Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

November 15, 2007

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

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

November 15, 2007

Welcome — **Frank Marascalco, RPh**

Old Business

- **Approval of Meeting Minutes**
- **Updates** — **Dennis Smith, RPh**
  - **Cost Management Analysis**
  - **DUR Activity Report**

Pharmacy Program Update — **Paige Clayton, Pharm.D.**

New Business — **Dennis Smith, RPh**

- **Review of 3rd Quarter Meeting Materials**
- **Alprazolam and Lorazepam Utilization**
- **Hydrocodone Utilization**
- **Impact of Quinine Removal on Utilization of Gabapentin and Lyrica®**
- **Duplicate Utilization of Risperdal Consta® and Oral Antipsychotic Agents**
- **Appropriate Antibiotic Use/Zyvox®**
- **Other Criteria Recommendations**
- **Boxed Warning Update**

Next Meeting Information — **Frank Marascalco, RPh**

Drug Utilization Review Board

Roy L. Arnold, Jr., R.Ph.
Clayton Drug Store
216 Main Street
Collins, MS 39428-0787
Term Expires: June 30, 2009

Harold B. Blakely, R.Ph.
Delta Area Hospice Care
5357 Cliff Gookin Boulevard
Tupelo, MS 38801
Term Expires: June 30, 2008

Laura Gray, M.D.
905 Garfield Street
Tupelo, MS 38801
Term Expires: June 30, 2008

John M. Wallace, M.D.
Jefferson Medical Clinic
1203 Jefferson Street
Laurel, MS 39440
Term Expires: June 30, 2009

Frank Marascalco, R.Ph
Sav-Mor Drugs
1967 Commerce Street
Grenada, MS 38901
Term Expires: June 30, 2008

Wallace Strickland
Rush Foundation Hospital
8219 Sycamore Creek Drive
Meridian, MS 39305
Term Expires: June 30, 2008

Lee Voulters, M.D.
1340 Broad Ave Suite 440
Gulfport, MS 39501
Term Expires: June 30, 2009

Upcoming Mississippi DUR Board Meeting Dates

February 21, 2008
May 15, 2008
August 21, 2008
November 20, 2008

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the May 17, 2007 Meeting

Members Attending: Billy Brown, Pharm.D.; Harold Blakely, R.Ph.; Laura Gray, M. D.; Frank Marascalco, R.Ph., Chair; Wallace Strickland; Lee Voulters, M.D.; John Wallace, M.D.

Members Absent: Roy Arnold, R.Ph.; Randy Calvert, R.Ph.; Lee Montgomery, M.D.; Andrea Phillips, M.D.; Troy Griffin.

Also Present:
DOM Staff: Judith Clark, R.Ph., Director of the Medicaid Pharmacy Bureau; Terri Kirby, R.Ph.; Paige Clayton, Pharm.D.

HID Staff: Dennis Smith, R.Ph., Project Manager; Ashleigh Holeman, Pharm.D.; Kathleen Burns, R.N.; Gail Franks, R.N.

Call to Order:
Frank Marascalco,R.Ph.,Chairman of the Board, called the meeting to order at 2:05 p.m.

Ms. Clark asked that the Board proceed with business that would not require a vote while awaiting arrival of enough members to constitute a quorum.

Updates:
Cost Management Analysis
Mr. Smith began by presenting a report reflecting pharmacy costs during the month of February 2007. The analysis began with the top 15 therapeutic classes by total costs in claims. The top therapeutic class by cost was the antipsychotic agents followed by monoclonal antibodies. The top 25 drugs based on the total number of claims were led by azithromycin. Mr. Smith continued the report with the top 25 drugs based on total claims cost, led by Synagis. It was pointed out that Synagis is a seasonal pharmaceutical with most utilization ending in March.

Approval of the Minutes:
With the arrival of a seventh Board member, Wallace Strickland made a motion to accept as submitted the minutes for the February 15, 2007 meeting. Dr. Voulters seconded the motion. All voted in favor of the approval.

DUR Activity Report:
Mr. Smith continued with a discussion of the role of the retrospective DUR program in encouraging proper utilization of medications. Dr. Voulters brought to the Board his input on the proper utilization of stimulants in both children and adults. It was suggested that HID develop criteria to alert the system of the use of stimulants, as well as Strattera. These initial retrospective reports will be presented at the next Board meeting.

Pharmacy Program Update:
Ms. Clark began her update by reviewing a handout concerning the removal of Zelnorm from the market by the FDA. In addition, she alerted the Board of the revised PDL that will be in place starting July 1, 2007. The new PDL will be published in the June Medicaid Bulletin.

New Business:
Ophthalmic Antibiotics
Mr. Smith began by presenting an extensive report on bacterial conjunctivitis and the appropriate use of ophthalmic antibiotics. Appropriate use of these agents has become a concern of many managed care organizations. As a result, many health insurers have limited access to these agents through prior authorization step-therapy requirements. These agents will be reviewed by the Mississippi Medicaid Pharmacy and Therapeutics Committee at the July meeting for the inclusion on the Preferred Drug List.

HID recommended distribution of a Medicaid Prescribing Update for this drug category. This is to be delivered to prescribers by the Academic Detailing staff of HID. This document should also be available by link from the Division of Medicaid's Website. In addition, HID recommended retrospective DUR criteria to focus on appropriate length of therapy and use in appropriate age patients. The motion was made by Harold Blakely and seconded by Dr. Laura Gray to accept these recommendations. All voted in favor of this motion.

HIV Therapy
Mr. Smith continued with a report based on the most recent NIH treatment guidelines for the treatment of HIV, updated in October 2006. He presented criteria based on these guidelines. After extensive discussions ranging from the total cost of the medications to the appropriate treatment for HIV patients, the criteria were brought to the Board for a vote. Dr. Voulters motioned that the criteria presented with requested changes be accepted. Mr. Strickland seconded the motion. All voted in favor of accepting the 83 criteria as presented by HID.

Other Criteria Recommendations
Continuing with a review of the remaining 31 criteria pertaining to several new drugs, Dr. Voulters made a motion to accept the criteria as presented with a second by Dr. Laura Gray. All voted in favor of the motion.

Mr. Smith asked the Board for input on developing a response to prescribers related to the removal of Zelnorm® from the market. The board recommended developing a Medicaid Prescribing Update (one pager) with the input of a gastroenterologist to help inform physicians of the appropriate approach to treatment of chronic idiopathic constipation and irritable bowel syndrome (IBS).

Mr. Smith introduced an off-the-agenda discussion of the antiplatelet class of medications. These medications were reviewed at the April meeting by the P& T Committee. It was noted that from April 2006 through April 2007, approximately 10,000

claims had been processed at a total of 1.4 million dollars. He continued that a Medicaid Prescribing Update (one pager) could be delivered to the physicians to educate them on the comparison studies available for this class of drugs. It is believed that the utilization of this class is appropriate but should be addressed educationally. All members supported the distribution of such a document by the Academic Detailers.

