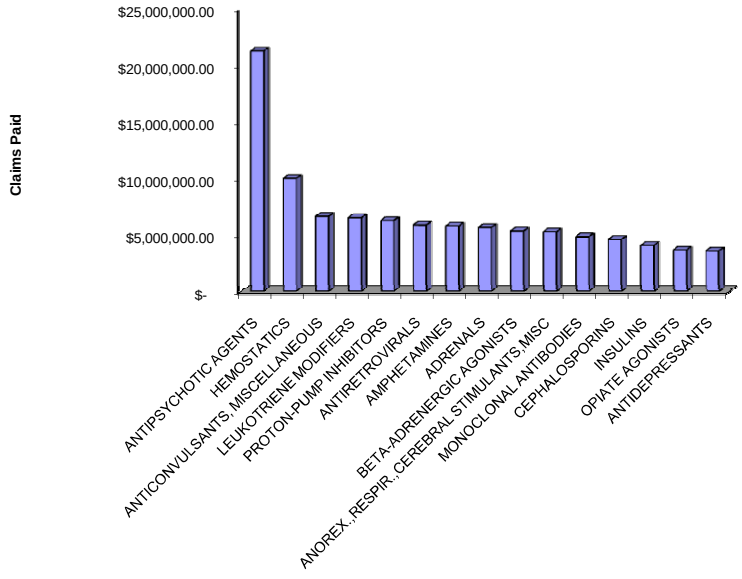
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 04/01/10-04/30/10

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	69,630	$ 21,235,339.13	$ 304.97	15.18%
HEMOSTATICS	330	$ 9,998,524.71	$30,298.56	0.07%
ANTICONVULSANTS, MISCELLANEOUS	77,471	$ 6,661,294.32	$ 85.98	16.88%
LEUKOTRIENE MODIFIERS	54,019	$ 6,546,706.62	$ 121.19	11.77%
PROTON-PUMP INHIBITORS	49,916	$ 6,297,008.81	$ 126.15	10.88%
ANTIRETROVIRALS	7,268	$ 5,896,438.19	$ 811.29	1.58%
AMPHETAMINES	38,999	$ 5,808,183.81	$ 148.93	8.50%
ADRENALS	78,882	$ 5,667,913.40	$ 71.85	17.19%
BETA-ADRENERGIC AGONISTS	90,619	$ 5,370,715.42	$ 59.27	19.75%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	37,702	$ 5,289,804.86	$ 140.31	8.22%
MONOCLONAL ANTIBODIES	3,048	$ 4,847,854.65	$ 1,590.50	0.66%
CEPHALOSPORINS	79,689	$ 4,622,085.44	$ 58.00	17.37%
INSULINS	23,948	$ 4,106,600.03	$ 171.48	5.22%
OPIATE AGONISTS	172,881	$ 3,680,892.62	$ 21.29	37.68%
ANTIDEPRESSANTS	90,852	$ 3,605,873.49	$ 39.69	19.80%
TOTAL TOP 15	875,254	$ 99,635,235.50	$ 113.84	190.76%

Total Rx Claims	458,824
From 04/01/10-04/30/10	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



Health Information Designs, Inc.
6/23/2010

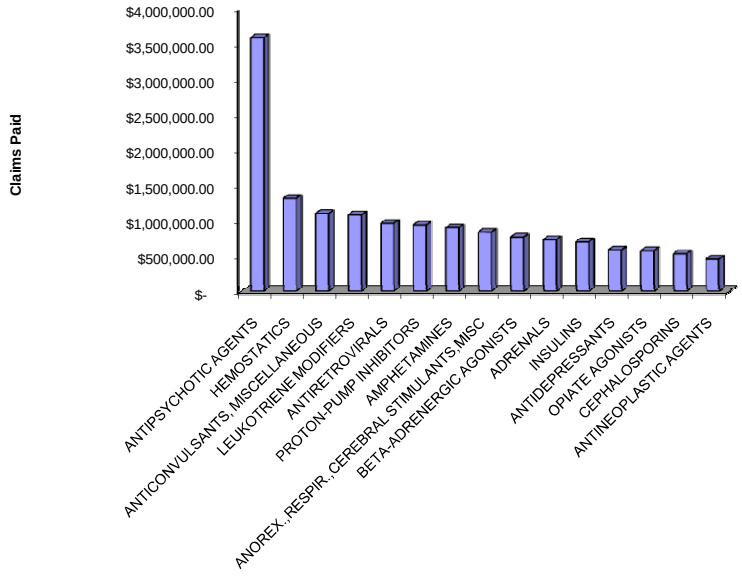
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 05/01/10-05/31/10

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	11,399	$ 3,585,106.77	$ 314.51	2.92%
HEMOSTATICS	55	$ 1,318,871.70	$23,979.49	0.01%
ANTICONVULSANTS, MISCELLANEOUS	12,670	$ 1,104,772.95	$ 87.20	3.25%
LEUKOTRIENE MODIFIERS	8,666	$ 1,084,841.57	$ 125.18	2.22%
ANTIRETROVIRALS	1,154	$ 967,586.01	$ 838.46	0.30%
PROTON-PUMP INHIBITORS	7,952	$ 944,967.87	$ 118.83	2.04%
AMPHETAMINES	5,947	$ 905,497.11	$ 152.26	1.52%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,746	$ 840,840.46	$ 146.33	1.47%
BETA-ADRENERGIC AGONISTS	11,863	$ 772,076.92	$ 65.08	3.04%
ADRENALS	10,669	$ 736,402.83	$ 69.02	2.73%
INSULINS	3,932	$ 707,498.75	$ 179.93	1.01%
ANTIDEPRESSANTS	14,563	$ 588,177.98	$ 40.39	3.73%
OPIATE AGONISTS	27,593	$ 579,667.15	$ 21.01	7.07%
CEPHALOSPORINS	9,791	$ 536,291.93	$ 54.77	2.51%
ANTINEOPLASTIC AGENTS	891	$ 461,830.84	$ 518.33	0.23%
TOTAL TOP 15	132,891	$ 15,134,430.84	$ 113.89	34.04%

Total Rx Claims	390,379
From 05/01/10-05/31/10	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

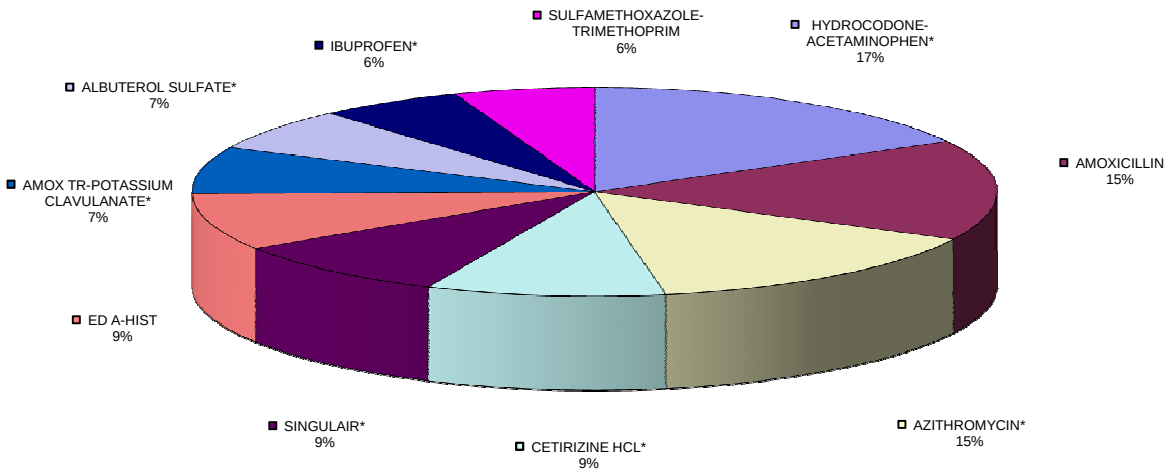
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 03/01/10-03/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	17,620	$ 252,546.47	1
AMOXICILLIN	PENICILLINS	16,103	$ 150,138.48	5
AZITHROMYCIN*	MACROLIDES	15,168	$ 449,293.30	6
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	9,932	$ 246,440.38	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	9,444	$ 1,181,600.27	4
ED A-HIST	PROPYLAMINE DERIVATIVES	9,152	$ 73,374.57	~
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	7,539	$ 384,201.17	32
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	6,837	$ 220,260.23	67
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	6,021	$ 47,523.28	18
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,833	$ 72,354.82	39
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	5,056	$ 55,866.99	59
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,889	$ 34,415.72	8
CEFDINIR	CEPHALOSPORINS	4,833	$ 357,501.81	68
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	4,367	$ 32,887.63	24
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,867	$ 376,985.21	140
CEPHALEXIN*	CEPHALOSPORINS	3,767	$ 55,266.44	22
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,539	$ 29,425.22	43
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	3,479	$ 154,975.66	14
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,090	$ 507,707.84	34
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	3,079	$ 21,160.07	~
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,978	$ 53,769.76	50
VYVANSE*	AMPHETAMINES	2,877	$ 391,645.23	97
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,877	$ 13,377.89	2
OMEPRAZOLE*	PROTON-PUMP INHIBITORS	2,863	$ 168,171.47	15
ADDERALL XR*	AMPHETAMINES	2,825	$ 597,269.91	30
TOTAL TOP 25		158,035	$ 5,928,159.82	

