Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

May 20, 2010

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

Drug Utilization Review Board

Lee Merritt, R.Ph.
Medfusion
2211 5th Street North
Columbus, MS 39705
Term expires: June 30, 2010

Edgar Donahoe, M.D.
Indianola Family Medical Group
122 Baker Street
Indianola, MS 38751
Term expires: June 30, 2010

Mark Reed, M.D.
University of Mississippi Medical Center
2500 North State Street, Trailer 16
Jackson, MS 39216
Term Expires: June 30, 2010

Vickie Veazey, R.Ph.
MS State Hospital at Whitfield
Building #50
Whitfield, MS 39193
Term expires: June 30, 2010

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

Upcoming Mississippi DUR Board Meeting Dates

August 19, 2010
February 17, 2011

November 18, 2010
May 19, 2011

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

May 20, 2010

Welcome	**Mark Reed, M.D.**
Old Business	**Mark Reed, M.D.**
Approval of Meeting Minutes	
Cost Management Analysis	**Ashleigh Holeman, Pharm.D.**
Pharmacy Program Update	**Paige Clayton, Pharm.D.**
New Business	**Ashleigh Holeman, Pharm.D.**

Duplicate Atypical Antipsychotic Therapy in Pediatric Beneficiaries

Attention Deficit Hyperactivity Disorder: A Medicaid Prescribing Update

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

The Role of Lipotropics in the Treatment of Cardiovascular Disease

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

Other Criteria Recommendations

Next Meeting Information	**Mark Reed, M.D.**

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the February 18, 2010 Meeting

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

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 2:00 p.m. Dr. Reed asked for a motion to accept the minutes from the meeting of November 19, 2009. Dr. Dees made the motion to accept the minutes with a second from Dr. Gray. All voted in favor of the motion.

Dr. Reed continued the meeting by moving into the new business under the direction of Dr. Holeman.

Cost Management Analysis:
Dr. Holeman began with the presentation of the Top 15 Therapeutic classes by the total cost of claims dating September 1, 2009 thru November 30, 2009. The Top Therapeutic class remains constant with Antipsychotic Agents leading. The Top 25 Drugs based on the number of claims for these same dates varied from the norm with Azithromycin leading the first month followed by hydrocodone-acetaminophen then these two shared the top two placements the following two months. The Top 25 Drugs based on total claims cost noted changes each month with Tamiflu® leading in September followed by Singulair® the second month then ending with Synagis® for November.

Pharmacy Program Update:
Dr. Clayton began by noting several implementations within the DOM pharmacy program. These were: the newest PDL introduced on January 1, 2010 and the age edits voted on by the Board for beneficiaries over the age of 21 for all ADHD medications. She continued by explaining that the age edits did not include quantity limits and this would be presented later during this meeting. It was noted that a contract had been granted to implement the E-Prescribing/Electronic Health Records that will go live soon. Physicians and pharmacists will have the opportunity to sign up for these programs which will greatly enhance their practices. Ms. Clark noted that this has been a work in progress for the DOM staff and the state will be one of the first to implement such programs. Ms. Clark also noted that with the recent legislation regarding pseudoephedrine products that DOM will continue to cover the OTC products with this formulation but the prescriptions will need renewing more often.

New Business:

Tamiflu® Utilization Update

In August 2009, a widespread outbreak of H1N1 influenza occurred in Mississippi. DOM, attempting to be proactive in discouraging stockpiling of medications and presenting potential antiviral resistance, asked the DUR Board to consider placing a limit on antiviral medications to two (2) prescriptions per calendar year. The Board voted unanimously on this recommendation. The claims count and the number of beneficiaries receiving an antiviral medication in 2009 were nearly 60 times higher than during the same time period in the previous year. This was notably a favorable move, on the part of DOM with the support of the DUR Board, as the utilization numbers for 2009 would have been even higher in the absence of the approved quantity limits.

Atypical Antipsychotics: Issues within the Mississippi Medical Population

On September 11, 2008, The Division of Medicaid implemented age edits for the atypical antipsychotic class based on the FDA-approved age for each agent. This proactive measure was the result of nationwide scrutiny regarding the growing use of this therapeutic class in pediatric beneficiaries. HID gathered claims data for the year prior to and the year after the implementation of the age edits for beneficiaries less than 13 years of age to see what the impact of these edits were for this population. The claims count for these medications decreased by 53% and the number of beneficiaries noted a decrease of 49%. Clearly, these edits were successful in encouraging responsible and informed prescribing of atypical antipsychotics in this population. DOM then asked HID to analyze utilization data for the atypical antipsychotics specifically related to possible duplicate therapy within the class. With the high cost associated with treatment in a single agent, duplicate therapy presents a great concern. HID gathered utilization data for the six-month period from 6/27/2009 to 12/26/2009. The results obtained indicated that there is a significant amount of duplicate therapy occurring within this class. Nearly 800 beneficiaries received two or more atypical antipsychotics within this six-month analysis. While there are no contraindications for duplicate atypical antipsychotic therapy, this practice causes concern due to the adverse events and high cost associated with single-agent use. HID will continue to monitor the activity of the previously approved RDUR criterion and intervene appropriately when necessary. HID does not recommend any additional action at this time.

ADHD Agents: Issues within the Mississippi Medicaid Population

ADHD agents continue to be one of the most utilized therapeutic classes within the Mississippi Medicaid population. Scrutiny also exists regarding the potential overprescribing of ADHD agents, particularly in young children. DOM monitors the ADHD agents continuously. With this being noted, HID gathered utilization data for the ADHD agents based on three different issues:

1. the impact of age edits implemented for the class in September 2008
2. use of ADHD agents in beneficiaries 21 years of age or older
3. use of multiple daily doses of short-acting ADHD agents

HID gathered claims data for the year prior to and the year after the implementation of the age edits for beneficiaries less than 6 years of age to see what the impact of these

edits was. There was a 341% increase in ADHD agent claims for this age group and a 274% increase in the number of beneficiaries under the age of 6 receiving an ADHD agent. DOM expected to see some increase but the degree of increased utilization in this age group was clearly unexpected by all. Dr. Holeman continued by moving to the new age edits approved by the DUR Board for ages 21 years and older at the last meeting. A total was noted by the data presented that 1189 beneficiaries ≥ 21 years of age received an ADHD agent in FY2009. Of these, 43% were 20 -29 years of age with the beneficiary count steadily declining with each decade of age. HID was also requested by the Board to submit data regarding multiple daily doses of short-acting ADHD agents in the Mississippi Medicaid population. Of all the claims for short-acting ADHD agents, 14% were for more than 62 tablets, followed by 5% for more than 93 tablets. From this data, it appears that a quantity limit may be necessary to curb the potential for abuse with short-acting agents and increase patient compliance by encouraging the use of long-acting agents that allow for once-daily dosing. HID recommends a cumulative quantity limit of 62 per every 31 days on the short-acting ADHD agents. This limit would be in line with the quantity limits present on most all other narcotics through the pharmacy benefit for Mississippi Medicaid. A motion was made by Lee Merritt seconded by Dr. Gray to implement this recommendation. All voted in favor of this motion. Dr. Dees suggested that the development of a Medicaid Prescribing Update for ADHD including information about proper diagnosis and treatment may be helpful, and that sharing this document with the state medical associations for pediatrics and family practice groups might be helpful to gain support throughout the state's medical community. HID was asked by the Board to bring data regarding compliance trends with ADHD agents to the next meeting for review.

Mississippi Medicaid Coverage of Topical Acne Agents

Dr. Holeman noted a common misconception in the retail pharmacy world is that DOM does not cover topical acne agents. DOM does in fact cover these agents for beneficiaries under the age of 21 with the PDL addressing preferred agents. DOM asked HID to develop a Medicaid Prescribing Update merging information from the most recent treatment guidelines for acne and the preferred drug list, in an effort to educate providers about the availability of treatment coverage for beneficiaries in Mississippi. This Medicaid Prescribing Update will be distributed to prescribers by the HID Academic Detailers. Dr. Dees noted that shared information with the school nurses association might be of benefit for beneficiaries with this diagnosis in this age group. He continued that this population has a tendency to have fewer physician visits, which may further limit their access to proper acne treatment. Dr. Reed asked the Board for a vote to approve the Acne Medicaid Prescribing Update to be distributed to providers by the Academic Detailers. All voted in favor.

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 updates. No questions were raised.

Dr. Reed called for the meeting to be adjourned at 3:10 p.m. The next meeting will be held at 2:00 p.m. on May 20, 2010.

Respectfully Submitted,
Health Information Designs, Inc.

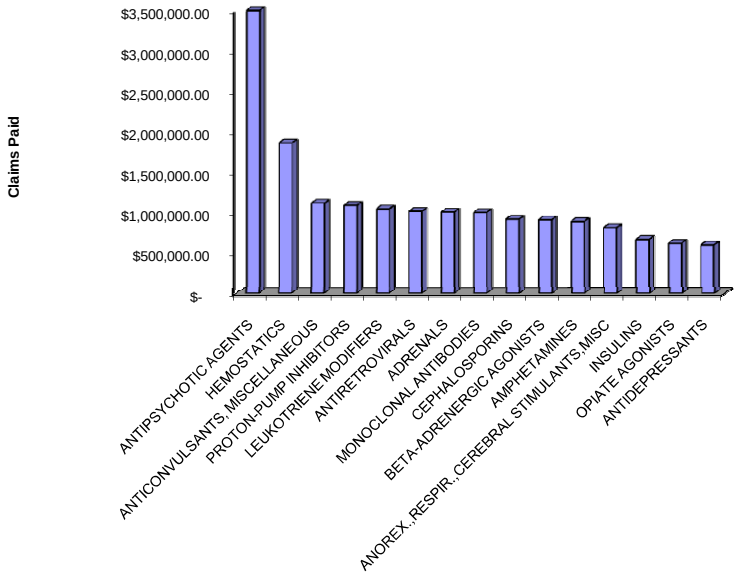
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 12/01/09-12/31/09