Boxed Warnings Update:
Mr. Smith presented black box warnings, other warnings, and labeling changes issued by the FDA concerning the following:

Actiq (fentanyl citrate) Oral Transmucosal Lozenge:
WARNINGS: IMPORTANCE OF PROPER PATIENT SELECTION
and POTENTIAL FOR ABUSE
See full prescribing information for complete boxed warning.

- Must not be used in opioid non-tolerant patients.
- Contains fentanyl, a Schedule II controlled substance with abuse liability similar to other opioid analgesics.
- Life-threatening hypoventilation could occur at any dose in patients not taking chronic opiates.
- Contraindicated in management of acute or postoperative pain.
- Contains medicine in an amount that can be fatal to a child. Keep out of reach of children and discard opened units properly.
- Use with strong and moderate CYP450 3A4 inhibitors may result in potentially fatal respiratory depression.

Femring (estradiol acetate vaginal ring):
BOXED WARNING: Cardiovascular and Other Risks
.....The estrogen-alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with oral conjugated estrogens (CE 0.625 mg) per day relative to placebo. The estrogen-plus-progestin substudy of WHI reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day, relative to placebo. The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with CE 0.625 mg alone and during 4 years of treatment with CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.....

Humira (adalimumab) Solution for Subcutaneous Injection:
BOXED WARNING
.....Patients should be evaluated for tuberculosis risk factors and be tested for latent tuberculosis infection prior to initiating Humira and during therapy.....

Ketek (telithromycin) Tablets:
BOXED WARNING
Ketek is contraindicated in patients with myasthenia gravis. There have been reports of fatal and life-threatening respiratory failure in patients with myasthenia gravis associated with the use of Ketek.

Benazepril-containing products (Lotensin, Lotensin HCT, Lotrel):
BOXED WARNING**:** Use in Pregnancy
When used in pregnancy, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, Lotensin should be discontinued as soon as possible.....

Next Meeting Information:
Ms. Clark announced that the next meeting would be on August 16, 2007. She continued with the information that there would be new additions to the Board at the next meeting.

Special recognition:
Billy Brown, Pharm.D., was complimented for his service on this Board as his term will end prior to the next meeting.

Frank Marascalco called for the meeting to be adjourned. Dr. Lee Voulters made the motion to adjourn and Harold Blakely seconded the motion. All voted in favor of the motion to adjourn.

Respectfully Submitted:
Health Information Designs

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the September 20, 2007 Meeting

Members Attending: Roy Arnold, R.Ph; Frank Marascalco, R.Ph, Chair; Wallace Strickland; Lee Voulters, M.D.; John Wallace, M.D.

Members Absent: Laura Gray, M.D.; Troy Griffin

Also Present:
DOM Staff: Judith Clark, R.Ph., Director of the Medicaid Pharmacy Bureau: Paige Clayton, Pharm D.; Rosie Moak, Administrative Assistant to the Division of Medicaid

HID Staff: Dennis Smith, R.Ph., Project Manager; Ashleigh Holeman, Pharm. D.; Chris Benton, Pharm. D.; Kathleen Burns, R.N.; Rob DiBenedetto, MBA (CEO, HID)

Call to Order:
Frank Marascalco, R.Ph., Chairman of the Board, called the meeting to order at 2:12 p.m.

Ms. Clark asked that the Board proceed with the meeting with the exception of voting, since a quorum was not present.

Updates:
Pharmacy Program Update

Ms. Clark addressed the upcoming tamper-resistant prescription pad mandate on October 1, 2007. She noted that refills for prescriptions written prior to October 1, 2007 will be exempt. Also exempt will be prescriptions telephoned or faxed from a physician's office. In addition, long term care facilities will be exempt, with the exception of prescriptions for C-2 controlled substances.

Ms. Clark introduced Paige Clayton, Pharm. D., as the new DOM Pharmacy Bureau DUR Coordinator. Also introduced to the Board was Ashleigh Holeman, Pharm. D., HID's newest Clinical Pharmacist.

Cost Management Analysis

Mr. Smith began by presenting reports reflecting pharmacy costs during the months of April 2007 through June 2007. The analysis began with the top 25 agents prescribed by total number of claims during these months. It was noted that in all three months hydrocodone-acetaminophen was the top drug. A lengthy discussion ensued among board members regarding the amount of hydrocodone prescribing. The top 25 drugs, based on total claims cost, were led by Singulair® in April 2007, followed by Risperdal® for the next two months. The top 15 therapeutic classes by total cost of claims over the three

month report time period were headed by antipsychotic agents, followed by anticonvulsants.

New Business:
Potential Misuse of ADHD Agents

At the May 17, 2007 DUR Board meeting, there was some discussion about the potential misuse of stimulants. Specific concerns were raised about the inappropriate use of these medications in the adult population for appetite suppression and weight loss.

Dr. Holeman presented a utilization analysis of these agents in the Mississippi Medicaid population. Utilization data was gathered through RxExplorer®, which searches paid claims data submitted to HID by the fiscal agent. Two unique searches were conducted for the period of 07/01/2006 through 05/25/2007. The search parameters were (1) stimulant utilization based on age and (2) Strattera® utilization based on age. As expected, utilization in both groups was found to be highest among children and adolescents ages five to 20. Utilization of both stimulants and Strattera® dropped to insignificant levels among adults 21 and older, indicating that widespread misuse in adults was not occurring. Dr. Voulters commented that it would be difficult to monitor the sharing of medications in the adult population.

Although the figures do not indicate extensive abuse of ADHD medications in the adult population, a retrospective DUR criterion is recommended to identify those adult patients (21 years and older) who may be using these medications inappropriately. This criterion will be introduced at the next Board meeting.

Inappropriate Use of Antibiotics

Mr. Smith presented introductory information on the inappropriate use of antibiotics. The emergence of bacterial strains that are increasingly resistant to antimicrobial agents is a growing national and worldwide concern. Currently, millions of courses of unnecessary antibiotics are prescribed and administered each year. This misuse may result from inappropriate diagnosis or inappropriate prescribing habits. It was noted that inappropriate antibiotic usage may have implications in addition to the development of multi-drug resistant microorganisms. A study published in the June issue of *Chest* found that children who were given antibiotics in the first year of life were significantly more likely to develop asthma by age seven. There was a positive correlation between the number of antibiotic courses received during the first year and an increased risk of developing asthma. In Mississippi, approximately 66,620 children (age <18) suffer from asthma. Asthma is the third leading cause of hospitalization in children – with an annual direct health care cost of approximately $11.5 billion. In addition, asthma is the leading cause of school absenteeism. Prevention of future asthma cases could present considerable cost savings to the State in drug expenditures alone.

In an effort to educate providers, HID recommends a retrospective DUR criterion to identify those patients less that one year of age that may have been prescribed over-utilized antibiotic treatments. Dr. Wallace noted that pediatrician involvement in this

effort might be beneficial in addressing over-prescription of antibiotics by physicians. Dr. Voulters recommended that physicians identified with these habits receive educational letters addressing this issue, adding that HID might identify the antibiotic treatments prescribed to patients under age one and the related diagnoses.