Total Rx Claims From 03/01/10-03/31/10	458,824

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

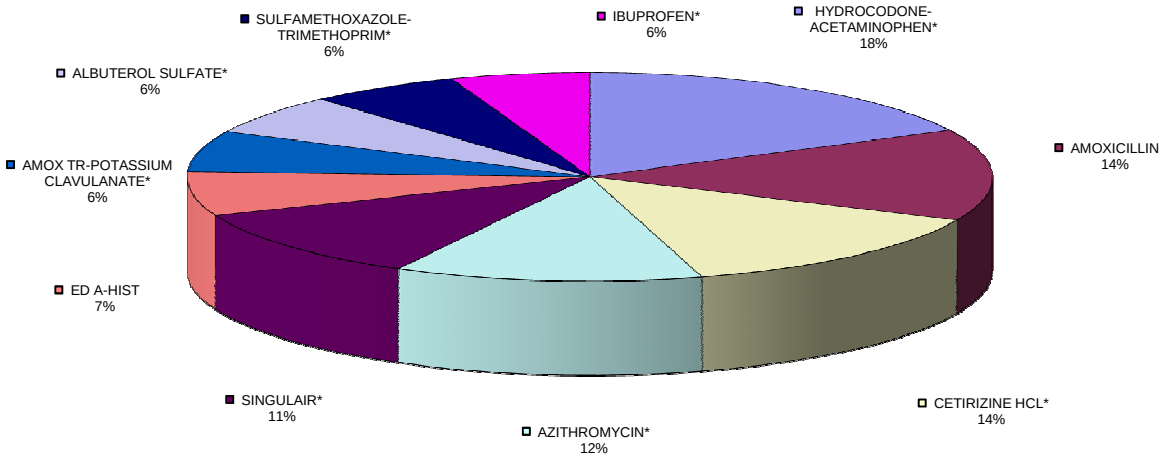
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/10-04/30/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	16,954	$ 246,628.87	1
AMOXICILLIN	PENICILLINS	13,621	$ 125,998.83	5
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	13,138	$ 332,853.47	~
AZITHROMYCIN*	MACROLIDES	11,849	$ 350,649.39	6
SINGULAIR*	LEUKOTRIENE MODIFIERS	10,650	$ 1,334,437.04	4
ED A-HIST	PROPYLAMINE DERIVATIVES	6,555	$ 55,822.41	~
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	6,083	$ 309,704.35	32
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	5,993	$ 200,247.11	67
SULFAMETHOXAZOLE-TRIMETHOPRIM*	SULFONAMIDES (SYSTEMIC)	5,853	$ 74,028.64	39
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,340	$ 40,864.25	18
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,899	$ 34,367.22	8
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	4,194	$ 32,340.10	24
CEFDINIR	CEPHALOSPORINS	4,021	$ 301,497.28	68
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,704	$ 355,087.60	140
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	3,517	$ 156,938.73	14
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,509	$ 29,002.29	43
CEPHALEXIN*	CEPHALOSPORINS	3,442	$ 50,324.88	22
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,321	$ 38,818.72	59
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	3,084	$ 21,182.24	~
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,017	$ 505,946.94	34
VYVANSE*	AMPHETAMINES	2,994	$ 407,952.93	97
FLUTICASONE PROPIONATE*	ANTI-INFLAMMATORY AGENTS (SKIN & MUCOUS)	2,907	$ 141,568.93	36
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,891	$ 13,639.76	2
OMEPRAZOLE*	PROTON-PUMP INHIBITORS	2,875	$ 167,166.48	15
ADDERALL XR*	AMPHETAMINES	2,784	$ 588,609.46	30
TOTAL TOP 25		147,195	$ 5,915,677.92	

Total Rx Claims From 04/01/10-04/30/10	458,824

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

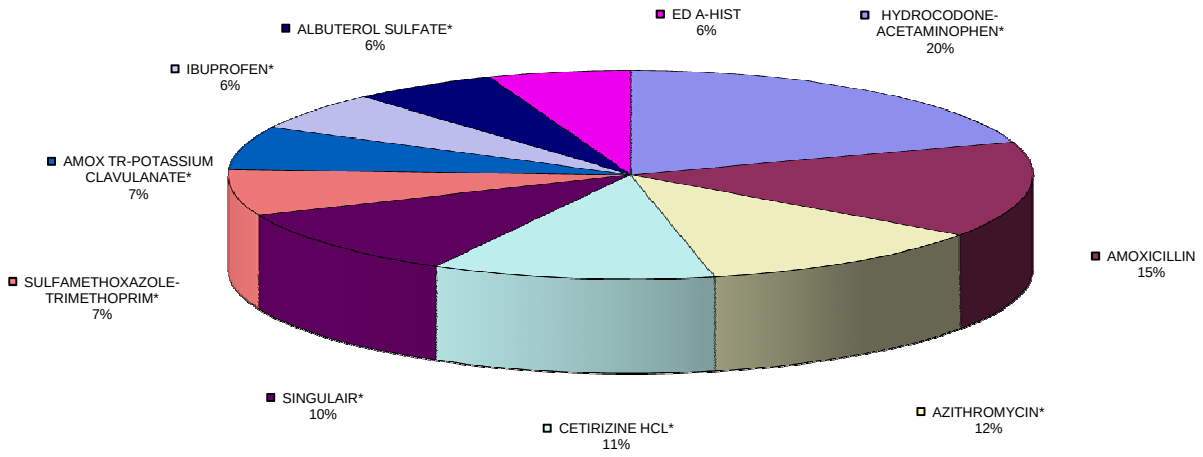
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 05/01/10-05/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	16,154	$ 232,099.80	1
AMOXICILLIN	PENICILLINS	12,068	$ 110,376.66	5
AZITHROMYCIN*	MACROLIDES	9,640	$ 291,675.23	6
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	9,196	$ 236,026.29	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,656	$ 1,083,301.32	4
SULFAMETHOXAZOLE-TRIMETHOPRIM*	SULFONAMIDES (SYSTEMIC)	5,796	$ 73,405.50	39
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	5,430	$ 274,746.96	32
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,847	$ 37,993.16	18
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	4,741	$ 153,894.46	67
ED A-HIST	PROPYLAMINE DERIVATIVES	4,620	$ 38,548.19	~
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,589	$ 32,132.56	8
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	4,021	$ 31,310.03	24
CEFDINIR	CEPHALOSPORINS	3,690	$ 267,257.53	68
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,495	$ 334,681.16	140
CEPHALEXIN*	CEPHALOSPORINS	3,117	$ 46,278.89	22
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,076	$ 25,331.72	43
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	2,892	$ 129,545.30	14
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,884	$ 33,773.86	59
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	2,830	$ 19,518.24	~
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,749	$ 104,352.47	107
OMEPRAZOLE*	PROTON-PUMP INHIBITORS	2,708	$ 161,556.71	15
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,703	$ 13,061.39	2
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,646	$ 443,937.08	34
NYSTATIN*	POLYENES	2,620	$ 32,356.67	142
CITALOPRAM HBR*	ANTIDEPRESSANTS	2,590	$ 19,225.41	25
TOTAL TOP 25		127,758	$ 4,226,386.59	