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	11,757	$ 3,496,899.42	$ 297.43	2.65%
HEMOSTATICS	60	$ 1,861,819.26	$31,030.32	0.01%
ANTICONVULSANTS, MISCELLANEOUS	13,095	$ 1,118,481.06	$ 85.41	2.95%
PROTON-PUMP INHIBITORS	8,177	$ 1,091,487.47	$ 133.48	1.84%
LEUKOTRIENE MODIFIERS	8,919	$ 1,046,579.68	$ 117.34	2.01%
ANTIRETROVIRALS	1,283	$ 1,017,063.52	$ 792.72	0.29%
ADRENALS	14,014	$ 1,008,474.24	$ 71.96	3.16%
MONOCLONAL ANTIBODIES	628	$ 1,003,231.92	$ 1,597.50	0.14%
CEPHALOSPORINS	15,319	$ 922,846.11	$ 60.24	3.45%
BETA-ADRENERGIC AGONISTS	16,235	$ 914,919.28	$ 56.35	3.66%
AMPHETAMINES	6,405	$ 894,473.94	$ 139.65	1.44%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,994	$ 815,490.32	$ 136.05	1.35%
INSULINS	4,142	$ 670,960.47	$ 161.99	0.93%
OPIATE AGONISTS	29,304	$ 624,029.31	$ 21.30	6.60%
ANTIDEPRESSANTS	15,445	$ 603,929.64	$ 39.10	3.48%
TOTAL TOP 15	150,777	$ 17,090,685.64	$ 113.35	33.98%

Total Rx Claims	443,713
From 12/01/09-12/31/09	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



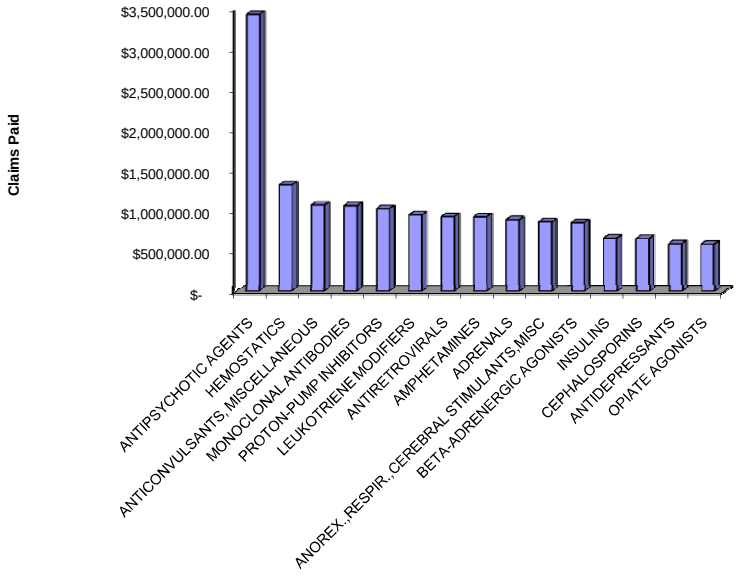
MISSISSIPPI MEDICAID
Cost Management Analysis

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

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	11,233	$ 3,423,685.67	$ 304.79	2.72%
HEMOSTATICS	39	$ 1,318,749.14	$33,814.08	0.01%
ANTICONVULSANTS, MISCELLANEOUS	12,498	$ 1,071,918.17	$ 85.77	3.03%
MONOCLONAL ANTIBODIES	659	$ 1,063,929.36	$ 1,614.46	0.16%
PROTON-PUMP INHIBITORS	8,120	$ 1,025,376.36	$ 126.28	1.97%
LEUKOTRIENE MODIFIERS	8,068	$ 949,256.20	$ 117.66	1.95%
ANTIRETROVIRALS	1,143	$ 928,203.01	$ 812.08	0.28%
AMPHETAMINES	6,093	$ 925,343.86	$ 151.87	1.48%
ADRENALS	11,989	$ 890,789.05	$ 74.30	2.90%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,143	$ 864,273.07	$ 140.69	1.49%
BETA-ADRENERGIC AGONISTS	14,188	$ 853,364.27	$ 60.15	3.44%
INSULINS	3,911	$ 661,000.44	$ 169.01	0.95%
CEPHALOSPORINS	11,861	$ 656,326.01	$ 55.33	2.87%
ANTIDEPRESSANTS	14,698	$ 591,860.33	$ 40.27	3.56%
OPIATE AGONISTS	28,126	$ 586,175.34	$ 20.84	6.81%
TOTAL TOP 15	138,769	$ 15,810,250.28	$ 113.93	33.62%

Total Rx Claims From 01/01/10-01/31/10	412,765

Top 15 Therapeutic Classes
Based on Total Cost of Claims



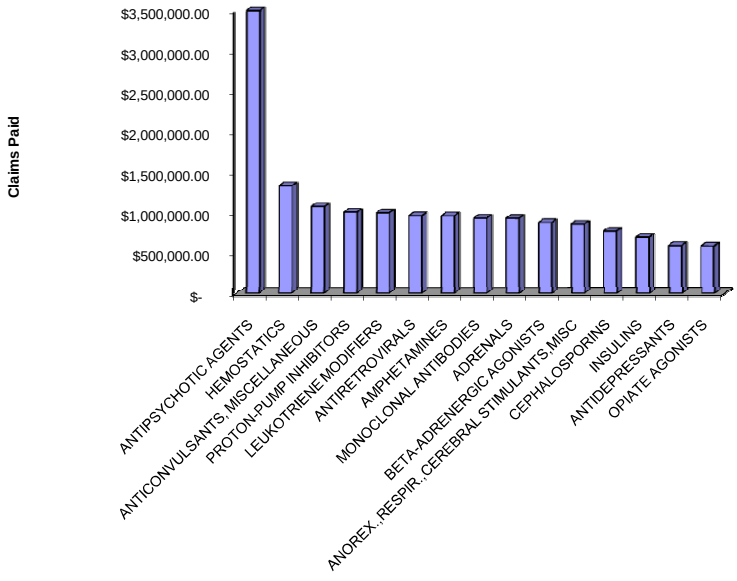
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 02/01/10-02/28/10

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	11,152	$ 3,494,333.30	$ 313.34	2.59%
HEMOSTATICS	55	$ 1,331,095.55	$24,201.74	0.01%
ANTICONVULSANTS, MISCELLANEOUS	12,470	$ 1,077,570.08	$ 86.41	2.90%
PROTON-PUMP INHIBITORS	8,202	$ 1,008,283.02	$ 122.93	1.91%
LEUKOTRIENE MODIFIERS	8,112	$ 999,406.47	$ 123.20	1.88%
ANTIRETROVIRALS	1,197	$ 963,484.69	$ 804.92	0.28%
AMPHETAMINES	6,204	$ 961,829.42	$ 155.03	1.44%
MONOCLONAL ANTIBODIES	568	$ 934,056.52	$ 1,644.47	0.13%
ADRENALS	12,733	$ 933,262.95	$ 73.29	2.96%
BETA-ADRENERGIC AGONISTS	14,578	$ 880,375.47	$ 60.39	3.39%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,085	$ 859,831.75	$ 141.30	1.41%
CEPHALOSPORINS	13,174	$ 773,477.26	$ 58.71	3.06%
INSULINS	3,868	$ 698,861.54	$ 180.68	0.90%
ANTIDEPRESSANTS	14,795	$ 594,908.37	$ 40.21	3.44%
OPIATE AGONISTS	27,156	$ 588,426.95	$ 21.67	6.31%
TOTAL TOP 15	140,349	$ 16,099,203.34	$ 114.71	32.61%

Total Rx Claims	430,404
From 02/01/10-02/28/10	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

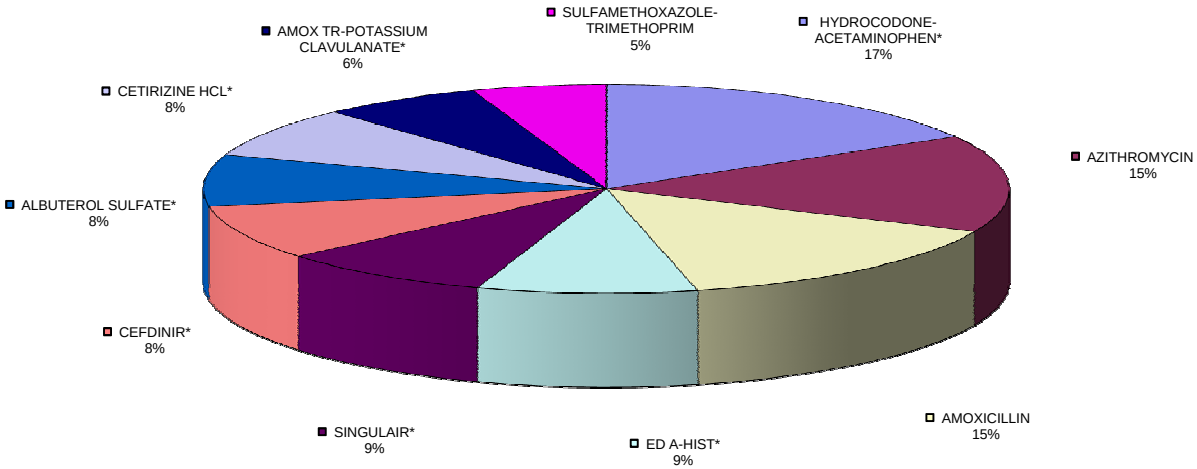
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 12/01/09-12/31/09

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	17,174	$ 247,544.11	1
AZITHROMYCIN*	MACROLIDES	15,557	$ 467,646.29	6
AMOXICILLIN	PENICILLINS	15,082	$ 137,849.13	5
ED A-HIST*	PROPYLAMINE DERIVATIVES	9,054	$ 72,638.21	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,907	$ 1,044,954.07	4
CEFDINIR*	CEPHALOSPORINS	8,697	$ 636,813.81	68
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	8,291	$ 267,841.13	67
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	8,137	$ 166,205.89	~
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	6,655	$ 331,686.70	32
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,538	$ 69,395.74	39
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,518	$ 43,795.70	18
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,900	$ 34,241.34	8
PREVACID*	PROTON-PUMP INHIBITORS	4,417	$ 772,209.55	7
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	4,278	$ 33,532.16	24
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,870	$ 44,273.91	59
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,659	$ 353,932.35	140
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	3,509	$ 147,483.27	14
CEPHALEXIN*	CEPHALOSPORINS	3,298	$ 46,820.32	22
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,170	$ 26,456.66	43
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	2,977	$ 20,436.97	~
CHERATUSSIN AC	ANTITUSSIVES	2,931	$ 14,804.98	105
PREDNISOLONE SODIUM PHOSPHATE	ADRENALS	2,883	$ 37,630.69	143
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,771	$ 12,714.38	2
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,749	$ 48,295.79	50
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,747	$ 432,637.23	34
TOTAL TOP 25		156,769	$ 5,511,840.38	