HIV Criteria Report

Dr. Holeman reported on several criteria approved by the DUR Board at the May 17, 2007 meeting that focus on HIV therapy. HID has designed a system that accounts for the individual patient factors which increase the risk for each criteria. This system also incorporates medical literature documentation of the adverse event related to each criteria. A focused inquiry into the severity of the exceptions generated in May and June revealed that there is not a significant drug therapy problem in HIV patients enrolled in Mississippi Medicaid. Dr. Holeman continued that since the appropriate use of HIV medications is imperative for each patient, retrospective DUR criteria will continue to be used to assist physicians in providing effective treatment for their HIV patients. Dr. Voulters encouraged the continued use of DUR criteria as an important tool for managing and supporting the efforts physicians deem helpful in the HIV patient population.

Proper Singulair Utilization

Montelukast (Singulair®) is indicated for the treatment of asthma and allergic rhinitis. As seen in the cost analysis presented by Mr. Smith, montelukast is consistently one of the highest cost agents to DOM. Due to the consistently large claims costs for Medicaid, there is some concern that this drug may be over-utilized for allergic rhinitis when less expensive alternatives are available. Mr. Smith presented an analysis of montelukast utilization from May 2006 to May 2007. This analysis revealed that approximately 62 percent of patients who received montelukast had a diagnosis of asthma, while approximately 65 percent had a diagnosis of allergic rhinitis. According to this information, there does not appear to be gross over-utilization of montelukast outside of the asthma population. Dr. Voulters voiced concern regarding the approximately 4,000 children identified in the study who did not have a diagnosis of asthma or allergic rhinitis. He continued that the costs to Medicaid on these claims should be identified by indicating the diagnoses that correlated with the dispensing. HID was requested to review these claims to identify the large number of beneficiaries receiving montelukast and report to the Board at the next meeting. All agreed that this was an important issue to pursue.

Criteria Recommendations

The criteria recommendations were read; however, a vote was not taken because a quorum was not present. These criteria will be presented for approval at the next board meeting.

Boxed Warning Update

Mr. Smith presented an overview of black box warnings, other warnings, and labeling changes recently issued by the FDA concerning the following:

Thiazolidinediones - Avandia (rosiglitazone maleate), Actos (pioglitazone) and combination products

After a review of postmarketing adverse event reports, FDA determined that an updated label with a boxed warning on the risks of heart failure was needed for the entire thiazolidinedione class of antidiabetic drugs. These drugs are used in conjunction with diet and exercise to improve blood sugar control in adults with type 2 diabetes. Manufacturers of certain drugs have agreed to the upgraded warning.

The strengthened warning advises healthcare professionals to observe patients carefully for the signs and symptoms of heart failure, including excessive, rapid weight gain, shortness of breath, and edema after starting drug therapy. Patients with these symptoms who then develop heart failure should receive appropriate management of the heart failure and use of the drug should be reconsidered. Patients with questions should contact their healthcare providers to discuss alternative treatments.

Exjade (deferasirox) tablets for oral suspension

Novartis and FDA notified healthcare professionals of changes to the WARNINGS and ADVERSE REACTIONS sections of the product labeling for Exjade, a drug used to treat chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients two years of age and older. Cases of acute renal failure, some with a fatal outcome, have been reported following the post marketing use of Exjade. Most of the fatalities occurred in patients with multiple co-morbidities and who were in advanced stages of their hematological disorders. Additionally, there were post-marketing reports of cytopenias, including agranulocytosis, neutropenia and thrombocytopenia in patients treated with Exjade where some of the patients died. The relationship of these episodes to treatment with Exjade is uncertain. Most of these patients had preexisting hematologic disorders that are frequently associated with bone marrow failure. Further, cases of leukocytoclastic vasculitis, urticaria, and hypersensitivity reactions (including anaphylaxis and angioedema) were reported.

Healthcare professionals should monitor serum creatinine in patients with increased risk of complications; that is, those who have preexisting renal conditions, are elderly, have co-morbid conditions, or are receiving medicinal products that depress renal function. Blood counts should also be monitored regularly and treatment should be interrupted in patients who develop unexplained cytopenia.

Propofol (marketed as Diprivan and generic products)

FDA informed healthcare professionals about several clusters of patients who experienced chills, fever, and body aches shortly after receiving propofol for sedation or general anesthesia. Multiple vials and several lots of propofol used in patients who experienced these symptoms were tested and there was no evidence that the propofol vials or prefilled syringes were contaminated with bacteria or endotoxins. Propofol is an

intravenous sedative-hypnotic agent used to induce and maintain anesthesia or sedation. To minimize the potential for bacterial contamination, propofol vials and prefilled syringes should be used within six hours of opening. Each vial should be used only for one patient. Patients who develop fever, chills, body aches or other symptoms of acute febrile reactions shortly after receiving propofol should be evaluated for bacterial sepsis. Healthcare professionals who administer propofol for sedation or general anesthesia should carefully follow the recommendations for handling and use in the product's full prescribing information.

Rocephin (ceftriaxone sodium) for Injection

Roche and FDA informed healthcare professionals of revisions to the CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections of the prescribing information for Rocephin for Injection. The revisions are based on new information that describes the potential risk associated with concomitant use of Rocephin with calcium or calcium-containing solutions or products. Cases of fatal reactions with calcium-ceftriaxone precipitates in the lungs and kidneys in both term and premature neonates were reported. Hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin. The drug must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines. Additionally, calcium-containing solutions or products must not be administered within 48 hours of the last ceftriaxone administration.

Next Meeting Information:

Ms. Clark reminded the Board of the next meeting on November 15, 2007.

Call for Adjournment:

Frank Marascalco called for the meeting to be adjourned at 3:40 p.m.

Respectfully Submitted:
Health Information Designs, Inc.