Total Rx Claims From 05/01/10-05/31/10	390,379

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

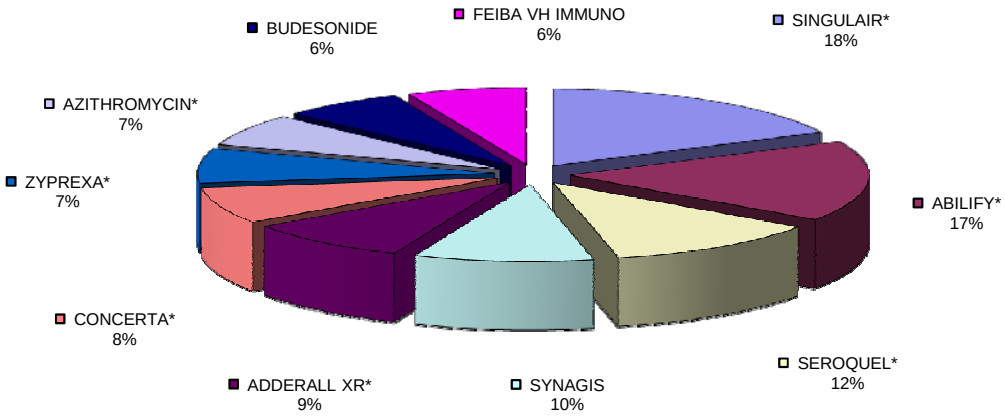
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 03/01/10-03/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	9,444	$ 1,181,600.27	7
ABILIFY*	ANTIPSYCHOTIC AGENTS	2,115	$ 1,122,770.58	12
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,904	$ 778,957.42	6
SYNAGIS	MONOCLONAL ANTIBODIES	409	$ 643,795.03	~
ADDERALL XR*	AMPHETAMINES	2,825	$ 597,269.91	23
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL	3,090	$ 507,707.84	33
ZYPREXA*	ANTIPSYCHOTIC AGENTS	757	$ 478,531.34	15
AZITHROMYCIN*	MACROLIDES	15,168	$ 449,293.30	3
BUDESONIDE	ADRENALS	1,691	$ 438,159.06	~
FEIBA VH IMMUNO	HEMOSTATICS	7	$ 425,963.15	~
PREVACID*	PROTON-PUMP INHIBITORS	2,402	$ 413,017.44	5
VYVANSE*	AMPHETAMINES	2,877	$ 391,645.23	96
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	7,539	$ 384,201.17	10
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,867	$ 376,985.21	24
HUMATE-P	HEMOSTATICS	10	$ 364,908.23	~
CEFDINIR	CEPHALOSPORINS	4,833	$ 357,501.81	17
GEODON*	ANTIPSYCHOTIC AGENTS	795	$ 354,595.42	45
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,670	$ 345,193.93	4
LANSOPRAZOLE*	PROTON-PUMP INHIBITORS	2,450	$ 327,668.51	~
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL	2,041	$ 298,546.35	113
ATRIPLA	ANTIRETROVIRALS	184	$ 280,082.47	39
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,599	$ 260,549.82	3
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	17,620	$ 252,546.47	1
EXJADE	HEAVY METAL ANTAGONISTS	50	$ 252,093.85	~
CETIRIZINE HCL*	SECOND GENERATION	9,932	$ 246,440.38	~
TOTAL TOP 25		95,279	$ 11,530,024.19	

Total Rx Claims	458,824
From 03/01/10-03/31/10	

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

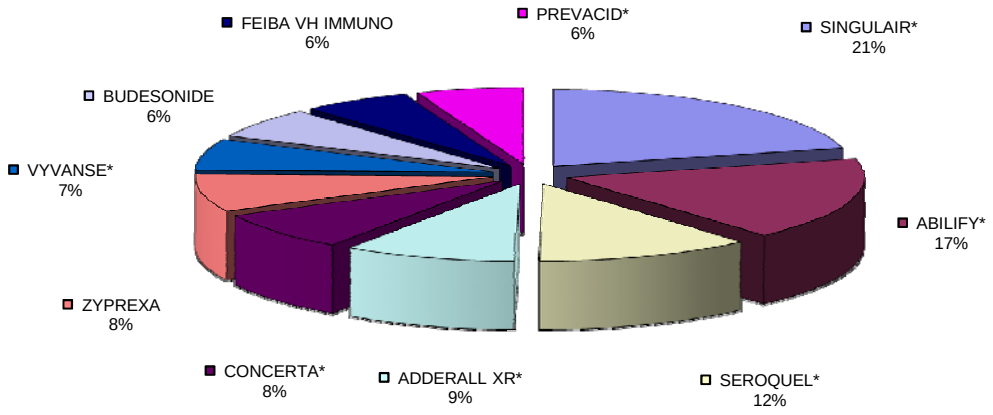
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/10-04/30/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	10,650	$ 1,334,437.04	7
ABILIFY*	ANTIPSYCHOTIC AGENTS	2,044	$ 1,089,990.98	12
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,806	$ 737,782.92	6
ADDERALL XR*	AMPHETAMINES	2,784	$ 588,609.46	23
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULA	3,017	$ 505,946.94	33
ZYPREXA	ANTIPSYCHOTIC AGENTS	767	$ 494,862.86	15
VYVANSE*	AMPHETAMINES	2,994	$ 407,952.93	96
BUDESONIDE	ADRENALS	1,560	$ 401,322.03	~
FEIBA VH IMMUNO	HEMOSTATICS	5	$ 373,734.27	~
PREVACID*	PROTON-PUMP INHIBITORS	2,076	$ 364,599.22	5
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,726	$ 355,090.65	4
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,704	$ 355,087.60	24
AZITHROMYCIN*	MACROLIDES	11,849	$ 350,649.39	3
LANSOPRAZOLE*	PROTON-PUMP INHIBITORS	2,541	$ 339,500.26	~
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINE	13,138	$ 332,853.47	~
GEODON*	ANTIPSYCHOTIC AGENTS	737	$ 325,931.58	45
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	6,083	$ 309,704.35	10
CEFDINIR	CEPHALOSPORINS	4,021	$ 301,497.28	17
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULA	2,015	$ 293,785.05	113
PLAVIX*	PLATELET-AGGREGATION	1,631	$ 266,421.20	3
ATRIPLA	ANTIRETROVIRALS	168	$ 262,085.84	39
EXJADE	HEAVY METAL ANTAGONISTS	50	$ 251,239.51	~
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	16,954	$ 246,628.87	1
NASONEX*	CORTICOSTEROIDS (EENT)	2,504	$ 244,196.47	42
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,767	$ 211,999.30	1
TOTAL TOP 25		96,591	$ 10,745,909.47	