Total Rx Claims From 12/01/09-12/31/09	443,713

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

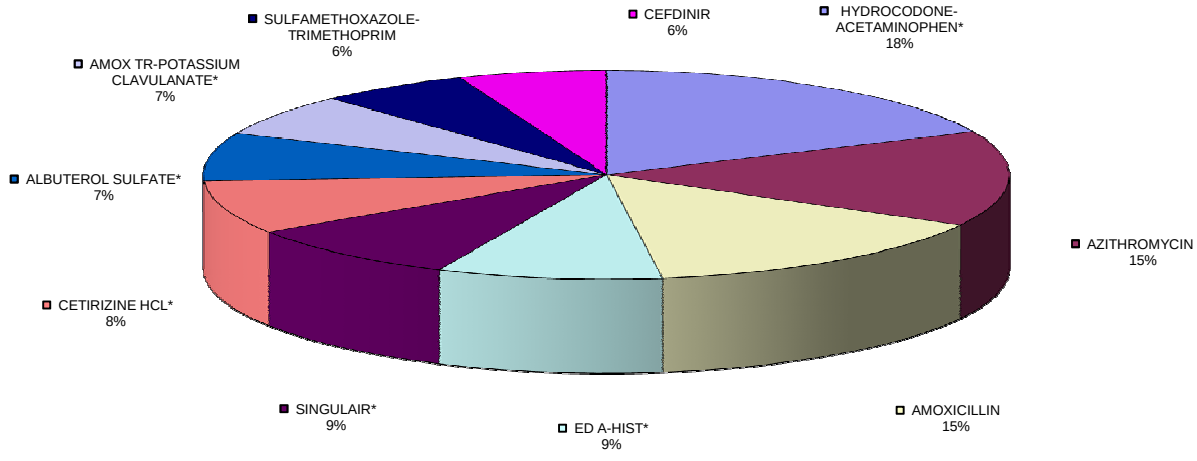
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 01/01/10-01/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	16,382	$ 235,823.24	1
AZITHROMYCIN*	MACROLIDES	13,287	$ 393,391.46	6
AMOXICILLIN	PENICILLINS	13,252	$ 121,039.95	5
ED A-HIST*	PROPYLAMINE DERIVATIVES	8,108	$ 64,132.51	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,059	$ 948,422.63	4
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	7,444	$ 159,881.43	~
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	6,685	$ 226,232.21	67
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	5,900	$ 296,083.91	32
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,417	$ 65,929.75	39
CEFDINIR	CEPHALOSPORINS	5,318	$ 389,779.29	68
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,297	$ 40,647.78	18
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	4,738	$ 51,994.03	59
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,638	$ 32,264.97	8
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	4,036	$ 30,903.96	24
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,543	$ 337,852.24	140
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	3,268	$ 137,932.42	14
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,206	$ 26,571.59	43
CEPHALEXIN*	CEPHALOSPORINS	3,193	$ 45,182.77	22
PREVACID*	PROTON-PUMP INHIBITORS	2,977	$ 518,339.37	7
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	2,849	$ 19,559.14	~
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,808	$ 438,686.67	34
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,669	$ 48,127.63	50
NYSTATIN*	ANTIFUNGALS (SKIN & MUCOUS MEMBRANE)	2,630	$ 30,682.92	142
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,627	$ 12,497.70	2
OMEPRAZOLE*	PROTON-PUMP INHIBITORS	2,574	$ 154,614.95	15
TOTAL TOP 25		140,905	$ 4,826,574.52	

Total Rx Claims From 01/01/10-01/31/10	412,765

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

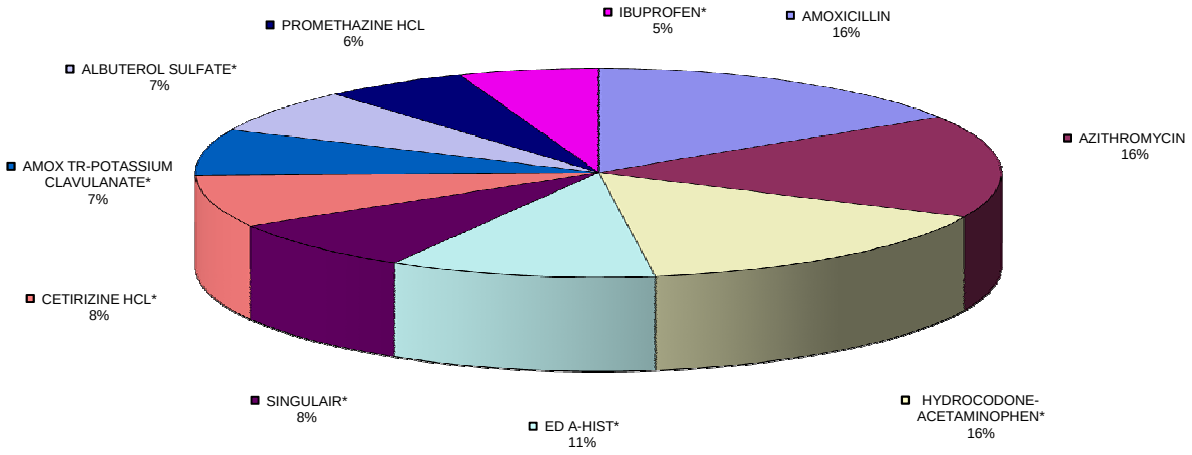
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 02/01/10-02/28/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
AMOXICILLIN	PENICILLINS	16,033	$ 148,237.99	5
AZITHROMYCIN*	MACROLIDES	15,974	$ 473,775.37	6
HYDROCODONE-ACETAMINOPHEN*	OPIATE AGONISTS	15,793	$ 228,129.53	1
ED A-HIST*	PROPYLAMINE DERIVATIVES	10,684	$ 84,718.31	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,102	$ 998,129.44	4
CETIRIZINE HCL*	SECOND GENERATION ANTIHISTAMINES	8,089	$ 194,207.34	~
AMOX TR-POTASSIUM CLAVULANATE*	PENICILLINS	7,197	$ 366,171.45	32
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	6,879	$ 227,063.17	67
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	5,790	$ 62,797.91	59
IBUPROFEN*	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,584	$ 43,788.61	18
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,306	$ 65,536.82	39
CEFDINIR	CEPHALOSPORINS	5,174	$ 397,468.16	68
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,545	$ 31,783.54	8
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,910	$ 30,484.45	24
CEPHALEXIN*	CEPHALOSPORINS	3,472	$ 51,032.55	22
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,437	$ 332,761.71	140
PROAIR HFA*	BETA-ADRENERGIC AGONISTS	3,265	$ 138,693.03	14
ACETAMINOPHEN-CODEINE*	OPIATE AGONISTS	3,182	$ 26,308.88	43
CHERATUSSIN AC	ANTITUSSIVES	3,062	$ 15,520.62	105
AMLODIPINE BESYLATE*	DIHYDROPYRIDINES	2,916	$ 20,045.11	~
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,746	$ 49,778.47	50
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,746	$ 429,218.92	34
LISINOPRIL*	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,702	$ 12,897.87	2
OMEPRAZOLE*	PROTON-PUMP INHIBITORS	2,652	$ 156,146.97	15
VYVANSE*	AMPHETAMINES	2,637	$ 359,971.42	97
TOTAL TOP 25		151,877	$ 4,944,667.64	

Total Rx Claims From 02/01/10-02/28/10	430,404

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

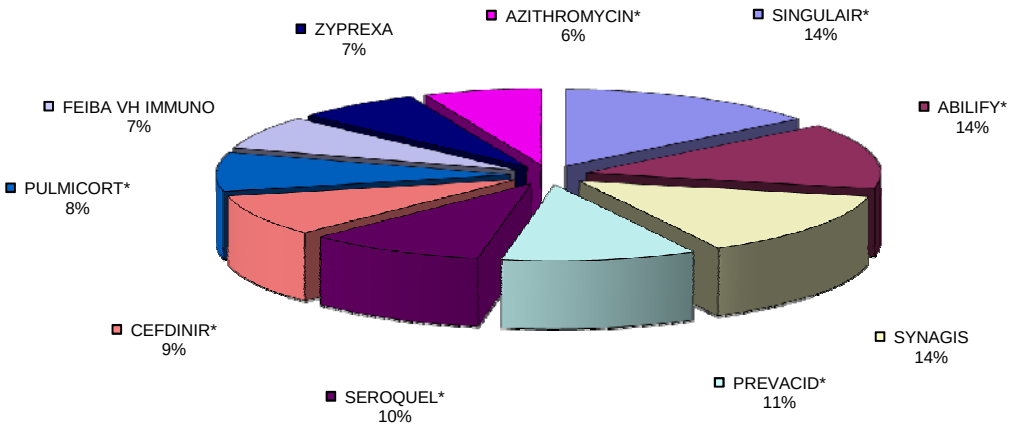
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 12/01/09-12/31/09

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,907	$ 1,044,954.07	7
ABILIFY*	ANTIPSYCHOTIC AGENTS	2,003	$ 1,005,979.65	12
SYNAGIS	MONOCLONAL ANTIBODIES	628	$ 1,003,231.92	~
PREVACID*	PROTON-PUMP INHIBITORS	4,417	$ 772,209.55	5
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,859	$ 705,359.83	6
CEFDINIR*	CEPHALOSPORINS	8,697	$ 636,813.81	17
PULMICORT*	ADRENALS	1,881	$ 594,137.53	55
FEIBA VH IMMUNO	HEMOSTATICS	6	$ 511,403.25	~
ZYPREXA	ANTIPSYCHOTIC AGENTS	801	$ 491,326.89	15
AZITHROMYCIN*	MACROLIDES	15,557	$ 467,646.29	3
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	2,747	$ 432,637.23	33
HUMATE-P	HEMOSTATICS	5	$ 407,109.21	~
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,659	$ 353,932.35	24
DEXTROAMPHETAMINE-AMPH	AMPHETAMINES	1,923	$ 345,446.19	~
AMOX TR-POTASSIUM CLAVU	PENICILLINS	6,655	$ 331,686.70	10
VYVANSE*	AMPHETAMINES	2,539	$ 325,174.03	96
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,615	$ 319,870.06	4
GEODON*	ANTIPSYCHOTIC AGENTS	766	$ 317,445.25	45
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	8,291	$ 267,841.13	63
ATRIPLA	ANTIRETROVIRALS	171	$ 254,223.46	39
HYDROCODONE-ACETAMINOI	OPIATE AGONISTS	17,174	$ 247,544.11	1
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,622	$ 245,380.73	3
EXJADE	HEAVY METAL ANTAGONISTS	53	$ 235,240.95	~
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	1,726	$ 234,113.04	113
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,150	$ 202,075.78	78
TOTAL TOP 25		94,852	$ 11,752,783.01	