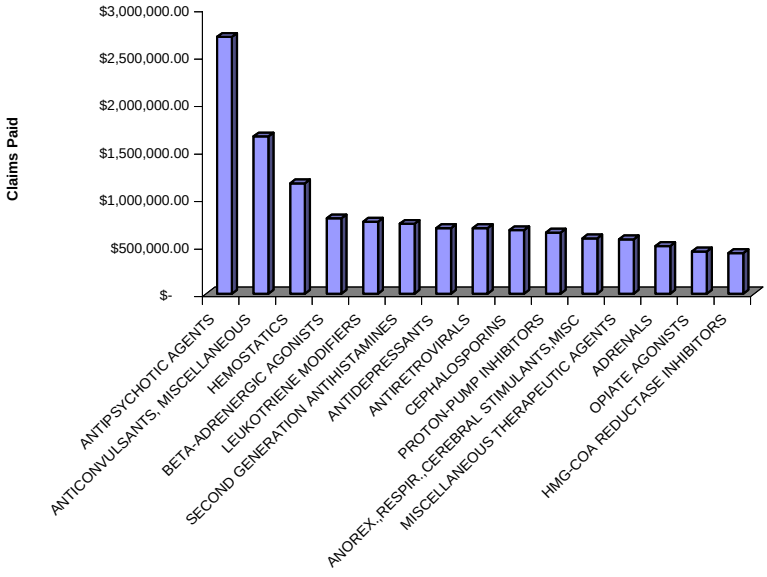
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 04/01/07-04/30/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	9,610	$ 2,704,581.53	$ 281.43	2.72%
ANTICONVULSANTS, MISCELLANEOUS	9,941	$ 1,656,651.23	$ 166.65	2.82%
HEMOSTATICS	41	$ 1,162,563.96	$28,355.22	0.01%
BETA-ADRENERGIC AGONISTS	10,985	$ 794,295.49	$ 72.31	3.11%
LEUKOTRIENE MODIFIERS	7,439	$ 759,935.34	$ 102.16	2.11%
SECOND GENERATION ANTIHISTAMINES	14,584	$ 737,084.01	$ 50.54	4.13%
ANTIDEPRESSANTS	13,069	$ 692,699.05	$ 53.00	3.70%
ANTIRETROVIRALS	1,058	$ 690,616.65	$ 652.76	0.30%
CEPHALOSPORINS	11,215	$ 669,489.82	$ 59.70	3.18%
PROTON-PUMP INHIBITORS	4,641	$ 645,192.90	$ 139.02	1.31%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,222	$ 584,756.89	$ 111.98	1.48%
MISCELLANEOUS THERAPEUTIC AGENTS	2,063	$ 573,026.03	$ 277.76	0.58%
ADRENALS	8,132	$ 501,866.81	$ 61.72	2.30%
OPIATE AGONISTS	22,922	$ 446,091.63	$ 19.46	6.49%
HMG-COA REDUCTASE INHIBITORS	4,671	$ 428,075.79	$ 91.65	1.32%
TOTAL TOP 15	125,593	$ 13,046,927.13	$ 103.88	35.57%

Total Rx Claims	353,044
From 04/01/07-04/30/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



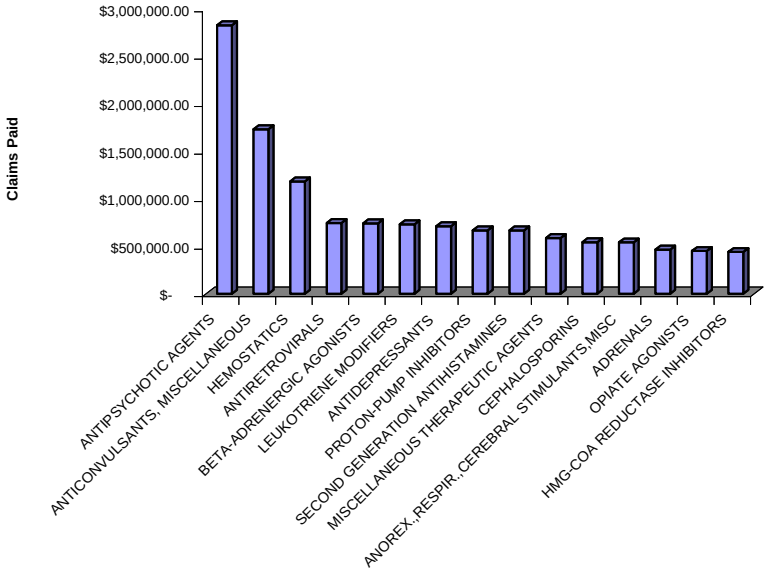
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 05/01/07-05/31/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	9,953	$ 2,826,486.82	$ 283.98	2.90%
ANTICONVULSANTS, MISCELLANEOUS	10,269	$ 1,732,759.83	$ 168.74	2.99%
HEMOSTATICS	49	$ 1,183,892.07	$24,161.06	0.01%
ANTIRETROVIRALS	1,096	$ 744,319.28	$ 679.12	0.32%
BETA-ADRENERGIC AGONISTS	10,202	$ 742,484.21	$ 72.78	2.97%
LEUKOTRIENE MODIFIERS	7,135	$ 731,487.37	$ 102.52	2.08%
ANTIDEPRESSANTS	13,389	$ 711,625.05	$ 53.15	3.90%
PROTON-PUMP INHIBITORS	4,807	$ 668,920.07	$ 139.16	1.40%
SECOND GENERATION ANTIHISTAMINES	13,340	$ 668,180.08	$ 50.09	3.89%
MISCELLANEOUS THERAPEUTIC AGENTS	2,146	$ 587,584.02	$ 273.80	0.63%
CEPHALOSPORINS	9,963	$ 544,324.64	$ 54.63	2.90%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,759	$ 541,489.88	$ 113.78	1.39%
ADRENALS	7,581	$ 464,644.88	$ 61.29	2.21%
OPIATE AGONISTS	23,044	$ 450,481.81	$ 19.55	6.71%
HMG-COA REDUCTASE INHIBITORS	4,820	$ 440,748.01	$ 91.44	1.40%
TOTAL TOP 15	122,553	$ 13,039,428.02	$ 106.40	35.69%

Total Rx Claims	343,357
From 05/01/07-05/31/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



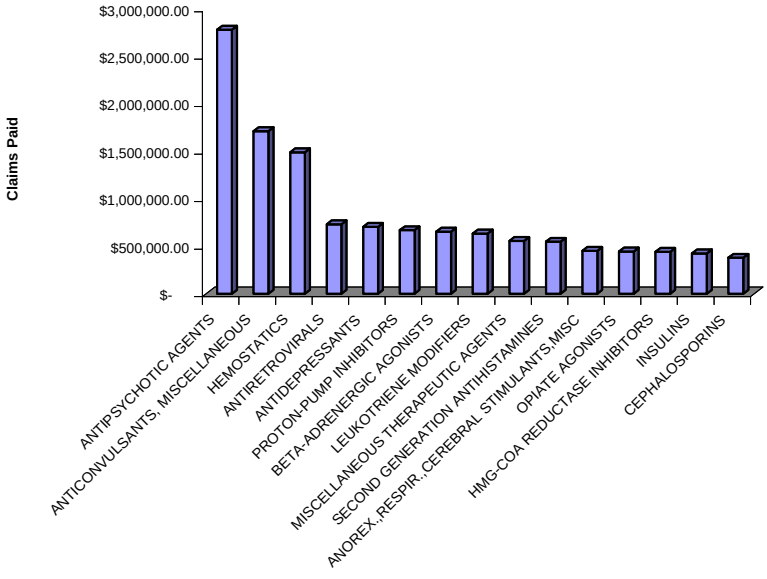
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 06/01/07-06/30/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	9,702	$ 2,779,742.93	$ 286.51	3.06%
ANTICONVULSANTS, MISCELLANEOUS	10,036	$ 1,711,302.07	$ 170.52	3.17%
HEMOSTATICS	54	$ 1,489,297.53	$27,579.58	0.02%
ANTIRETROVIRALS	1,114	$ 732,695.54	$ 657.72	0.35%
ANTIDEPRESSANTS	13,222	$ 705,548.69	$ 53.36	4.17%
PROTON-PUMP INHIBITORS	4,768	$ 669,269.62	$ 140.37	1.50%
BETA-ADRENERGIC AGONISTS	8,770	$ 654,974.07	$ 74.68	2.77%
LEUKOTRIENE MODIFIERS	6,185	$ 633,899.34	$ 102.49	1.95%
MISCELLANEOUS THERAPEUTIC AGENTS	2,187	$ 556,509.96	$ 254.46	0.69%
SECOND GENERATION ANTIHISTAMINES	10,896	$ 548,262.98	$ 50.32	3.44%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,907	$ 452,161.71	$ 115.73	1.23%
OPIATE AGONISTS	22,819	$ 445,823.03	$ 19.54	7.20%
HMG-COA REDUCTASE INHIBITORS	4,856	$ 441,505.19	$ 90.92	1.53%
INSULINS	3,382	$ 424,370.42	$ 125.48	1.07%
CEPHALOSPORINS	7,892	$ 379,685.81	$ 48.11	2.49%
TOTAL TOP 15	109,790	$ 12,625,048.89	$ 114.99	34.65%