Total Rx Claims	458,824
From 04/01/10-04/30/10	

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

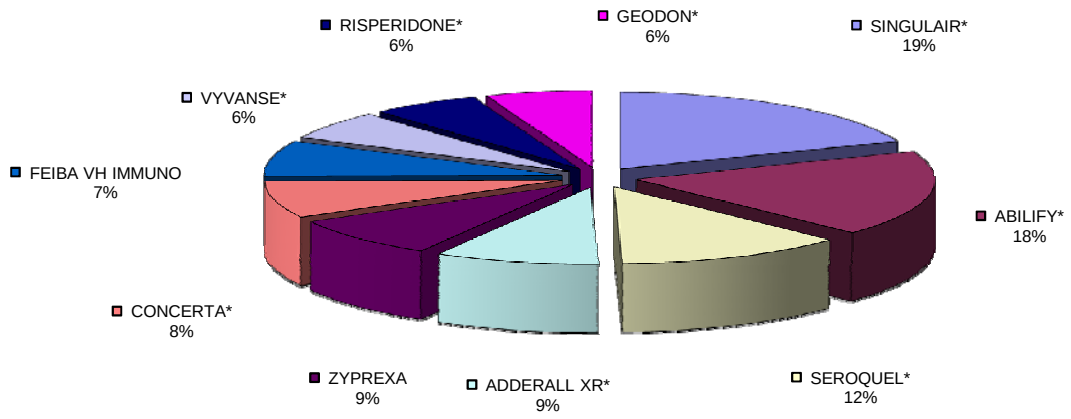
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 05/01/10-05/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,656	$ 1,083,301.32	7
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,935	$ 1,019,596.89	12
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,700	$ 700,220.92	6
ADDERALL XR*	AMPHETAMINES	2,374	$ 502,049.16	23
ZYPREXA	ANTIPSYCHOTIC AGENTS	743	$ 484,956.26	15
CONCERTA*	STIMULANTS,MISC	2,646	$ 443,937.08	33
FEIBA VH IMMUNO	HEMOSTATICS	6	$ 418,432.69	~
VYVANSE*	AMPHETAMINES	2,532	$ 343,492.70	96
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,495	$ 334,681.16	24
GEODON*	ANTIPSYCHOTIC AGENTS	729	$ 327,083.96	45
BUDESONIDE	ADRENALS	1,285	$ 325,756.85	~
LANSOPRAZOLE*	PROTON-PUMP INHIBITORS	2,435	$ 325,109.36	~
PREVACID*	PROTON-PUMP INHIBITORS	1,823	$ 322,217.71	5
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,491	$ 307,937.79	4
AZITHROMYCIN*	MACROLIDES	9,640	$ 291,675.23	3
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	5,430	$ 274,746.96	10
CEFDINIR	CEPHALOSPORINS	3,690	$ 267,257.53	17
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULA	1,754	$ 256,209.85	113
ATRIPLA	ANTIRETROVIRALS	159	$ 248,997.62	39
PLAVIX*	PLATELET-AGGREGATION	1,504	$ 245,141.05	3
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINE	9,196	$ 236,026.29	~
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	16,154	$ 232,099.80	1
EXJADE	HEAVY METAL ANTAGONISTS	45	$ 230,970.58	~
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,644	$ 197,654.03	1
FEIBA NF	HEMOSTATICS	4	$ 192,100.74	~
TOTAL TOP 25		81,070	$ 9,611,653.53	

Total Rx Claims From 05/01/10-05/31/10	390,379

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



Long-Acting Injectable Antipsychotic Use in Long-Term Care Settings

Injectable antipsychotic formulations can be divided into two groups based on their pharmacokinetic features: short-acting and long-acting or depot preparations. Short-acting formulations are used for acute psychotic episodes, whereas long-acting antipsychotics are primarily used as maintenance therapy to guarantee compliance and eliminate bioavailability issues related to absorption and metabolism.

Residents of long-term care (LTC) settings are provided assistance with activities of daily living and instrumental activities of daily living, such as medication management. By law, Mississippi Medicaid beneficiaries are limited to five prescriptions per month, and prior authorization is required for all long-acting injectable antipsychotic medications. LTC beneficiaries are exempt from monthly prescription drug limits and currently do not require prior authorization for the use of long-acting injectable antipsychotics.

HID conducted a claims analysis for the 2009 calendar year on the utilization of long-acting injectable antipsychotic medications in LTC beneficiaries. There were a total of 248 claims for 33 beneficiaries, leading to a total cost of $132,926.91 for the Division of Medicaid. The results of the analysis are provided below.

Drug Name	Rx Num	Total DOM Cost
FLUPHENAZINE DECANOATE	45	$2,743.74
HALDOL DECANOATE	9	$604.55
INVEGA SUSTENNA	5	$6,328.31
RISPERDAL CONSTA	189	$123,250.31
Totals	248	$132,926.91

There are several explanations as to the need of long-acting injectable antipsychotic medications in this community setting. Nonadherence to oral antipsychotic medication is one of the most significant clinical challenges in mental healthcare. Long-acting injectable antipsychotics have typically been reserved for the most difficult patients where nonadherence to oral medication has been identified as a primary obstacle. Other advantages of long-acting antipsychotic injections over oral medications include guaranteed delivery of medication, reliable monitoring of treatment adherence, increased opportunities to intervene as soon as a dose is missed, and reduction in hospitalizations due to relapse or suicide attempts. Significant issues within the LTC environment itself may be low nurse-to-resident ratio and time requirements for medication administration. Although medication administration may seem to be a simple nursing task, the combination of polypharmacy and medical complexity in this patient population presents challenges in itself. Cognitive, behavioral, or swallowing problems may complicate the direct administration of a single medication. These are all common problems in the LTC population.

Conclusion

Concerns have been raised over the need for long-acting injectable antipsychotic medications in a LTC setting when beneficiaries live in a controlled environment where medication administration is supervised. However, leaving a limited nursing staff responsible for the care and safety of a large number of highly vulnerable and complex patients, especially those with medication management problems, increases the risk of missed doses of oral medication. Clinical research indicates that nonadherence with oral antipsychotic medications is the most common reason for initiating long-acting injections. DOM seeks the DUR Board's counsel regarding whether long-acting injectable antipsychotic medications for long-term care beneficiaries should require prior authorization.

Addendum

After this report was presented to the DUR Board at the May 2010 meeting, members requested cost-comparison information for the long-acting injectable antipsychotics and the oral atypical antipsychotics. Members wanted to know if required prior authorization for long-term care beneficiaries would result in a cost savings for DOM. HID reviewed the claims data from a cost perspective and the results are included in the table below.

	LA INJ PSY	PO PSY
Claims	38	3412
Cost	$22,450.27	$1,260,327.35
Cost/Claim	$590.80	$369.38
Savings/Rx switched from INJ to PO		$221.42
Total Beneficiaries ID'd		33
Total Potential Savings		$7,306.86
Total Potential Annual Savings		$87,682.32

If all of the beneficiaries identified in the earlier report (33) were switched from a long-acting injectable antipsychotic to an oral atypical antipsychotic, the Division of Medicaid would realize an estimated cost savings of $7,306.72 per month or nearly $88,000 annually.

Evaluating Ondansetron Quantity Limits

On November 1, 2005 the Division of Medicaid implemented quantity limits for Zofran® (ondansetron) products. These limits were put into place as an attempt to prevent overuse for non-approved indications such as gastroenteritis and nausea and vomiting due to pregnancy. At the time the limits were put in place, ondansetron products were available as branded products only and were quite costly. These limits are still in place, with beneficiaries allowed 12 tablets or 100mL per every 31 days. The only exception to this limit is for Zofran® 24mg tablets, which have a limit of 5 tablets per every 31 days. Prescribers have the option to submit a Maximum Unit Override request for those beneficiaries whom they feel require more than the quantity allowed by these limits.

It was mentioned at the April P&T Committee meeting that the University of Mississippi Medical Center has recently changed its protocol from using promethazine IM to ondansetron IM for nausea and vomiting of any cause due to serious tissue injury associated with the promethazine injection. In September 2009, the FDA required the manufacturers of parenteral promethazine to include a boxed warning emphasizing the established risk of severe tissue damage associated with intravenous administration of promethazine. Based on this warning, the preferred route of administration is deep intramuscular injection. Inadvertent intra-arterial or subcutaneous injection of the dug is likely to result in major adverse reactions ranging from burning, irritation, and pain to tissue necrosis and gangrene in the affected extremity. Some reported injuries have even resulted in amputation of the affected extremity.