Total Rx Claims From 12/01/09-12/31/09	443,713

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

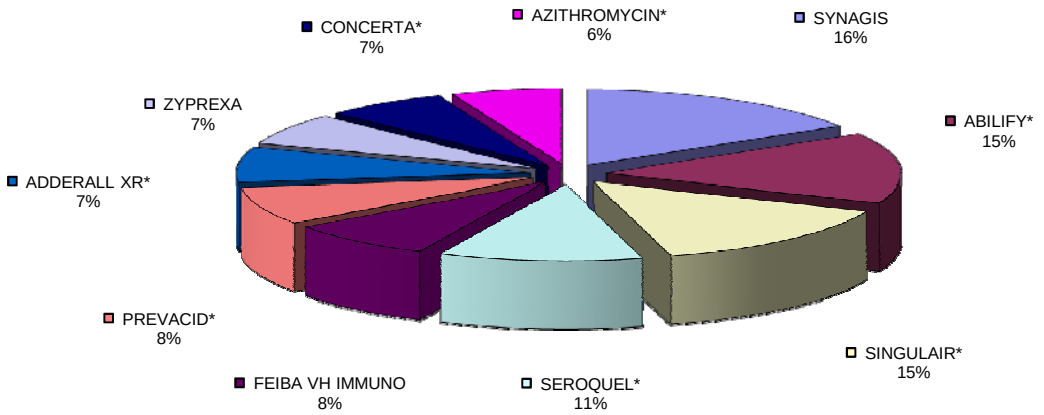
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 01/01/10-01/31/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SYNAGIS	MONOCLONAL ANTIBODIES	659	$ 1,063,929.36	~
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,857	$ 972,971.33	12
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,059	$ 948,422.63	7
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,808	$ 726,059.28	6
FEIBA VH IMMUNO	HEMOSTATICS	7	$ 526,119.05	~
PREVACID*	PROTON-PUMP INHIBITORS	2,977	$ 518,339.37	5
ADDERALL XR*	AMPHETAMINES	2,299	$ 486,820.53	23
ZYPREXA	ANTIPSYCHOTIC AGENTS	736	$ 441,057.88	15
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	2,808	$ 438,686.67	33
AZITHROMYCIN*	MACROLIDES	13,287	$ 393,391.46	3
CEFDINIR	CEPHALOSPORINS	5,318	$ 389,779.29	17
VYVANSE*	AMPHETAMINES	2,554	$ 343,201.78	96
BUDESONIDE	ADRENALS	1,322	$ 339,738.51	~
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,543	$ 337,852.24	24
GEODON*	ANTIPSYCHOTIC AGENTS	720	$ 326,114.67	45
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,529	$ 310,962.72	4
AMOX TR-POTASSIUM CLAV*	PENICILLINS	5,900	$ 296,083.91	10
PULMICORT*	ADRENALS	781	$ 285,537.47	55
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	1,808	$ 261,528.20	113
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,610	$ 242,748.29	3
ATRIPLA	ANTIRETROVIRALS	158	$ 239,125.72	39
HYDROCODONE-ACETAMIN*	OPIATE AGONISTS	16,382	$ 235,823.24	1
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	6,685	$ 226,232.21	63
LANSOPRAZOLE*	PROTON-PUMP INHIBITORS	1,682	$ 225,493.86	~
EXJADE	HEAVY METAL ANTAGONISTS	43	$ 212,315.87	~
TOTAL TOP 25		84,532	$ 10,788,335.54	

Total Rx Claims From 01/01/10-01/31/10	412,765

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

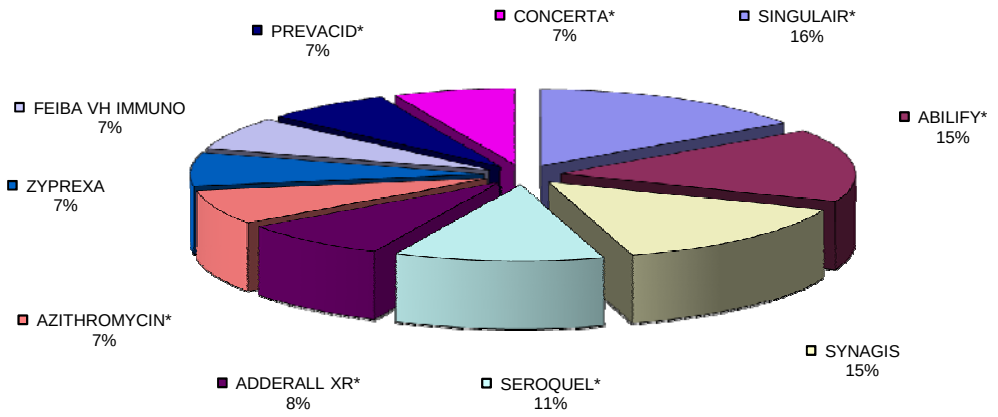
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 02/01/10-02/28/10

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,102	$ 998,129.44	7
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,881	$ 997,942.27	12
SYNAGIS	MONOCLONAL ANTIBODIES	568	$ 934,056.52	~
SEROQUEL*	ANTIPSYCHOTIC AGENTS	1,781	$ 739,926.02	6
ADDERALL XR*	AMPHETAMINES	2,477	$ 528,377.71	23
AZITHROMYCIN*	MACROLIDES	15,974	$ 473,775.37	3
ZYPREXA	ANTIPSYCHOTIC AGENTS	747	$ 455,934.78	15
FEIBA VH IMMUNO	HEMOSTATICS	7	$ 446,119.10	~
PREVACID*	PROTON-PUMP INHIBITORS	2,570	$ 445,264.59	5
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	2,746	$ 429,218.92	33
CEFDINIR	CEPHALOSPORINS	5,174	$ 397,468.16	17
BUDESONIDE	ADRENALS	1,532	$ 396,742.27	~
AMOX TR-POTASSIUM CLAV*	PENICILLINS	7,197	$ 366,171.45	10
VYVANSE*	AMPHETAMINES	2,637	$ 359,971.42	96
RISPERIDONE*	ANTIPSYCHOTIC AGENTS	3,437	$ 332,761.71	24
GEODON*	ANTIPSYCHOTIC AGENTS	718	$ 322,577.41	45
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,532	$ 316,261.15	4
LANSOPRAZOLE*	PROTON-PUMP INHIBITORS	2,066	$ 278,327.24	~
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MIS	1,810	$ 266,341.40	113
PULMICORT*	ADRENALS	636	$ 249,207.42	55
ATRIPLA	ANTIRETROVIRALS	163	$ 248,305.51	39
HUMATE-P	HEMOSTATICS	5	$ 243,736.96	~
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,528	$ 240,693.26	3
HYDROCODONE-ACETAMIN*	OPIATE AGONISTS	15,793	$ 228,129.53	1
ALBUTEROL SULFATE*	BETA-ADRENERGIC AGONISTS	6,879	$ 227,063.17	63
TOTAL TOP 25		87,960	$ 10,922,502.78	

Total Rx Claims	430,404
From 02/01/10-02/28/10	

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



Duplicate Atypical Antipsychotic Therapy in Pediatric Beneficiaries

Data regarding atypical antipsychotic use has been presented to the DUR Board over the last several years in many varying forms, including off-label use in ADHD and/or ODD, duplicate therapy with oral and long-acting injectable formulations, and concerns of increased risk of metabolic adverse effects with atypical antipsychotic use. At the 1st Quarter 2010 DUR Board meeting, data was presented indicating that duplicate therapy with multiple atypical antipsychotics may be a concern in Mississippi Medicaid beneficiaries. Although there are currently RDUR criteria in place to monitor the incidence of duplicate therapy, DUR Board members felt that it may still be necessary to implement duplicate therapy edits at the point of sale to prohibit duplicate therapy with multiple agents without prior authorization. Additionally, DOM and HID pharmacists recently attended the 2010 American Drug Utilization Review Symposium in February 2010, where a nationally recognized expert in pediatric bipolar disorder, Dr. Kiki Chang, presented information pertaining to pediatric mental health. Dr. Chang specifically pointed out that although children with bipolar disorder typically require more than one agent for the management of their disorder, prescribers should avoid using two or more atypical antipsychotics concurrently.

Based on this revelation, HID analyzed claims data to determine the incidence of duplicate atypical antipsychotic therapy in pediatric Mississippi Medicaid beneficiaries. Claims for calendar year 2009 for beneficiaries under the age of 18 were reviewed to determine how many beneficiaries received more than one atypical antipsychotic and for how long the duplicate therapy occurred. The results are provided in the table below.

Duration of Duplicate Therapy	Beneficiary Count	% of Total Beneficiaries
30 days	262	3.6%
60 days	165	2.3%
90 days	105	1.4%
120 days	74	1%

A total of 7,308 beneficiaries 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 with atypical antipsychotics appears to be minimal, based on these results. However, when considering the potential metabolic and extrapyramidal effects associated with this therapeutic class in conjunction with expert opinion that duplicate therapy in pediatric patients should be discouraged, the implementation of duplicate therapy edits at the point of sale may need to be considered.

Recommendation

HID recommends establishing edits at the point of sale that prohibit duplicate therapy with two or more atypical antipsychotics in pediatric beneficiaries. This 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.

Attention Deficit Hyperactivity Disorder: A Medicaid Prescribing Update

ADHD agents continue to be one of the most utilized therapeutic classes within the Mississippi Medicaid population, with agents within this class consistently appearing in the cost analyses presented to the DUR Board. Scrutiny also exists regarding the potential overprescribing of ADHD agents, particularly in young children. Information presented at the 1st Quarter 2010 DUR Board meeting led to fervent discussions about proper diagnosis and treatment of ADHD.