Total Rx Claims	316,818
From 06/01/07-06/30/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



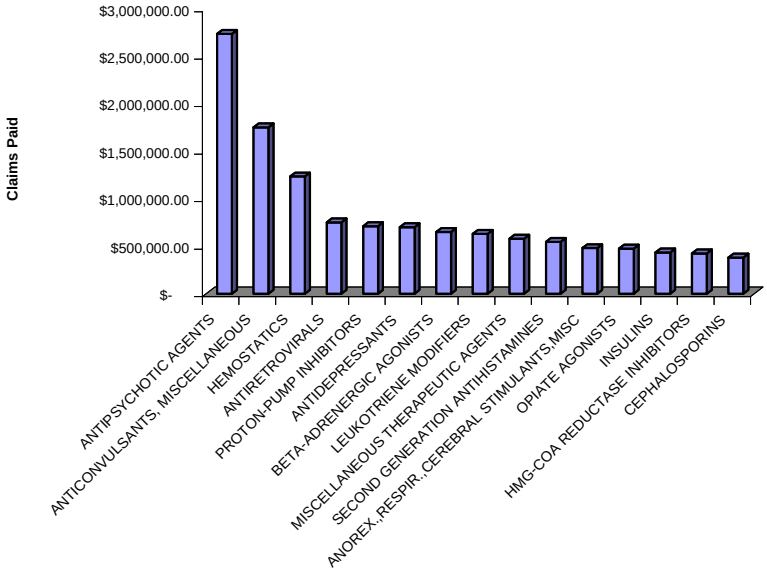
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 07/01/07-07/31/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	9,427	$ 2,735,264.81	$ 290.15	2.89%
ANTICONVULSANTS, MISCELLANEOUS	10,159	$ 1,751,771.97	$ 172.44	3.12%
HEMOSTATICS	45	$ 1,235,746.72	$27,461.04	0.01%
ANTIRETROVIRALS	1,127	$ 752,222.14	$ 667.46	0.35%
PROTON-PUMP INHIBITORS	4,956	$ 710,590.59	$ 143.38	1.52%
ANTIDEPRESSANTS	13,373	$ 701,482.76	$ 52.46	4.11%
BETA-ADRENERGIC AGONISTS	8,824	$ 650,014.25	$ 73.66	2.71%
LEUKOTRIENE MODIFIERS	6,175	$ 631,564.24	$ 102.28	1.90%
MISCELLANEOUS THERAPEUTIC AGENTS	2,184	$ 578,941.55	$ 265.08	0.67%
SECOND GENERATION ANTIHISTAMINES	10,613	$ 547,915.31	$ 51.63	3.26%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,166	$ 481,095.35	$ 115.48	1.28%
OPIATE AGONISTS	24,289	$ 474,578.96	$ 19.54	7.46%
INSULINS	3,492	$ 434,344.89	$ 124.38	1.07%
HMG-COA REDUCTASE INHIBITORS	4,669	$ 425,343.59	$ 91.10	1.43%
CEPHALOSPORINS	7,935	$ 382,184.20	$ 48.16	2.44%
TOTAL TOP 15	111,434	$ 12,493,061.33	$ 112.11	34.21%

Total Rx Claims	325,725
From 07/01/07-07/31/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



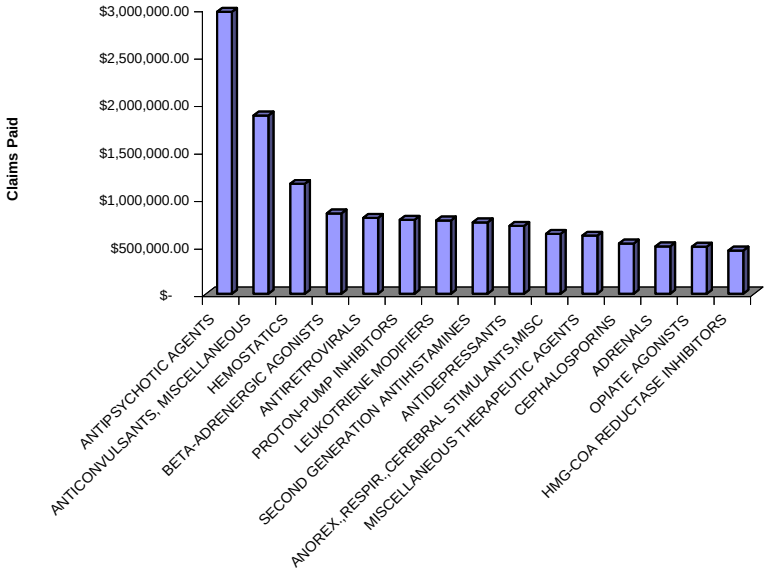
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 08/01/07-08/31/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	10,207	$ 2,969,763.42	$ 290.95	2.75%
ANTICONVULSANTS, MISCELLANEOUS	10,831	$ 1,878,201.97	$ 173.41	2.91%
HEMOSTATICS	41	$ 1,158,330.38	$28,251.96	0.01%
BETA-ADRENERGIC AGONISTS	11,841	$ 845,446.99	$ 71.40	3.19%
ANTIRETROVIRALS	1,181	$ 800,110.87	$ 677.49	0.32%
PROTON-PUMP INHIBITORS	5,377	$ 779,661.12	$ 145.00	1.45%
LEUKOTRIENE MODIFIERS	7,554	$ 773,437.62	$ 102.39	2.03%
SECOND GENERATION ANTIHISTAMINES	13,791	$ 752,589.70	$ 54.57	3.71%
ANTIDEPRESSANTS	14,058	$ 715,925.32	$ 50.93	3.78%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,515	$ 630,221.83	$ 114.27	1.48%
MISCELLANEOUS THERAPEUTIC AGENTS	2,282	$ 612,214.89	$ 268.28	0.61%
CEPHALOSPORINS	10,520	$ 529,479.57	$ 50.33	2.83%
ADRENALS	8,043	$ 499,742.94	$ 62.13	2.16%
OPIATE AGONISTS	26,008	$ 494,673.55	$ 19.02	7.00%
HMG-COA REDUCTASE INHIBITORS	5,020	$ 455,105.01	$ 90.66	1.35%
TOTAL TOP 15	132,269	$ 13,894,905.18	$ 105.05	35.60%