Additionally, it has been noticed with the recent occurrence of several gastrointestinal stomach viruses being transmitted rapidly within the metro area that many prescribers are issuing ondansetron prescriptions for nausea and vomiting rather than promethazine or other antiemetics. DOM asked HID to analyze claims data for ondansetron and promethazine and compare the utilization based on diagnoses. HID gathered claims data for the six-month period from 10/1/09 – 3/31/10. A summary of the findings is provided below.

	Ondansetron		Promethazine	
Diagnosis	Claims	Beneficiaries	Claims	Beneficiaries
Enteritis	3,075 (53%)	2,799 (54%)	17,758 (56%)	14,429 (57%)
Pregnancy	1,757 (30%)	1,405 (27%)	4,190 (13%)	3,091 (12%)
All Diagnoses	5,790	5,189	31,577	25,469

For both ondansetron and promethazine, over 50% of the utilization during the six months reviewed could be attributed to a gastroenteritis diagnosis. Additionally, from the data gathered, it appears that providers are more comfortable using ondansetron for nausea and vomiting due to pregnancy than promethazine, with 30% of claims for ondansetron versus 13% of promethazine claims possibly credited to a pregnancy diagnosis. Conversely, HID also looked at the ondansetron claims that could be the result of chemotherapy or radiation treatment. From 10/1/09 – 3/31/10, only 138 claims (2%) for ondansetron were found in the presence of a chemotherapy or radiation diagnosis.

As mentioned above, one of the reasons provided for implementing the quantity limits for ondansetron products in November 2005 was cost of the products. As such, HID conducted a cost analysis of the ondansetron products for the six-month period assessed and compared it to the same six-month period surrounding the implementation of the ondansetron quantity limits. The results are provided in the chart below.

Drug	Cost/Rx (Current)	Cost/Rx (Previous)
ONDANSETRON 4 MG/5 ML SOL	$148.43	$258.43
ONDANSETRON HCL 4 MG TABLET	$15.07	$394.83
ONDANSETRON HCL 8 MG TABLET	$23.04	$794.70
ONDANSETRON ODT 4 MG TABLET	$106.52	$252.30
ONDANSETRON ODT 8 MG TABLET	$211.39	$554.25

Clearly, the arrival of a generic equivalent to the market has driven down the cost of ondansetron products. For example, the 4mg tablets have decreased from $394.83 to $15.07 per prescription, a 96% decline in cost. Considering an average prescription cost of approximately $11.00 for promethazine, ondansetron 4mg and 8mg tablets are now a cost-effective option for the treatment of nausea and vomiting of any origin.

Even with the price decrease afforded by the availability of generic ondansetron, the ODT dosage forms still remain considerably more expensive than the regular oral tablets. For instance, the ondansetron 8mg ODT tablets are nearly ten times more expensive than the 8mg tablets. Because of this significant price difference, the Division of Medicaid began requiring prior authorization for the ODT dosage form of ondansetron for beneficiaries 12 years of age and older beginning July 1, 2010. Pediatric beneficiaries ages 0-11 do not require prior authorization for ondansetron ODT, ensuring product availability for those beneficiaries who are unable to swallow a tablet.

Conclusion

In an effort to prevent overuse of an expensive product for unapproved indications, DOM implemented quantity limits for the ondansetron products in November 2005. Recent changes in a local hospital's antiemetic protocol and concerns regarding the use of older antiemetics in certain populations has continued to drive the use of ondansetron for general nausea and vomiting. However, the price of these products has significantly decreased since the implementation of these quantity limits in 2005. HID recommends no changes to the current quantity limits in place for ondansetron products. These limits ensure availability for the products for less severe conditions such as gastroenteritis, with a timely prior authorization request option in those instances where a larger quantity of ondansetron may be required.

Low-Dose Seroquel® Utilization

Seroquel® (quetiapine) is an atypical antipsychotic agent structurally similar to clozapine. Like clozapine, quetiapine has been shown to improve symptoms of schizophrenia without producing extrapyramidal side effects. The effect of quetiapine on positive and negative symptoms has been shown to be equivalent to haloperidol, but without the considerable extrapyramidal symptoms and hyperprolactinemia associated with first-generation antipsychotic use. Seroquel® is FDA-approved for the treatment of bipolar disorder and schizophrenia for patients 10 years of age and older, with therapeutic doses ranging from 300-800mg/day for both indications.

Concerns were raised at the 2nd quarter 2010 Drug Utilization Review Board meeting regarding potential misuse of low-dose quetiapine as a sleeping and/or anxiety aid. A review of Medicaid DUR initiatives nationwide mirrors these concerns, as several state Medicaid agencies have either implemented or are in the process of implementing minimum-dose edits for this agent. HID gathered claims data for calendar year 2009 (1/1/09 – 12/1/09) for Seroquel® 25mg and 50mg tablets, and drilled the analysis down to those claims for quantities less than 93 tablets. The chart below details the findings of this examination.

Label Name	Rx Count	Qty Dispensed	Total DOM Cost
SEROQUEL 25 MG TABLET	1773	87387	$223,348.50
SEROQUEL 50 MG TABLET	2405	102273	$429,653.25
Total	4178	189660	$653,001.75

In 2009, there were a total of 21,178 prescriptions for all strengths of Seroquel ® (immediate-release). Of these, 4,178 (20%) were for sub-therapeutic doses of the 25mg and 50mg tablets as identified by this claims analysis. HID further reviewed these claims to determine if beneficiaries were receiving low-dose Seroquel ® prescriptions on a monthly basis, in an attempt to eliminate those beneficiaries receiving lower doses of Seroquel ® as part of a titration schedule to a higher dose. In October 2009, a total of 344 beneficiaries received a prescription for low-dose Seroquel ®. Of these beneficiaries, 157 (46%) continued to receive such prescriptions in November and December, well outside the suggested one week titration schedule proposed in the product labeling.

At an average cost of approximately $156 per prescription, the use of low-dose Seroquel® as a sleep aid is not a cost-efficient option for Mississippi Medicaid beneficiaries, compared to an average cost of $25 per prescription for a sedative/hypnotic. The results of this analysis seem to have authenticated the misgivings voiced at the 2nd quarter 2010 DUR Board meeting.

Conclusion

Seroquel® is an atypical antipsychotic indicated for the treatment of bipolar disorder and schizophrenia in adolescents and adults. Discussions took place at the 2nd quarter 2010 DUR Board meeting regarding the suspected off-label use of Seroquel®. Based on data presented in the claims analysis above, it appears that these suspicions have been validated. DOM seeks direction from the DUR Board to

determine what steps are necessary to discourage the cost-prohibitive use of Seroquel® as a sleep aid and/or anxiolytic.

Appropriate Duration of Therapy with Proton Pump Inhibitors (PPIs)

Proton pump inhibitors are one of the most widely used therapeutic classes, as evidenced by their constant placement in the cost analysis reports provided to the DUR Board at each meeting. These drugs are potent inhibitors of H^+,K^+-ATPase, an enzyme located in the apical secretory membrane of the parietal cell. This enzyme plays a key role in the secretion of hydrogen ions (protons) into the gastric lumen. PPIs can completely inhibit acid secretion and have a long duration of action. They promote ulcer healing and are also key components of H. pylori eradication regimens. Because of faster onset of action and greater efficacy, proton pump inhibitors have replaced H_2-blockers in most clinical situations.

The PPIs are approved for varying diagnoses, ranging from erosive esophagitis, GERD, Zollinger-Ellison syndrome, and duodenal ulcers, among others. These medications are also FDA-approved for differing lengths of therapy, depending on whether they are being used for treatment of active symptoms/disease or maintenance therapy. These approved durations of therapy are summarized in the table below.