One of the requests that stemmed from the discussions at this meeting was the development of a Medicaid Prescribing Update that outlines 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.

HID developed the following Medicaid Prescribing Update based on the *Clinical Practice Guideline: Diagnosis and Evaluation of the Child with Attention Deficit/Hyperactivity Disorder* from the American Academy of Pediatrics in May 2000. This Medicaid Prescribing Update will be distributed to prescribers by the HID Academic Detailers; it will also be available, along with others on additional topics, by a link from the Division of Medicaid website.

Prescribing Information Update

Attention Deficit/Hyperactivity Disorder (ADHD)

Mississippi Division of Medicaid

- *The core symptoms of ADHD include inattention, hyperactivity and impulsivity.*
- *According to the AAP, a child should meet the DSM-IV criteria in order to be diagnosed with ADHD.*
- *Prior authorization, including an appropriate diagnosis, is required for **all** ADHD agents for beneficiaries ≥ 21 years old.*
- *Beginning 7/15/10, Mississippi Medicaid will implement quantity limits for the ADHD therapeutic class.*

Attention deficit/hyperactivity disorder (ADHD) is one of the most common chronic health conditions that affects school-aged children. Children with ADHD tend to experience considerable functional problems such as school difficulties, academic underachievement, and troubled interpersonal relationships. The core symptoms of ADHD include inattention, hyperactivity, and impulsivity. Because symptoms of ADHD often continue into adolescence and adulthood, early recognition and treatment of the disorder are vital, as proper treatment can redirect the educational, psychological and social development of children with ADHD.

AAP Guidelines for the Diagnosis/Evaluation of Children with ADHD

The American Academy of Pediatrics published clinical guidelines for the diagnosis and evaluation of children with ADHD in May 2000. These guidelines are summarized below.

- A child that presents to a primary care provider with inattention, hyperactivity, impulsivity, academic underachievement, or behavior problems should be evaluated for ADHD.
- In order for a diagnosis of ADHD to be made, the child must meet DSM-IV criteria for such a diagnosis. This strategy is recommended in order to minimize inappropriate diagnoses of ADHD, by decreasing the variation in how a diagnosis is made.
- The assessment of a child suspected to have ADHD should include reports obtained directly from the parents/caregivers and classroom schoolteacher (or other school professional) regarding the core symptoms of ADHD in various settings, the age on onset, duration of symptoms, and the degree of functional impairment.
- Evaluation of the child for ADHD should also include assessment for other coexisting conditions, such as oppositional defiant disorder, anxiety disorder, and depression.
- Other diagnostic tests, such as blood lead levels, thyroid hormone levels, and brain imaging, are not routinely indicated for establishment of an ADHD diagnosis.
- Children who present with behavioral symptoms of ADHD but do not suffer from functional impairment ***do not*** meet diagnostic criteria for ADHD.
- Although ADHD rating scales can be helpful in the evaluation of a child for ADHD, their results may be inaccurate due to the subjective nature of the questions and must be interpreted in context of the overall evaluation of the child.

Mississippi Medicaid: Preferred ADHD Agents

The ADHD agents are addressed by the Mississippi Medicaid Preferred Drug List. The preferred products on the Mississippi Medicaid PDL are provided in the chart below.

Short-acting stimulants	Amphetamine salt combination, dexmethylphenidate IR, dextroamphetamine IR, Focalin®, Methylin® chewable tablets and solution, methylphenidate IR
Long-acting stimulants	Adderall XR®, Concerta®, Daytrana®, Focalin XR®, Metadate CD®, methylphenidate ER, Vyvanse®
Non-stimulants	Intuniv®

- Prior authorization with an appropriate diagnosis is required for all ADHD agents for beneficiaries ≥ 21 years old.
- Prior authorization is required for beneficiaries under the FDA-approved age for each ADHD agent.
- Beginning 7/15/10, quantity limits will be implemented for the ADHD agents. For a complete listing of these limits, please visit http://www.medicaid.ms.gov/Documents/Pharmacy/ProductswQuantityLimits.pdf .

References:

Clinical Practice Guidelines: Diagnosis and Evaluation of the Child with Attention Deficit/Hyperactivity Disorder. Pediatrics, Vol 105, No 5, May 2000.

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.

The Role of Lipotropics in the Treatment of Cardiovascular Disease

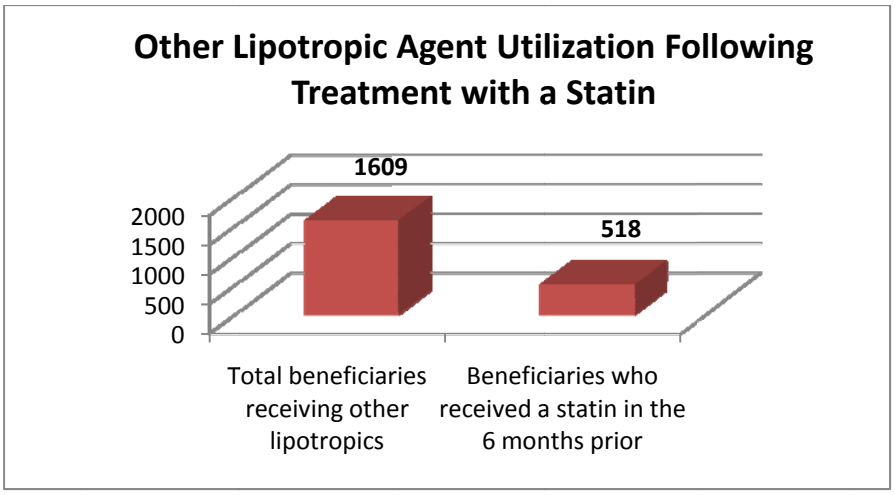
During the March 2010 Pharmacy and Therapeutics (P & T) Meeting, there were discussions regarding the role of non-statin lipotropics in the treatment of cardiovascular disease. The point was raised that, although these agents lower LDL, non-statin lipotropics have not been proven to reduce morbidity and mortality related to cardiovascular disease. Several P & T Committee members agreed that 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. As mentioned in the discussion, there seems to be a false sense of protection of the patient's wellbeing for both the prescriber and the patient.

Based on this discussion, the P & T Committee and DOM are requesting that the DUR Board review the utilization of this class to determine if the non-statin lipotropics were being used appropriately. If the data analysis verify improper utilization of the non-statin lipotropics, P&T Committee members wanted to identify what steps may be necessary to encourage appropriate use and improve outcomes for Mississippi Medicaid beneficiaries. P & T committee members outlined two particular areas that should be covered in this analysis:

1) Are beneficiaries being given a trial of a statin prior to attempting treatment with a non-statin lipotropic?
2) Of those beneficiaries being treated with a non-statin lipotropic, how many have a hypertriglyceridemia diagnosis?

1) Prior treatment with a statin

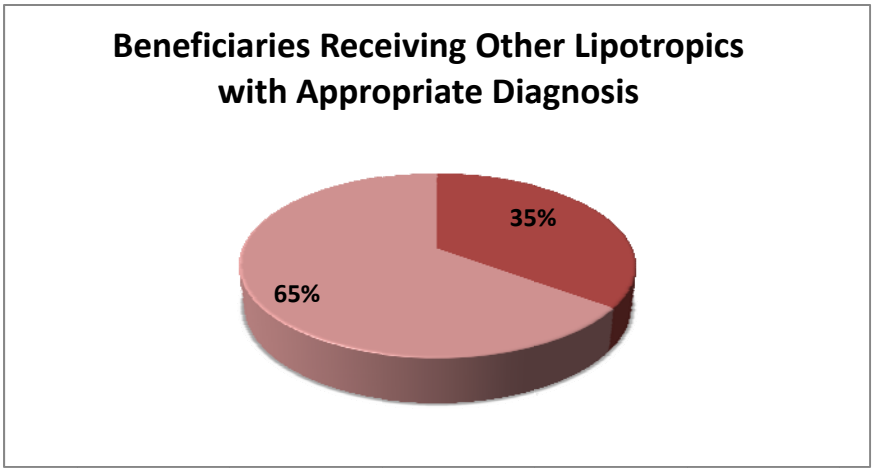
The ATP III Final Report from the National Heart Lung and Blood Institute supports the use of statins as first-line therapy for LDL-reduction based on results from 5 large clinical trials. These trials showed a documented decrease in cardiovascular disease and total mortality as well as reductions in myocardial infarctions, revascularization procedures, stroke, and peripheral vascular disease across all genders and ages with statin therapy. P & T committee members agreed that statins should be the first line treatment for a beneficiary with high cholesterol due to the strong data confirming their ability to decrease morbidity and mortality in cardiovascular disease. These members wanted to know if Mississippi Medicaid beneficiaries were in fact being treated with a statin first before moving on to other lipotropic therapies. HID gathered utilization data of the non-statin lipotropics from 7/1/09 – 12/31/09 and the statins from 1/1/09 – 6/30/09 and then compared the data to determine if this was the case. The chart below illustrates the findings of this analysis.



Of the 1609 beneficiaries who received a non-statin lipotropic from 7/1/09 – 12/31/09, 518 (32%) received a statin in the prior 6 months. This would indicate that a majority of Mississippi Medicaid beneficiaries being treated with non-statin lipotropics have not been given a trial of a statin prior to initiating therapy with the other lipotropics.

2) Hypertriglyceridemia

P & T committee members acknowledged that the non-statin lipotropics are an important tool in managing hypertriglyceridemia and that prescribers should not be required to attempt treatment with a statin prior to initiating therapy with other lipotropics in beneficiaries affected with this disease. According to the ATP III Final Report, however, statins should be used first-line 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 ATP III Final Report does recommend the use of fibrates or nicotinic acid as first-line therapy to lower triglyceride levels. P&T committee members were not confident that utilization of these agents in the Mississippi Medicaid population could be attributed to a hypertriglyceridemia diagnosis. As such, HID agreed to analyze utilization data of the non-statin lipotropics to determine what percentage of utilization could be credited to a hypertriglyceridemia diagnosis. The chart below illustrates the findings of this analysis.



As the chart above shows, 35% of Mississippi Medicaid beneficiaries receiving a non-statin lipotropic have a documented diagnosis of elevated triglycerides. Based on these findings, it appears that the assumption of P & T committee members that most utilization of these agents cannot be attributed to a hypertriglyceridemia diagnosis was correct.