Total Rx Claims	371,591
From 08/01/07-08/31/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

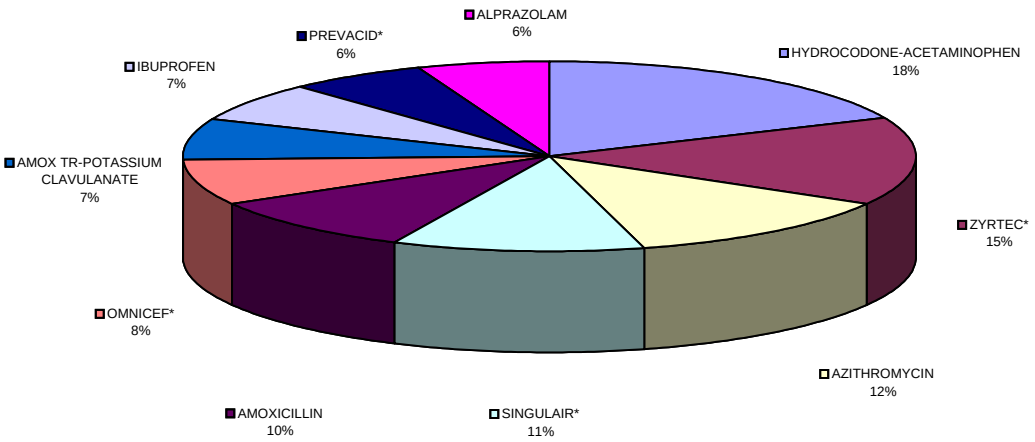
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/07-04/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	12,350	$ 130,490.39	1
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	10,268	$ 550,672.80	12
AZITHROMYCIN	MACROLIDES	8,473	$ 302,315.33	9
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,434	$ 759,350.79	7
AMOXICILLIN	PENICILLINS	6,643	$ 56,005.42	3
OMNICEF*	CEPHALOSPORINS	5,270	$ 479,727.67	45
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	4,776	$ 253,898.39	22
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,466	$ 35,334.94	13
PREVACID*	PROTON-PUMP INHIBITORS	4,100	$ 577,472.85	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,006	$ 32,942.41	7
ED A-HIST	PROPYLAMINE DERIVATIVES	3,865	$ 36,411.75	-------
SULFAMETHOXAZOLE/TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	3,723	$ 44,096.80	40
AMOXICILLIN TRIHYDRATE	PENICILLINS	3,637	$ 42,782.68	-------
CEPHALEXIN	CEPHALOSPORINS	3,621	$ 58,667.27	14
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,198	$ 37,792.30	53
ACETAMINOPHEN W/CODEINE	OPIATE AGONISTS	3,182	$ 27,118.37	31
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	3,176	$ 80,675.60	61
ADDERALL XR*	AMPHETAMINES	3,090	$ 386,459.74	42
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,022	$ 56,657.02	23
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,890	$ 70,211.25	11
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,801	$ 719,307.82	48
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,635	$ 70,758.64	19
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,572	$ 323,113.63	46
FERROUS SULFATE	IRON PREPARATIONS	2,462	$ 9,414.04	106
NYSTATIN	ANTIFUNGALS (SKIN & MUCOUS MEMBRANE)	2,422	$ 33,131.42	144
TOTAL TOP 25		114,082	$ 5,174,809.32	

Total Rx Claims From 04/01/07-04/30/07	353,044

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

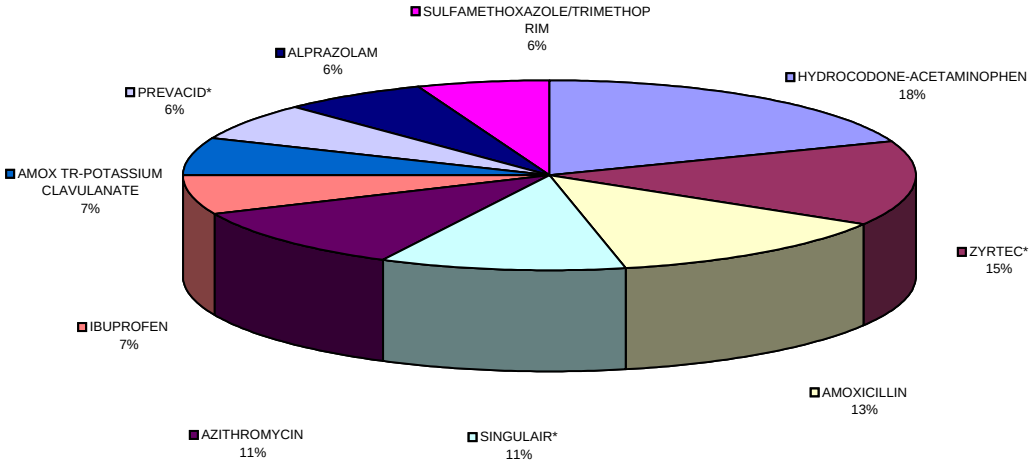
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 05/01/07-05/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	12,471	$ 130,138.86	1
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,580	$ 511,949.13	12
AMOXICILLIN	PENICILLINS	8,584	$ 81,041.88	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,129	$ 731,059.75	7
AZITHROMYCIN	MACROLIDES	6,998	$ 248,580.68	9
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,312	$ 34,384.48	13
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	4,263	$ 221,330.33	22
PREVACID*	PROTON-PUMP INHIBITORS	4,238	$ 595,373.55	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,172	$ 34,509.41	7
SULFAMETHOXAZOLE/TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	3,791	$ 44,816.69	40
CEPHALEXIN	CEPHALOSPORINS	3,311	$ 52,885.97	14
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,202	$ 59,941.67	23
ACETAMINOPHEN W/CODEINE	OPIATE AGONISTS	3,110	$ 25,539.40	31
ED A-HIST	PROPYLAMINE DERIVATIVES	2,967	$ 27,363.59	--------
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,905	$ 35,246.84	53
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,864	$ 73,072.22	61
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,857	$ 736,294.75	48
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,806	$ 74,163.97	19
ADDERALL XR*	AMPHETAMINES	2,767	$ 348,180.79	42
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,750	$ 67,430.59	11
OMNICEF*	CEPHALOSPORINS	2,558	$ 238,240.03	45
FERROUS SULFATE	IRON PREPARATIONS	2,551	$ 9,193.21	106
NYSTATIN	ANTIFUNGALS (SKIN & MUCOUS MEMBRANE)	2,430	$ 33,016.78	144
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,396	$ 90,503.84	119
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,261	$ 285,862.24	46
TOTAL TOP 25		107,273	$ 4,790,120.65	