	FDA-approved Length of Therapy	
Drug	Treatment	Maintenance
Dexlansoprazole (Dexilant®)	8 weeks	6 months
Esomeprazole (Nexium®)	8 weeks	6 months
Lansoprazole (Prevacid®)	8-12 weeks	12 months
Omeprazole and Sodium Bicarbonate (Zegerid®)	12 weeks	12 months
Omeprazole (Prilosec®)	8 weeks	5 years
Pantoprazole (Protonix®)	16 weeks	12 months
Rabeprazole (Aciphex®)	16 weeks	12 months

HID was asked to review PPI utilization to determine if long-term treatment with these products was an issue in the Mississippi Medicaid population. HID gathered claims data for the month of January in 2008, 2009, and 2010, then intersected these searches to determine the degree of long-term treatment occurring over one- and two-year periods. The results are provided below.

Treatment duration		Beneficiary Count
1 year	(1/08-1/09)	2153
	(1/09-1/10)	2516
2 years	(1/08-1/10)	1139

Chronic use of PPIs has been identified as the possible culprit for several health problems. PPI treatment leads to increased levels of gastrin, which can translate into an increased risk of gastric cancer

due to dysplasia with chronic use. Long term treatment with a PPI has been identified as possibly increasing the risk of developing *Clostridium difficile* infection and decreasing vitamin B12 absorption. Additionally, patients who use PPIs for more than one year have been identified as being at a higher risk for hip and vertebral fractures.

Health concerns aside, the cost of PPI treatment is a factor to be considered. At an average cost of $125 per month for a PPI prescription, the cost for treating a single patient for one year with a PPI amounts to almost $1,500. When these numbers are extrapolated out with the number of beneficiaries identified in the searches above, Mississippi Medicaid paid over $3 million for beneficiaries who received PPI treatment for 12 months or more.

Conclusion

PPIs are considered first line therapy for acid reduction in a variety of clinical settings due to their rapid onset of action and superb efficacy. However, the need for chronic treatment with a PPI is questionable, considering that the majority of indications that these products are approved for are considered to be treatable within 8-12 weeks. When considering the risks and costs associated with chronic use, limitations on the length of therapy with the PPIs may need to be considered for the Mississippi Medicaid pharmacy benefit. HID recommends an edit at the point of sale that would deny claims for a proton pump inhibitor when the beneficiary has been treated with any PPI for more than 6 months. This edit can be overridden with a prior authorization request providing medical justification for chronic therapy with a PPI.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3rd Quarter 2010

Criteria Recommendations	*Approved*	*Rejected*

1. ActoPlus Met XR /Overutilization _____ _____

Alert Message: ActoPlus Met XR (extended-release pioglitazone/metformin) may be over-utilized. The manufacturer's maximum recommended daily dose is 45 mg pioglitazone / 2000 mg metformin.

Conflict Code: ER – Overutilization
Drug/Disease:

Util A	Util B	Util C
ActoPlus Met XR		

Max Dose: 45mg pioglitazone -2000mg metformin extended-release per day

References:
Facts & Comparisons, 2010 Updates.
ActoPlus Met XR Prescribing Information, March 2009, Takeda Pharmaceuticals.

2. ActoPlus Met XR /Non-adherence _____ _____

Alert Message: Non-adherence to ActoPlus Met XR (extended-release pioglitazone/metformin) therapy may result in loss of glycemic control and an increased risk of developing diabetic-related complications.

Conflict Code: LR – Non-adherence
Drug/Disease:

Util A	Util B	Util C
ActoPlus Met XR		

References:
Facts & Comparisons, 2010 Updates.
ActoPlus Met XR Prescribing Information, March 2009, Takeda Pharmaceuticals.

3. Dutasteride/tamsulosin / Overutilization _____ _____

Alert Message: Jalyn (dutasteride/tamsulosin) may be over-utilized. The manufacturer's maximum recommended daily dose is one capsule (0.5 mg dutasteride/0.4 mg tamsulosin) daily.

Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Dutasteride/tamsulosin		

Max Dose: 0.5 mg dutasteride/0.4 mg tamsulosin per day

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.

Criteria Recommendations ***Approved*** ***Rejected***

4. Tamsulosin / Strong CYP 3A4 Inhibitors _____ _____

Alert Message: Tamsulosin-containing products should not be co-administered with strong CYP3A4 Inhibitors (e.g. ketoconazole, itraconazole, and ritonavir). Tamsulosin is metabolized via CYP3A4 isoenzyme and concurrent use with a strong inhibitor can significantly decrease tamsulosin metabolism and increase tamsulosin exposure.

Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B		Util C
Tamsulosin-All	Ketoconazole	Ritonavir	
	Itraconazole	Saquinavir	
	Nefazodone	Indinavir	
	Clarithromycin	Nelfinavir	
	Telithromycin	Atazanavir	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

5. Tamsulosin / CYP2D6 Inhibitors & Moderate 3A4 Inhibitors _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with moderate CYP3A4 inhibitors, moderate or strong CYP2D6 inhibitors or in patients known to be poor2D6 metabolizers. Tamsulosin is metabolized via CYP3A4 and CYP2D6 and concurrent use with Inhibitors of these isoenzymes or in poor 2D6 metabolizers may result in a significant increase in tamsulosin exposure.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B			Util C
Tamsulosin-All	Erythromycin	Paroxetine	Terbinafine	
	Aprepitant	Bupropion		
	Fluconazole	Fluoxetine		
	Verapamil	Quinidine		
	Diltiazem	Duloxetine		

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

6. Tamsulosin-All / Cimetidine _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with cimetidine (an inhibitor of both CYP3A4 and 2D6). Concurrent use of these agents has resulted in a moderate increase in tamsulosin AUC (44%) with a 26% decrease in tamsulosin clearance.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Tamsulosin-All	Cimetidine	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

Criteria Recommendations ***Approved*** ***Rejected***

7. Tamsulosin-All / Warfarin _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with warfarin. Results from limited in vitro and in vivo studies are inconclusive concerning this interaction, therefore caution should be exercised with concurrent use.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Tamsulosin-All	Warfarin	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

8. Alpha-1-Adrenergic Receptor Blockers/ Duplicate Therapy _____ _____

Alert Message: Therapeutic duplication of alpha-1-adrenergic blockers may be occurring. These agents should not be used concurrently due to the increased risk of hypotension.

Conflict Code: TD – Therapeutic Duplication
Drug/Disease:

Util A	Util B	Util C
Tamsulosin-all		
Prazosin		
Terazosin		
Doxazosin		
Alfuzosin		
Silodosin		

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.
Minipress Prescribing Information, July 2009, Pfizer Labs.

9. Dutasteride / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Dutasteride-containing products are contraindicated during pregnancy and in women of childbearing potential due to risk for fetal harm. In animal studies dutasteride, an androgen hormone inhibitor, inhibited the normal development of external genitalia in male fetuses. Dutasteride-containing products are pregnancy category X.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drug/Disease:

Util A	Util B	Util C (Negating)
Tamsulosin	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

Age: 12 – 999 years of age

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Facts & Comparisons, 2010 Updates.
Avodart Prescribing Information, June 2010, GlaxoSmithKline.

FDA Updates

The following information is provided to the DUR Board to assist in identifying drug products with potential for concern surrounding safety and appropriate utilization. Most of the safety alert information provided is derived from recent FDA safety alerts. While many of the alerts included are not Black Box Warning additions or updates, they are labeling changes or updates with relevance worthy of action by FDA.

Included for reference, the following is the Code of Federal Regulations definition for Black Box Warnings. (Citation: Title 21 CFR 201.57 Section E)

(e) Warnings. Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and Usage: section of labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease of condition, and there is lack of substantial evidence of effectiveness for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these adverse reactions and, if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective used of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

Propylthiouracil-Boxed Warning Added
FDA has added a Boxed Warning to the label for propylthiouracil, to include information about reports of severe liver injury and acute liver failure, some of which have been fatal, in adult and pediatric patients using this medication.
Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Online: www.fda.gov/MedWatch/report.htm
- Phone: 1-800-332-1088
- Mail: return the postage-paid FDA form 3500, which may be downloaded from the MedWatch "Download Forms" page, to address on the pre-addressed form
- Fax: 1-800-FDA-0178

McNeil Consumer Healthcare Over-the-Counter Infants' and Children's Products: Recall including Tylenol, Motrin, Zyrtec, and Benadryl products

McNeil Consumer Healthcare and FDA notified healthcare professionals of a voluntary recall of certain over-the-counter (OTC) Children's and Infants' liquid products manufactured in the United States, including Tylenol, Motrin, Zyrtec, and Benadryl products. Some of these products may not meet required quality standards. This recall is not being undertaken on the basis of adverse medical events. However, as a precautionary measure, parents and caregivers should not administer these products to their children. These products were distributed in the United States, Canada, Dominican Republic, Dubai (UAE), Fiji, Guam, Guatemala, Jamaica, Puerto Rico, Panama, Trinidad & Tobago, and Kuwait. See the company Press Release for a list of products affected by this recall.