Conclusion

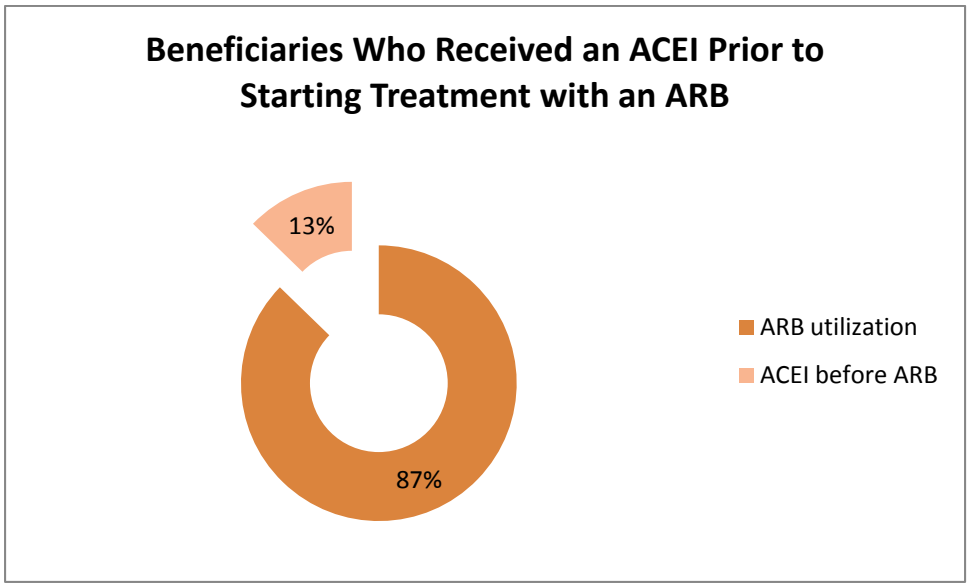
Mississippi Medicaid P & T Committee members voiced concerns at the March 2010 meeting regarding appropriate utilization of the non-statin lipotropics. As shown earlier, it appears that a majority of beneficiaries receiving these medications had not been tried on a statin and/or did not have a hypertriglyceridemia diagnosis. DOM is requesting direction from the DUR Board regarding promoting appropriate use of the non-statin lipotropics in the Mississippi Medicaid population.

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

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) play an important role in the management of hypertension and heart disease. A review of the literature shows that ACEIs and ARBs appear to provide added benefit beyond blood pressure lowering in those patients with hypertension accompanied by other comorbidities, such as heart failure, myocardial infarction, diabetes, chronic kidney disease and stroke. Clinical trials have also shown that ACEIs and ARBs may also be beneficial in the prevention of diabetes, atrial fibrillation and recurrent stroke.

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 JNC 7 report and the ACC/AHA Heart Failure guidelines both recommend ACEI as the primary therapy over ARBs.

Consequently, DOM asked HID to review the utilization data for these agents to determine what percentage of Mississippi Medicaid beneficiaries received an ACEI before attempting treatment with an ARB. HID gathered utilization data for the ACEIs from 1/1/09 through 6/30/09 and for the ARBs from 7/1/09 through 12/31/09. These searches were then intersected to identify the number of beneficiaries who received an ACEI before starting treatment with an ARB. The results of this analysis are included below.



From 7/1/09 through 12/31/09, **7,050** beneficiaries received an ARB through the Mississippi Medicaid pharmacy benefit. Of these beneficiaries, **899 (13%)** received an ACEI in the six months prior to this search. It appears that an overwhelming majority of Mississippi Medicaid beneficiaries being treated with an ARB for hypertension and/or heart disease have not been managed based on current treatment guidelines and medical literature. While some of the beneficiaries identified in this search being treated with an ARB may have been receiving ARB therapy for a prolonged period of time and attempted

treatment with an ACEI in months or years before the time periods selected for this report, the argument could be made that inclusion of these beneficiaries would still not constitute a majority of beneficiaries who were identified by this search being treated with an ARB.

Conclusion

In April, P&T Committee members recommended that Mississippi Medicaid require beneficiaries to attempt and fail treatment with an ACEI before starting therapy with an ARB, based on current literature and treatment guidelines that maintain that ARBs do not provide any additional clinical benefit over ACEIs. Based on the data presented in this report, it appears that most Mississippi Medicaid beneficiaries are not being treated in accordance with these guidelines. DOM would like to know what steps the DUR Board feels may be necessary to promote appropriate use of ARBs in the Mississippi Medicaid population.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2nd QUARTER 2010

Criteria Recommendations	*Approved*	*Rejected*

1. Milnacipran / Over-utilization _____ _____

Alert Message: The recommended dose of Savella (milnacipran) is 100 mg per day given in two divided doses. Milnacipran therapy should always begin with dosing at 12.5 mg and increase to 100 mg per day over a 1-week period. The daily dose may be increased to 200 mg per day based on individual response.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

Max Dose: 200 mg per day

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

2. Milnacipran / Nonadherence _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Savella (milnacipran) may result in loss of therapeutic effect.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

Less than 75 days in 90 day review.

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

3. Milnacipran / Monoamine Oxidase Inhibitors _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a monoamine oxidase inhibitor (MAOI) is contraindicated. Milnacipran has serotonin reuptake inhibitor activity and the use of this agent with a MAOI may cause a rapid, excessive accumulation of serotonin resulting in serious, sometimes, fatal reactions. Milnacipran should not be used within 14 days of discontinuing an MAOI and at least 5 days should elapse after stopping milnacipran before starting an MAOI.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Isocarboxazid	
	Tranylcypromine	
	Phenelzine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

Criteria Recommendations ***Approved Rejected***

4. Milnacipran / Risk of Suicide (Black Box Warning) _____ _____

Alert Message: Savella (milnacipran) is a selective serotonin and norepinephrine reuptake inhibitor (SNRI), similar to some drugs used for the treatment of depression and other psychiatric disorders. SNRIs may increase the risk compared to placebo of suicidal thinking and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Monitor patients closely for unusual changes in behavior.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

References:
Savella Prescribing Information, Jan 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

5. Milnacipran / Uncontrolled Narrow Angle Glaucoma _____ _____

Alert Message: The use of Savella (milnacipran) is contraindicated in patients with uncontrolled narrow angle glaucoma. In clinical trials, milnacipran was associated with an increased risk of mydriasis. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and mydriasis has been reported with other dual reuptake inhibitors agents.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Narrow Angle Glaucoma	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

6. Milnacipran / Serotonergic Drugs _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a serotonergic drug is not recommended. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin and increase the risk of serotonin syndrome (e.g., mental status changes, hypertension, vasoconstriction, and neuronal aberrations).

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Milnacipran	Triptans	TCAs	
	Tramadol	Mirtazapine	
	SSRIs	Bupropion	
	SNRIs	Trazodone	
	Nefazodone	Codeine	
	Fentanyl	Zyvox	
	Lithium		

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations ***Approved Rejected***

7. Milnacipran / Clonidine _____ _____

Alert Message: Concurrent use of Savella (milnacipran) and clonidine may result in the loss of blood pressure control. Clonidine acts to decrease norepinephrine (NE) release in the brain which leads to a reduction in arterial blood pressure. Milnacipran inhibits NE reuptake, thereby increasing NE levels and inhibiting the effects of clonidine.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Clonidine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

8. Milnacipran / Seizures _____ _____

Alert Message: Savella (Milnacipran) should be used with caution in patients with a history of seizure disorders. Seizures have been reported, infrequently, in patients treated with milnacipran for disorders other than fibromyalgia.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Seizures	
	Epilepsy	
	Convulsions	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

9. Milnacipran / Hypertension _____ _____

Alert Message: Savella (milnacipran) may cause elevated blood pressure and heart rate. Monitor blood pressure and heart rate prior to initiating milnacipran therapy and periodically throughout treatment.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Hypertension ICD-9	
	Beta Blockers	
	ACE Inhibitors	
	ARBs	
	Diuretics	
	Calcium Channel Blockers	
	Antiadrenergic Agents - Centrally Acting & Peripherally	
	Peripheral Vasodilators	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

Criteria Recommendations ***Approved Rejected***

10. Febuxostat / Over utilization _____ _____

Alert Message: The recommended starting dose of Uloric (febuxostat) is 40 mg once daily and may be increased to 80 mg once daily in patients who do not achieve a serum uric acid (sUA) less than 6 mg per dL after 2 weeks with the 40 mg. Exceeding the recommended daily dose may cause a risk of adverse effects (e.g., rash, arthralgia, nausea, and liver function abnormalities).

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Max Dose: 80 mg per day

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

11. Febuxostat / Nonadherence _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Uloric (febuxostat) may result in loss of therapeutic effect.

Conflict Code: LR – Underutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Less than a 75 day supply in 90 days

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

12. Febuxostat / Azathioprine, Mercaptopurine & Theophylline _____ _____

Alert Message: Uloric (febuxostat) is contraindicated in patients being treated with drugs metabolized by xanthine oxidase (i.e., azathioprine, mercaptopurine, and theophylline). Febuxostat is a xanthine oxidase (XO) inhibitor and concurrent use of febuxostat with drugs metabolized by XO may cause substantially increased plasma concentrations of the XO metabolized drug leading to severe toxicity.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Febuxostat	Azathioprine Mercaptopurine Theophylline	

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

Criteria Recommendations ***Approved Rejected***

13. Febuxostat / Cardiovascular Events (Warning) _____ _____
Alert Message: In clinical trials, patients treated with Uloric (febuxostat) had a higher rate of cardiovascular thromboembolic events than allopurinol-treated patients. Monitor patients for signs and symptoms of MI or stroke.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A Util B Util C
Febuxostat

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

14. Febuxostat / Liver Enzyme Elevation (Warning) _____ _____
Alert Message: It is recommended that patients receiving Uloric (febuxostat) receive laboratory assessment of liver function at 2 and 4 months following Initiation of febuxostat and periodically thereafter. In controlled studies, elevated transaminase elevations were observed and were the most common adverse event that led to discontinuation of the drug.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A Util B Util C
Febuxostat

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

15. Liraglutide / Over-utilization _____ _____
Alert Message: The recommended maximum dose of Victoza (liraglutide) is 1.8 mg per day. Exceeding this dose may result in the increased risk of adverse effects (e.g. nausea and vomiting).