Total Rx Claims From 05/01/07-05/31/07	343,357

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

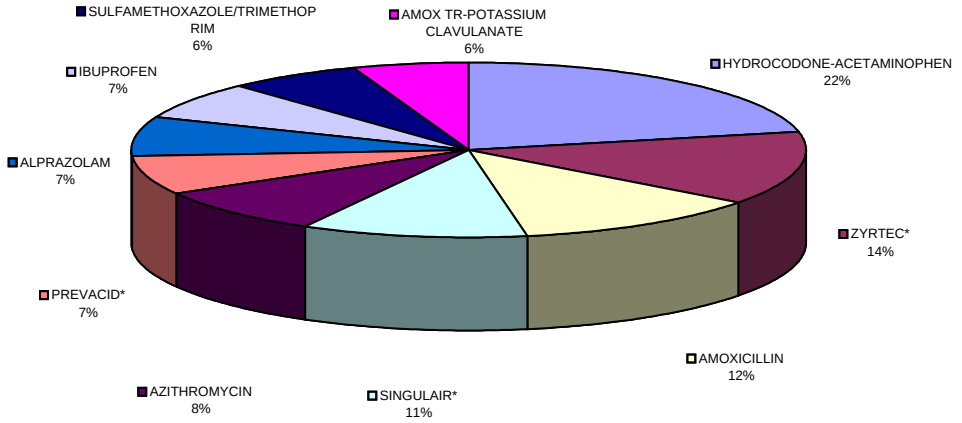
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 06/01/07-06/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	12,332	$ 130,086.45	1
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	7,839	$ 422,201.09	12
AMOXICILLIN	PENICILLINS	6,878	$ 63,465.32	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,178	$ 632,765.05	7
AZITHROMYCIN	MACROLIDES	4,787	$ 169,986.64	9
PREVACID*	PROTON-PUMP INHIBITORS	4,211	$ 598,410.12	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,186	$ 34,737.76	7
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	3,830	$ 30,342.72	13
SULFAMETHOXAZOLE/TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	3,685	$ 44,867.88	40
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	3,205	$ 167,658.01	22
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,073	$ 57,473.57	23
ACETAMINOPHEN W/CODEINE	OPIATE AGONISTS	2,953	$ 23,519.73	31
CEPHALEXIN	CEPHALOSPORINS	2,922	$ 45,933.42	14
CEFDINIR	CEPHALOSPORINS	2,907	$ 205,577.93	--------
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,824	$ 731,482.24	48
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,744	$ 72,039.43	19
FERROUS SULFATE	IRON PREPARATIONS	2,528	$ 8,791.19	106
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,508	$ 61,854.71	11
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,452	$ 92,466.81	119
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,384	$ 29,858.53	53
FUROSEMIDE	LOOP DIURETICS	2,342	$ 12,209.76	8
ADDERALL XR*	AMPHETAMINES	2,311	$ 293,719.28	42
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,215	$ 59,394.97	61
NYSTATIN	POLYENES	2,180	$ 30,604.59	144
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,080	$ 47,834.09	2
TOTAL TOP 25		95,554	$ 4,067,281.29	

Total Rx Claims From 06/01/07-06/30/07	316,818

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

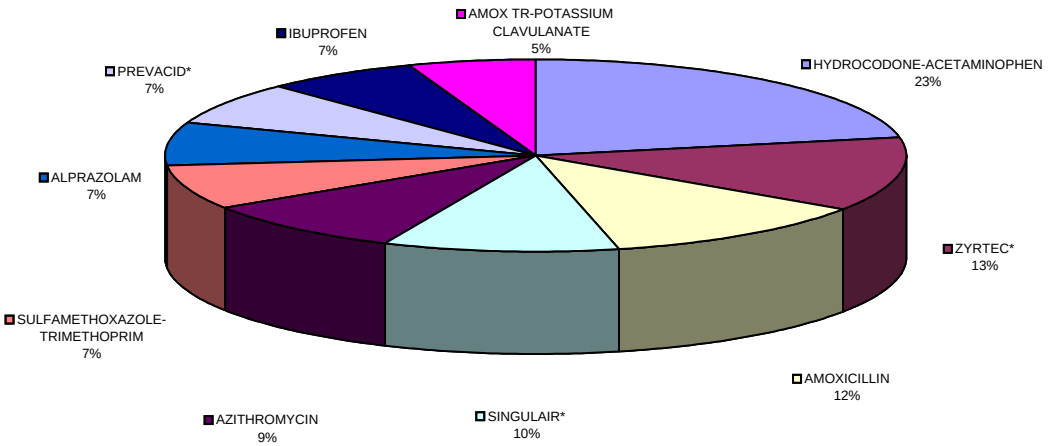
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 07/01/07-07/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	13,115	$ 138,012.79	1
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	7,524	$ 420,896.26	12
AMOXICILLIN	PENICILLINS	7,072	$ 64,370.08	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,171	$ 631,214.36	7
AZITHROMYCIN	MACROLIDES	5,522	$ 197,073.62	9
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,410	$ 52,988.34	40
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,395	$ 36,197.79	7
PREVACID*	PROTON-PUMP INHIBITORS	4,382	$ 633,566.57	8
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,001	$ 31,563.29	13
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	3,251	$ 176,305.58	22
ACETAMINOPHEN W/CODEINE	OPIATE AGONISTS	3,174	$ 25,741.78	31
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,131	$ 59,446.26	23
CEFDINIR	CEPHALOSPORINS	3,112	$ 222,963.82	-------
CEPHALEXIN	CEPHALOSPORINS	3,009	$ 46,771.16	14
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,844	$ 730,280.72	48
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,772	$ 104,978.79	119
FERROUS SULFATE	IRON PREPARATIONS	2,770	$ 10,153.36	106
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,752	$ 74,849.67	19
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,596	$ 80,360.28	42
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,478	$ 60,544.31	11
ADDERALL XR*	AMPHETAMINES	2,384	$ 300,579.71	42
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,328	$ 29,482.16	53
NYSTATIN	POLYENES	2,313	$ 32,997.65	144
PROPOXYPHENE NAPSYLATE-APAP	OPIATE AGONISTS	2,251	$ 19,185.46	17
FUROSEMIDE	LOOP DIURETICS	2,244	$ 11,546.41	8
TOTAL TOP 25		100,001	$ 4,192,070.22	