Consumers can contact the company at 1-888-222-6036 and also at www.mcneilproductrecall.com

GnRH Agonists: Safety Review of Drug Class Used to Treat Prostate Cancer

FDA notified healthcare professionals and patients of FDA's preliminary and ongoing review which suggests an increase in the risk of diabetes and certain cardiovascular diseases in men treated with GnRH agonists, drugs that suppress the production of testosterone, a hormone that is involved in the growth of prostate cancer.

Most of the studies reviewed by FDA reported small, but statistically significant increased risks of diabetes and/or cardiovascular events in patients receiving GnRH agonists. FDA's review is ongoing and the agency has not made any conclusions about GnRH agonists and whether they increase the risk of diabetes and cardiovascular disease in patients receiving these medications for prostate cancer.

Healthcare professionals and patients should be aware of these potential safety issues and carefully weigh the benefits and risks of GnRH agonists when determining treatment choices. FDA recommends that patients receiving GnRH agonists should be monitored for development of diabetes and cardiovascular disease. Patients should not stop their treatment with GnRH agonists unless told to do so by their healthcare professional.

Some GnRH agonists are also used in women and in children for other indications than those above. There are no known comparable studies that have evaluated the risk of diabetes and heart disease in women and children taking GnRH agonists.

Vivitrol (naltrexone for extended-release injectable suspension): Medication Guide Required for Patients

Alkermes and FDA notified healthcare professionals and patients of an update to the Warnings, Information for Patients, and Dosage and Administration sections of the Prescribing Information to strengthen language regarding the risk of injection site reactions based on postmarketing reports that had been received prior to June 2009.

FDA requires that a Medication Guide, which communicates this and other important information about treatment be provided to all patients. Healthcare professionals should also counsel patients about the risks and benefits of Vivitrol before an initial prescription, including those risks and benefits set forth in the new Medication Guide and Prescribing Information, and should ensure that patients understand these risks.

Intravenous Medications Manufactured by Claris: Recall due to contamination of products Metronidazole, Ciprofloxacin and Ondansetron sold under the Claris, Sagent Pharmaceuticals, Pfizer, and West-Ward Pharmaceuticals labels.

FDA notified healthcare professionals not to use the intravenous medications, metronidazole, ciprofloxacin and ondansetron manufactured by Claris Lifesciences due to contamination. These products were all manufactured on the same manufacturing line and sold under the Claris, Sagent Pharmaceuticals, Pfizer, and West-Ward Pharmaceuticals labels. The FDA received reports of floating matter in intravenous bags of metronidazole and ondansetron. Foreign matter should not be present in a sterile injectable product. Healthcare professionals should not use these products and should immediately remove them from their pharmacy inventories. Claris is initiating a recall of all lots of these products. FDA is further investigating the situation and will notify the public when new information becomes available. Please review the linked Public Health Alert for a list of the affected and recalled products.

Tramadol: Changes to Warnings section of Prescribing Information

Ortho-McNeil-Janssen and FDA notified healthcare professionals of changes to the Warnings section of the prescribing information for tramadol, a centrally acting synthetic opioid analgesic indicated for the management of moderate to moderately severe chronic pain. The strengthened Warnings information emphasizes the risk of suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs and also warns of the risk of overdosage. Tramadol-related deaths have occurred in patients with previous histories of emotional disturbances or suicidal ideation or attempts, as well as histories of misuse of tranquilizers, alcohol, and other CNS-active drugs. Tramadol may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs that cause central nervous system depression. Serious potential consequences of overdosage with tramadol are central nervous system depression, respiratory depression and death. Tramadol has mu-opioid agonist activity, can be abused and may be subject to criminal diversion.

Proton Pump Inhibitors (PPI): Class Labeling Change

including Nexium, Dexilant, Prilosec, Zegerid, Prevacid, Protonix, Aciphex, Vimovo, Prilosec OTC, Zegerid OTC, and Prevacid 24HR

FDA notified healthcare professionals and patients of revisions to the prescription and over-the-counter [OTC] labels for proton pump inhibitors, which work by reducing the amount of acid in the stomach, to include new safety information about a possible increased risk of fractures of the hip, wrist, and spine with the use of these medications.

The new safety information is based on FDA's review of several epidemiological studies that found those at greatest risk for these fractures received high doses of proton pump inhibitors or used them for one year or more. The majority of the studies evaluated individuals 50 years of age or older and the increased risk of fracture primarily was observed in this age group. While the greatest increased risk for fractures in these studies involved people who had been taking prescription proton pump inhibitors for at least one year or who had been taking high doses of the prescription medications (not available over-the-counter), as a precaution, the "Drug Facts" label on the OTC proton pump inhibitors (indicated for 14 days of continuous use) also is being revised to include information about this risk. FDA recommends healthcare professionals, when prescribing proton pump inhibitors, should consider whether a lower dose or shorter duration of therapy would adequately treat the patient's condition.

The safety communication includes a data summary with a table and references which support the epidemiological studies reviewed for this communication.

Orlistat (marketed as Alli and Xenical): Labeling Change

FDA notified healthcare professionals and patients that it has approved a revised label for Xenical to include new safety information about cases of severe liver injury that have been reported rarely with the use of this medication. The agency is also adding a new warning about rare reports of severe liver injury to the OTC Drug Facts label for Alli.

Xenical and Alli are medications used for weight-loss that contain different strengths of the same active ingredient, orlistat. Xenical (orlistat 120 mg) is available by prescription and Alli (orlistat 60 mg) is sold over-the-counter without a prescription. This new safety information, originally announced in August 2009, is based on FDA's completed review of orlistat.

Healthcare professionals should weigh the benefits of weight-loss with the potential risks associated with Xenical and Alli before prescribing or recommending these medications to their patients; patients should stop use of orlistat and contact their healthcare professional if they develop the signs and symptoms of liver injury, including itching, yellow eyes or skin, dark urine, light-colored stools, or loss of appetite.

GammaGard Liquid, Immune Globulin Intravenous (Human)

ISSUE: Baxter BioScience and FDA notified healthcare professionals of a market withdrawal being conducted as a precautionary measure due to an increased number of adverse event reports of allergic reactions associated with two lots of the product.

BACKGROUND: GammaGard Liquid is indicated for the treatment of primary immunodeficiency disorders associated with defects in humoral immunity.

RECOMMENDATION: Customers are asked to contact Baxter BioScience for Urgent Market Withdrawal instructions. See the Market Withdrawal Notice for information on affected lots.

Benicar (olmesartan): Ongoing Safety Review

ISSUE: FDA is evaluating data from two clinical trials in which patients with type 2 diabetes taking the blood pressure medication, Benicar (olmesartan), an angiotensin II receptor blocker, had a higher rate of death from a cardiovascular cause compared to patients taking a placebo. FDA's review is ongoing and the Agency has not concluded that Benicar increases the risk of death. FDA currently believes that the benefits of Benicar in patients with high blood pressure continue to outweigh its potential risks.

BACKGROUND: The Agency plans to review the primary data from the two studies of concern, ROADMAP and ORIENT, and is considering additional ways to assess the cardiovascular effects of Benicar. ROADMAP and ORIENT are both long-term clinical trials. In both trials, patients with type 2 diabetes were given either Benicar or placebo to determine if treatment with Benicar would slow the progression of kidney disease. An unexpected finding observed in both trials was a greater number of deaths from a cardiovascular cause (heart attack, sudden death, or stroke) in the Benicar-treated patients compared to placebo.