Conflict Code: ER – Overuse
Drug/Disease
Util A Util B Util C
Liraglutide

Max Dose: 1.8 mg/day

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

16. Liraglutide / Non-adherence _____ _____
Alert Message: Non-adherence to Victoza (liraglutide) therapy may result in loss of glycemic control and an increased risk of developing adverse diabetic-related complications.

Conflict Code: LR - Nonadherence
Drug/Disease
Util A Util B Util C
Liraglutide

Nonadherence: ≤ 75% refill in current 90 days

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

Criteria Recommendations ***Approved Rejected***

17. Liraglutide / Black Box Warning – Thyroid Cancer _____ _____

Alert Message: Victoza (liraglutide) causes thyroid C-cell tumors in clinically relevant exposure in rodents. It is unknown whether liraglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans. Counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness).

Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease

Util A	Util B	Util C
Liraglutide		

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

18. Liraglutide / Medullary Thyroid Carcinoma & Multiple Endocrine Neoplasia Syndrome (Black Box Contraindication) _____ _____

Alert Message: Victoza (liraglutide) is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome. Liraglutide has been shown to cause thyroid C-cell tumors in rats, the human relevance is unknown. It is recommended to counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness).

Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning-Contraindication)
Drug/Disease

Util A	Util B	Util C
Liraglutide	Medullary Thyroid Carcinoma	
	Multiple Endocrine Neoplasia Syndrome	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

19. Liraglutide / Type 1 Diabetes & Ketoacidosis _____ _____

Alert Message: Victoza (liraglutide) should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Drug/Disease

Util A	Util B	Util C
Liraglutide	Type 1 Diabetes ICD-9s	
	Ketoacidosis ICD-9	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

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

20. Liraglutide / Insulin Secretagogues _____ _____

Alert Message: The coadministration of Victoza (liraglutide) and an insulin secretagogue may increase the risk of hypoglycemia. Consider lowering the dose of the insulin secretagogue to reduce the risk.

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

Util A	Util B	Util C
Liraglutide	Repaglinide	
	Nateglinide	
	Chlorpropamide	
	Glimepiride	
	Glipizide	
	Glyburide	
	Tolazamide	
	Tolbutamide	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

21. Liraglutide / Pancreatitis _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with a history of pancreatitis. In clinical trials, there were more cases of pancreatitis among liraglutide-treated patients than placebo-treated. Counsel patients on symptoms of pancreatitis. If pancreatitis is suspected during liraglutide therapy, liraglutide and any other suspect drugs should be discontinued.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drug/Disease

Util A	Util B	Util C
Liraglutide	Pancreatitis	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

22. Liraglutide / Pediatric Patients _____ _____

Alert Message: Safety and efficacy of Victoza (liraglutide) have not been established in pediatric patients and the drug is therefore not recommended for use in this population.

Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease

Util A	Util B	Util C
Liraglutide		

Age Range: 0 – 18 year of age
References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

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

23. Liraglutide / Renal Impairment _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with renal impairment due to limited data for the drug in this population. Compared to healthy subjects, liraglutide AUC in mild, moderate, and severe renal impairment and ESRD was on average 35%, 19%, 29% and 30% lower, respectively.

Conflict Code: DB – Drug/Drug Marker and/or Diagnosis Precaution/Warning Drug/Disease

Util A	Util B	Util C
Liraglutide	Renal Impairment ICD-9s	
	Fosrenol	
	PhosLo	
	Zemplar	
	Renagel	
	Renvela	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

24. Liraglutide / Hepatic Impairment _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with hepatic impairment due to limited data for the drug in this population. Compared to healthy subjects, liraglutide AUC in subjects with mild, moderate and severe hepatic impairment was on average 11%, 14% and 42% lower, respectively.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning Drug/Disease

Util A	Util B	Util C
Liraglutide	Hepatic Impairment	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

25. Liraglutide / Gastroparesis _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with gastroparesis. Liraglutide slows gastric emptying and may exacerbate the condition.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning Drug/Disease

Util A	Util B	Util C
Liraglutide	Gastroparesis	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

Criteria Recommendations ***Approved Rejected***

26. Liraglutide / Oral Drugs _____ _____

Alert Message: Caution should be exercised when Victoza (liraglutide), a GLP-1 receptor agonist, is coadministered with oral medications. Liraglutide causes delayed gastric emptying and has the potential to impact the rate and extent of absorption of the oral agent.

Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease

Util A	Util B	Util C
Liraglutide		

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

27. Raltegravir / Non-Preferred Dual NRTIs/ Truvada _____ _____

Alert Message: The preferred INSTI-based antiretroviral regimen for treatment-naïve HIV-1 infected patients involves raltegravir plus 2 NRTIs, preferably tenofovir plus emtricitabine. The use of raltegravir with other dual NRTIs (such as abacavir/lamivudine or zidovudine/lamivudine) may be acceptable, but more definitive data for these regimens are needed.

Conflict Code: DD - Appropriate Drug Combination
Drug/Disease:

Util A	Util B	Util C (Negating)
Raltegravir	Zidovudine/Lamivudine	Tenofovir/Emtricitabine
	Lamivudine/Abacavir	
	Didanosine	
	Stavudine	
	Abacavir	
	Zidovudine	
	Lamivudine	
	Emtricitabine	
	Tenofovir	
	Zidovudine/Lamivudine/Abacavir	

References:
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents - A Working Group of the Office of AIDS Research Advisory Council. December 1, 2009.

**All existing HAART criteria have been updated – this is new guideline recommendation involving raltefravir.

28. PrandiMet / Nonadherence _____ _____

Alert Message: Non-adherence to PrandiMet (repaglinide/metformin) therapy may result in loss of glycemic control and an increased risk of developing adverse diabetic-related complications.

Conflict Code: LR - Nonadherence
Drug/Disease:

Util A	Util B	Util C
Repaglinide/Metformin		

References:
Lau DT, Nau DP, Oral Antihyperglycemic Medication Nonadherence and Subsequent Hospitalization Among Individuals with Type 2 Diabetes, Diabetes Care. 27:2149-2153, 2004.
Miller KE, Medication Nonadherence Affects Diabetes Treatment, Am Family Phys. Vol. 75 No. 6, March 15, 2007.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus, Cardiology Review, April 2007.

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.

Alli 60 mg capsules (120 count refill kit): Counterfeit Product

FDA notified consumers and healthcare professionals about a counterfeit and potentially harmful version of Alli 60 mg capsules (120 count refill kit). The counterfeit version contained the controlled substance sibutramine and did not contain orlistat, the active ingredient. Sibutramine is a drug that should not be used in certain patient populations or without physician oversight. Sibutramine can also interact in a harmful way with other medications the consumer may be taking. GSK has determined that the counterfeit product has been sold over the internet. However, there is no evidence at this time that the counterfeit Alli product has been sold through other channels, such as retail stores. The differences between the counterfeit and authentic products are described in both text and photos in the FDA news release.

Consumers who believe they have received counterfeit Alli are asked to contact the FDA's Office of Criminal Investigations (OCI) by calling 800-551-3989 or by visiting the OCI Web site (http://www.fda.gov/OCI).

Any adverse events that may be related to use should be reported to the FDA's MedWatch Safety Information and Adverse Event Reporting Program online [at www.fda.gov/MedWatch/report.htm], by phone 1-800-332-1088, or by returning the postage-paid FDA form 3500 [which may be downloaded

from the MedWatch "Download Forms" page] by mail [to address on the pre-addressed form] or fax [1-800-FDA-0178].

Meridia (sibutramine hydrochloride): Follow-Up to an Early Communication about an Ongoing Safety Review

FDA notified healthcare professionals that the review of additional data indicates an increased risk of heart attack and stroke in patients with a history of cardiovascular disease using sibutramine. Based on the serious nature of the review findings, FDA requested and the manufacturer agreed to add a new contraindication to the sibutramine drug label stating that sibutramine is not to be used in patients with a history of cardiovascular disease, including:

- History of coronary artery disease (e.g., heart attack, angina)
- History of stroke or transient ischemic attack (TIA)
- History of heart arrhythmias
- History of congestive heart failure
- History of peripheral arterial disease
- Uncontrolled hypertension (e.g., > 145/90 mmHg)

Patients currently using sibutramine should talk with their healthcare professional to determine if continued use of sibutramine is appropriate and discuss any questions they may have about their treatment.

Nipro GlucoPro Insulin Syringes: Recall

Nipro Medical Corporation and FDA notified healthcare professionals of a voluntary nationwide recall of all GlucoPro Insulin Syringes. These syringes may have needles that detach from the syringe. If the needle becomes detached from the syringe during use, it can become stuck in the insulin vial, push back into the syringe, or remain in the skin after injection. This recall includes all product codes and lot numbers with expiration dates before 2011-11 (November 1, 2011). Product was distributed nationwide, including Puerto Rico. Consumers who have GlucoPro Insulin Syringes should stop using and return them to point of sale for reimbursement.

Zyprexa (olanzapine): Use in Adolescents

Lilly and FDA notified healthcare professionals of changes to the Prescribing Information for Zyprexa related to its indication for use in adolescents (ages 13-17) for treatment of schizophrenia and bipolar I disorder [manic or mixed episodes]. The revised labeling states that:

> Section 1, Indications and Usage: When deciding among the alternative treatments available for adolescents, clinicians should consider the increased potential (in adolescents as compared with adults) for weight gain and hyperlipidemia. Clinicians should consider the potential long-term risks when prescribing to adolescents, and in many cases this may lead them to consider prescribing other drugs first in adolescents.
>
> Section 17.14, Need for comprehensive Treatment Program in Pediatric Patients: Zyprexa is indicated as an integral part of a total treatment program for pediatric patients with schizophrenia and bipolar disorder that may include other measures (psychological, educational, social) for patients with the disorder. Effectiveness and safety of ZYPREXA have not been established in pediatric patients less than 13 years of age.

Videx/Videx EC (didanosine): Labeling Revision - Risk of Non-Cirrhotic Portal Hypertension

FDA notified healthcare professionals and patients about a rare, but serious, complication in the liver known as non-cirrhotic portal hypertension in patients using Videx or Videx EC (didanosine), a

medication used to treat human immunodeficiency virus (HIV) infection. FDA became aware of cases of non-cirrhotic portal hypertension through adverse event reports submitted to FDA's Adverse Event Reporting System. Based on the number of well-documented cases and exclusion of other causes of portal hypertension such as alcohol-related cirrhosis or hepatitis C, FDA concludes there is an association between use of didanosine and development of non-cirrhotic portal hypertension. Because of the potential severity of portal hypertension, including death from hemorrhaging esophageal varices, FDA has revised the Warning and Precautions section of the didanosine drug label to assure safe use of the medication. FDA believes the clinical benefits of didanosine for certain patients with HIV continue to outweigh its potential risks. The decision to use this drug, however, must be made on an individual basis between the treating physician and the patient.