RECOMMENDATION: Follow the recommendations in the drug label when prescribing Benicar. Additional Information for Patients, for Healthcare Professionals and a Data Summary are provided in the Drug Safety Communication below. Additional information about ROADMAP and ORIENT can be found at clinicaltrials.gov.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Qualaquin (quinine sulfate): New Risk Evaluation and Mitigation Strategy - Risk of serious hematological reactions

ISSUE: Due to continued reports of serious side effects in patients using Qualaquin "off-label" for night time leg cramps, FDA has approved a risk management plan to warn against the use of this drug for such unapproved uses. Qualaquin should not be used for night time leg cramps. Qualaquin use may result in serious and life-threatening hematological reactions, including serious bleeding due to thrombocytopenia, and hemolytic-uremic syndrome/ thrombotic thrombocytopenic purpura, which in some cases may result in permanent kidney damage. In some patients, adverse reactions result in hospitalization and death.

BACKGROUND: Qualaquin is only FDA-approved for the treatment of uncomplicated malaria caused by the parasite Plasmodium falciparum, primarily in travelers returning from malaria-endemic areas. However, the majority of Qualaquin's use in the United States is for the treatment or prevention of night time leg cramps. The product labeling states that the risks associated with the use of Qualaquin in the absence of evidence of its effectiveness for treatment or prevention of nocturnal leg cramps outweigh any potential benefits.

The risk management plan (REMS) requires that patients be given a Medication Guide explaining what this medication is and is not approved for, as well as the potential side effects of this drug. In addition, the REMS requires that the manufacturer issue a Dear Health Care Provider Letter warning of the risk of serious and life-threatening hematologic reactions.

A data summary of adverse event reports received by FDA from April 2005 to October 2008 is provided in the Drug Safety Communication below.

RECOMMENDATION: Healthcare professionals should discuss with patients the warning signs of thrombocytopenia, such as easy bruising, severe nose bleeds, blood in the urine or stool, bleeding gums, and the appearance of unusual purple, brown, or red spots on the skin. Patients are encouraged to read the Medication Guide given to them at the pharmacy before starting Qualaquin and each time they get a refill.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Arava (leflunomide): Boxed Warning - Risk of Severe Liver Injury

ISSUE: FDA is adding information on severe liver injury to the Boxed Warning of Arava (leflunomide) a drug used to treat rheumatoid arthritis - to highlight the risk of severe liver injury in patients using this drug and how this risk may be reduced. FDA previously required a Boxed Warning stating that leflunomide was contraindicated in pregnant women, or women of childbearing potential who were not using reliable contraception.

BACKGROUND: The decision to add information on severe liver injury to the Boxed Warning was based on FDA’s review of adverse event reports which identified 49 cases of severe liver injury, including 14 cases of fatal liver failure, between August 2002 and May 2009. In this review, the greatest risk for liver injury was seen in patients taking other drugs known to cause liver injury, and patients with pre-existing liver disease.

RECOMMENDATIONS**:** The information on severe liver injury being added to the Boxed Warning states:

- Patients with pre-existing liver disease should not receive leflunomide.
- Patients with elevated liver enzymes (ALT greater than two times the upper limit of normal) should not receive leflunomide.
- Caution should be used in patients who are taking other drugs that can cause liver injury.

- Liver enzymes should be monitored at least monthly for three months after starting leflunomide and at least quarterly thereafter.
- If the ALT rises to greater than two times the upper limit of normal while the patient is on leflunomide – leflunomide should be stopped, cholestryamine washout begun to speed the removal of leflunomide from the body and follow-up liver function tests conducted at least weekly until the ALT value is within normal range.

Coumadin 1 mg Tablet Blister Packs: Recall
ISSUE: Bristol-Myers Squibb determined that some of the tablets, over time, may not meet specification for isopropanol. Isopropanol is used to maintain the active ingredient, Coumadin, in the crystalline state, and could affect the therapeutic levels of the active ingredient. A decrease of active ingredient may increase the risk of clots which could lead to heart attack or stroke, and if there is too much active ingredient, there is an increased risk of bleeding. The following lot numbers are included in this recall: Physician Sample Blister Packs: Lot# 9A48931A, 9A48931B, 9A48931C, expiration January 2012; HUD Blister Pack: Lot# 8F34006B, 8K44272A, 8K46168A, 9F44437A and 9K58012B with expiry dates between June 2011 and November 2012.
BACKGROUND: The recall only involves Coumadin 1 mg tablet blister-packs distributed in the U.S. This recall does not involve Coumadin 1 mg supplied in bottles or any other strengths and dosage forms of the product. Patients who may have product from the subject lots should contact their physicians to ensure that their anticoagulation therapy is not interrupted.
RECOMMENDATION: See the company Press Release for additional contact information. Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Angiotensin Receptor Blockers (ARBs): Ongoing Safety Review for Cancer Risk
ISSUE: A recently published study - a meta-analysis combining cancer-related findings from several clinical trials - suggested use of ARBs may be associated with a small increased risk of cancer.
BACKGROUND: ARBs are used in patients with high blood pressure and other conditions. Brand names include Atacand, Avapro, Benicar, Cozaar, Diovan, Micardis, and Teveten. The meta-analysis included data from over 1,000 patients in several long-term, randomized, controlled clinical trials evaluating ARBs for which adverse events related to cancer were captured during the study. The mean duration of follow-up ranged from 1.7 to 4.8 years. The study reported the frequencies of new cancer occurrence to be 7.2% for patients receiving ARBs compared to 6.0% for those not receiving ARBs (risk ratio = 1.08, 95% Confidence Interval: 1.01-1.15). No statistically significant difference in cancer deaths was noted.
RECOMMENDATION: FDA has not concluded that ARBs increase the risk of cancer. The Agency is reviewing information related to this safety concern and will update the public when additional information is available. FDA believes the benefits of ARBs continue to outweigh their potential risks. Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

Advair Diskus (fluticasone propionate and salmeterol inhalation powder): Stolen Product Warning
ISSUE: Certain Advair Diskus inhalers stolen from a distribution warehouse in 2009 have been found in some pharmacies. The safety and effectiveness of the stolen inhalers cannot be assured and they should not be used. The lot numbers, doses, and quantities of the stolen Advair Diskus inhalers are:

- Lot 9ZP2255 - NDC 0173-0696-00, Advair Diskus 250/50, 60 Dose, Exp: Sep 2010 (14,400 inhalers)

- Lot 9ZP3325 - NDC 0173-0697-00, Advair Diskus 500/50, 60 Dose, Exp: Sep 2010 (11,200 inhalers)

BACKGROUND: Advair Diskus (fluticasone propionate and salmeterol inhalation powder) is an inhaler used to treat patients with asthma and chronic obstructive pulmonary disease. The products were reported stolen in August 2009 from a GlaxoSmithKline warehouse near Richmond, Va. The inhalers found recently were the first from the stolen lots to be found in commerce. However, more stolen product may still be on the market and the FDA continues to aggressively investigate the matter. Stolen medicine may be harmful because it may have been stored at the wrong temperature or humidity or other improper conditions, may degrade or lose potency, become contaminated, or may have been tampered with or handled improperly while outside of the legitimate supply chain. RECOMMENDATION: Patients who have products with these lot numbers should immediately stop using them, contact GlaxoSmithKline's Customer Response Center at 888-825-5249, and follow-up with their physician or pharmacist to obtain a proper replacement. Pharmacists and wholesalers who find Advair Diskus inhalers bearing these lot numbers should remove them from shelves and contact the FDA's Office of Criminal Investigations (OCI) at 800-551-3989. The agency also is asking for the public's help in reporting any information regarding these inhalers, including suspicious or unsolicited offers for the Advair Diskus lots in question, to OCI or by visiting the OCI website.