Erythropoiesis-Stimulating Agents (ESAs): Procrit, Epogen and Aranesp: Drug Safety Communication
FDA and Amgen notified healthcare professionals and patients that all ESAs must be used under a REMS risk management program. As part of the risk management program, a Medication Guide explaining the risks and benefits of ESAs must be provided to all patients receiving an ESA. Under the ESA APPRISE Oncology program, Amgen will ensure that only those hospitals and healthcare professionals who have enrolled and completed training in the program will prescribe and dispense ESAs to patients with cancer. Amgen is also required to oversee and monitor the program to ensure that hospitals and healthcare professionals are fully compliant with all aspects of the program. FDA is requiring a REMS because studies show that ESAs can increase the risk of tumor growth and shorten survival in patients with cancer who use these products. Studies also show that ESAs can increase the risk of heart attack, heart failure, stroke or blood clots in patients who use these drugs for other conditions.

Maalox Total Relief and Maalox Liquid Products: Medication Use Errors
FDA notified consumers and healthcare professionals about reports of serious medication errors involving consumers who used Maalox Total Relief when they had intended to use a Maalox liquid antacid product. Maalox Total Relief and the traditional Maalox products are both liquid medications available without a prescription, but are not interchangeable and are intended to treat different medical conditions. Maalox Total Relief is an upset stomach reliever and anti-diarrheal medication, while traditional Maalox liquid products Maalox Advanced Regular Strength and Maalox Advanced Maximum Strength are antacids.
Maalox Total Relief is not appropriate for individuals who want to use an antacid, since it contains the active ingredient bismuth subsalicylate which is chemically related to aspirin and may cause serious adverse effects such as bleeding. Maalox Total Relief should not be used in people who have or have a history of gastrointestinal ulcers or a bleeding disorder. It also should not be taken by children and teens if they are recovering from a viral infection, nor by individuals who are taking certain medications including: oral antidiabetic drugs (OADs), anticoagulation (thinning the blood) drugs such as warfarin (Coumadin) and clopidogrel (Plavix), non-steroidal anti-inflammatory drugs (NSAIDS), and other anti-inflammatory drugs.
The Drug Safety Communication contains additional information for consumers and healthcare professionals, as well as product label photos.

Exjade (deferasirox): Boxed Warning
Novartis Oncology and FDA notified healthcare professionals about recent changes in the Prescribing Information (PI) for Exjade, indicated for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older. New language was added to the Contraindications, Warnings and Precautions, and Drug Interactions sections of the PI, including a Boxed Warning, that the product may cause:

- renal impairment, including failure
- hepatic impairment, including failure
- gastrointestinal hemorrhage

In some reported cases, these reactions were fatal. These reactions were more frequently observed in patients with advanced age, high risk myelodysplastic syndromes, underlying renal or hepatic impairment or low platelet counts. Exjade therapy requires close patient monitoring, including measurement of serum creatinine and/or creatinine clearance as specified in the PI and serum transaminases and bilirubin as specified in the PI.

Long-Acting Beta-Agonists (LABAs): New Safe Use Requirements

FDA notified healthcare professionals and consumers that, due to safety concerns, FDA is requiring a risk management strategy (REMS) and class-labeling changes for all LABAs. The REMS will require a revised Medication Guide written specifically for patients, and a plan to educate healthcare professionals about the appropriate use of LABAs. These changes are based on FDA's analyses of studies showing an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations in pediatric and adult patients as well as death in some patients using LABAs for the treatment of asthma. Healthcare professionals are reminded that to ensure the safe use of these products:

- Single-ingredient LABAs should only be used in combination with an asthma controller medication; they should not be used alone.
- LABAs should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medications.
- LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. Patients should then be maintained on an asthma controller medication.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure compliance with both medications.

FDA has determined that the benefits of LABAs in improving asthma symptoms outweigh the potential risks when used appropriately with an asthma controller medication in patients who need the addition of LABAs. FDA believes the safety measures recommended will improve the safe use of these drugs.

Avandia (rosiglitazone): Ongoing Review of Cardiovascular Safety

FDA notified healthcare professional and patients that it is reviewing the primary data from a large, long-term clinical study, RECORD, on possible cardiovascular risks with the diabetes drug, Avandia (rosiglitazone). In addition to the clinical trial, a number of observational studies of the cardiovascular safety of rosiglitazone have been published and FDA has been reviewing these on an ongoing basis. These reviews are ongoing and no new conclusions or recommendations about the use of rosiglitazone in the treatment of type 2 diabetes have been made at this time. Once FDA completes its review of the data from the RECORD study, the agency will present the totality of new and existing cardiovascular safety data on rosiglitazone at a public meeting in July 2010. The Agency will provide an updated assessment of the risks and benefits of rosiglitazone in the treatment of type 2 diabetes. FDA recommends that healthcare professionals follow the recommendations in the drug label when prescribing rosiglitazone. This includes a Boxed Warning. Patients should continue taking rosiglitazone unless told by their healthcare professional to stop. Patients who are concerned about the possible risks associated with using rosiglitazone should talk to their healthcare professional.

Invirase (saquinavir): Ongoing safety review of clinical trial data

FDA notified healthcare professionals and patients that it is reviewing clinical trial data about a potentially serious effect on the heart from the use of Invirase (saquinavir) in combination with Norvir (ritonavir), antiviral medications given together to treat HIV infection.

The data suggest that together the two drugs may affect the electrical activity of the heart, known as prolonged QT or PR intervals. A prolonged QT interval can increase the risk for a serious abnormal rhythm called torsades de pointes. A prolonged PR interval can cause the electrical signal responsible for generating a heartbeat to slow or even stop, known as heart block.

FDA's analysis of these data is ongoing. The agency will update the public as soon as this review is complete. However, healthcare professionals should be aware of this potential risk for changes to the electrical activity of the heart. Invirase and Norvir should not be used in patients already taking medications known to cause QT interval prolongation such as Class IA (such as quinidine,) or Class III (such as amiodarone) antiarrhythmic drugs, or in patients with a history of QT interval prolongation. Patients should not stop taking their prescribed antiviral medications. Patients who are concerned about possible risks associated with using Invirase and Norvir should talk to their healthcare professional. 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:

- 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

OneTouch SureStep Test Strips (LifeScan): Recall

LifeScan and FDA notified healthcare professionals of a voluntary recall of eight lots of OneTouch SureStep Test Strips, used by people with diabetes to measure their blood glucose levels at home. The test strips are being recalled because they may provide falsely low glucose results when the glucose level is higher than 400 mg/dL.

If patients use the falsely low test results to determine their insulin dose, they may give themselves too little insulin, which could result in poor blood glucose control. High blood glucose must be recognized and treated promptly to avoid serious complications, such as coma and death.

The eight lots of consumer OneTouch SureStep Test Strips being recalled are identified in the firm's press release. Lot numbers are located on the outer carton and test strip vial. LifeScan estimates approximately fourteen thousand packages (50- and 100-count) of consumer OneTouch SureStep Test Strips were distributed nationwide between August 1, 2009 and January 28, 2010.

It is important that patients with recalled test strips continue to test their blood glucose. Patients with access to a meter that does not use OneTouch SureStep Test Strips should use this other meter to test their blood glucose until replacement product from LifeScan arrives. If an alternate meter is not available, patients may continue to test using the recalled OneTouch SureStep Test Strips. However, if patients obtain results above 400 mg/dL, they should contact their healthcare professional for further instructions because their glucose may be significantly higher.

Plavix (clopidogrel): Reduced effectiveness in patients who are poor metabolizers of the drug
FDA notified healthcare professionals and patients that a Boxed Warning has been added to the prescribing information for Plavix, an anti-blood clotting medication. The Boxed Warning in the drug label will include information to:

- Warn about reduced effectiveness in patients who are poor metabolizers of Plavix. Poor metabolizers do not effectively convert Plavix to its active form in the body.
- Inform healthcare professionals that tests are available to identify genetic differences in CYP2C19 function.
- Advise healthcare professionals to consider use of other anti-platelet medications or alternative dosing strategies for Plavix in patients identified as poor metabolizers.

Plavix is given to reduce the risk of heart attack, unstable angina, stroke, and cardiovascular death in patients with cardiovascular disease. Plavix works by decreasing the activity of blood cells called platelets, making platelets less likely to form blood clots. A data summary and additional information for healthcare professionals and patients are provided in the linked Drug Safety Communication.

Zocor (simvastatin): increased risk of muscle injury with high doses
FDA notified healthcare professionals and patients that, based on review of data from a large clinical trial and other sources, there is an increased risk of muscle injury in patients taking the highest approved dose of the cholesterol-lowering medication, Zocor (simvastatin) 80 mg, compared to patients taking lower doses of simvastatin and possibly other drugs in the "statin" class. FDA is also reviewing data from other clinical trials, observational studies, adverse event reports, and data on prescription use of simvastatin to better understand the relationship between high-dose simvastatin use and muscle injury.
Recommendations for healthcare professionals, recommendations for patients and a data summary of information used in this ongoing review are provided in the Drug Safety Communication.

Stalevo (entacapone/carbidopa/levodopa): Ongoing Safety Review
FDA notified healthcare professionals and patients that it is evaluating data from a long-term clinical trial called Stalevo Reduction in Dyskinesia Evaluation - Parkinson's Disease (STRIDE-PD) that may suggest that patients taking Stalevo may be at an increased risk for developing prostate cancer. Other controlled clinical trials evaluating Stalevo or Comtan (entacapone) did not find an increased risk of prostate cancer. FDA is still reviewing the available information and has not concluded that Stalevo increases the risk of developing prostate cancer. Healthcare professionals should be aware of this possible risk and follow current guidelines for prostate cancer screening. FDA recommends that healthcare professionals follow the recommendations in the drug label when prescribing Stalevo and Comtan. Patients should not stop taking their medication unless directed to do so by their healthcare professional.