Total Rx Claims From 07/01/07-07/31/07	325,725

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

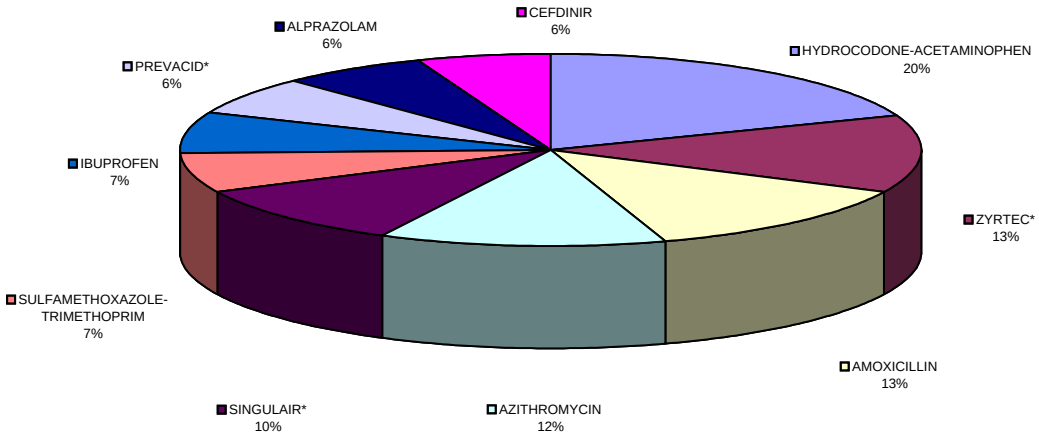
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 08/01/07-08/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	14,048	$ 144,101.64	1
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,669	$ 572,569.60	12
AMOXICILLIN	PENICILLINS	9,531	$ 89,218.37	3
AZITHROMYCIN	MACROLIDES	9,116	$ 325,421.77	9
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,549	$ 772,820.87	7
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,057	$ 60,071.53	40
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,006	$ 40,545.96	13
PREVACID*	PROTON-PUMP INHIBITORS	4,770	$ 699,259.38	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,590	$ 37,956.17	7
CEFDINIR	CEPHALOSPORINS	4,377	$ 321,946.58	-------
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	4,145	$ 228,229.98	22
CEPHALEXIN	CEPHALOSPORINS	3,652	$ 57,499.59	14
ACETAMINOPHEN W/CODEINE	OPIATE AGONISTS	3,336	$ 26,612.54	31
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,292	$ 63,162.78	23
ED A-HIST	PROPYLAMINE DERIVATIVES	3,271	$ 30,065.84	0
ALBUTEROL	BETA-ADRENERGIC AGONISTS	3,206	$ 79,482.97	11
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,190	$ 838,727.02	48
ADDERALL XR*	AMPHETAMINES	3,187	$ 396,453.10	42
FERROUS SULFATE	IRON PREPARATIONS	2,966	$ 10,754.46	106
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,959	$ 77,975.62	61
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,953	$ 79,977.63	19
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,918	$ 36,250.22	53
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,858	$ 107,523.09	119
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,768	$ 87,911.32	42
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,523	$ 317,519.58	46
TOTAL TOP 25		120,937	$ 5,502,057.61	

Total Rx Claims From 08/01/07-08/31/07	371,591

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

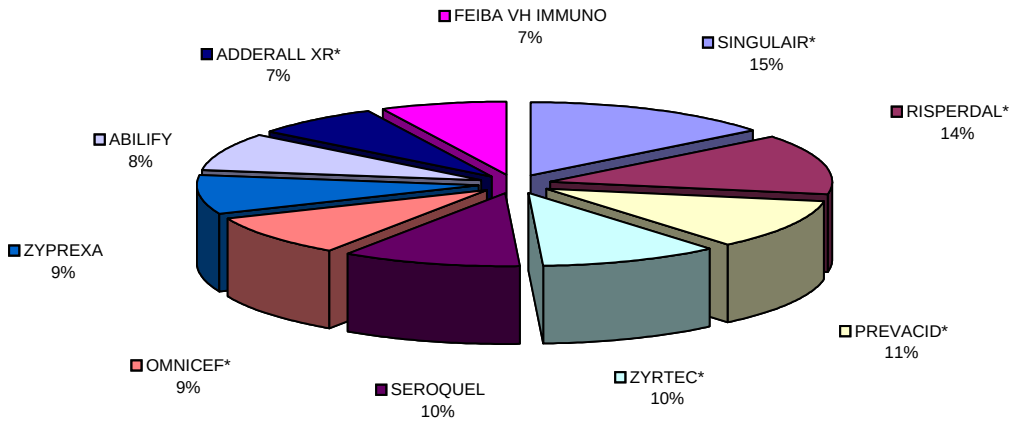
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/07-04/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,434	$ 759,350.79	5
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,801	$ 719,307.82	18
PREVACID*	PROTON-PUMP INHIBITORS	4,100	$ 577,472.85	3
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	10,268	$ 550,672.80	29
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,860	$ 547,554.19	11
OMNICEF*	CEPHALOSPORINS	5,270	$ 479,727.67	49
ZYPREXA	ANTIPSYCHOTIC AGENTS	1,022	$ 463,778.87	19
ABILIFY	ANTIPSYCHOTIC AGENTS	1,041	$ 444,327.66	24
ADDERALL XR*	AMPHETAMINES	3,090	$ 386,459.74	33
FEIBA VH IMMUNO	HEMOSTATICS	6	$ 376,259.11	----------
PULMICORT*	ADRENALS	1,600	$ 375,466.03	73
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,197	$ 327,059.26	20
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,572	$ 323,113.63	41
AZITHROMYCIN	MACROLIDES	8,473	$ 302,315.33	3
XOPENEX*	BETA-ADRENERGIC AGONISTS	1,749	$ 266,296.55	107
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,490	$ 260,962.90	4
AMOX TR-POTASSIUM CL	PENICILLINS	4,776	$ 253,898.39	6
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,141	$ 217,035.93	74
GEODON*	ANTIPSYCHOTIC AGENTS	741	$ 215,867.26	72
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	697	$ 205,824.43	26
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,368	$ 199,841.31	63
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,725	$ 197,524.39	5
EXJADE	HEAVY METAL ANTAGONISTS	49	$ 188,226.38	----------
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,757	$ 178,146.57	1
EFFEXOR XR*	ANTIDEPRESSANTS	1,137	$ 169,587.30	6
TOTAL TOP 25		67,364	$ 8,986,077.16	

Total Rx Claims From 04/01/07-04/30/07	353,044

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

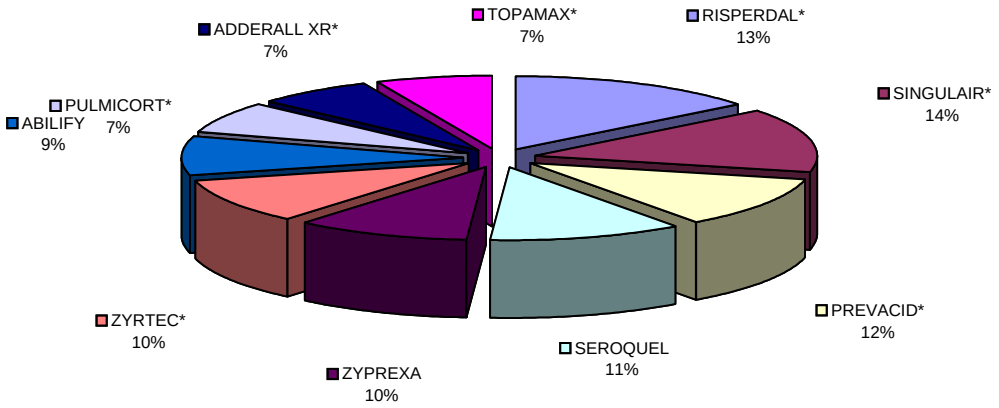
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 05/01/07-05/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,857	$ 736,294.75	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,129	$ 731,059.75	5
PREVACID*	PROTON-PUMP INHIBITORS	4,238	$ 595,373.55	3
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,905	$ 562,895.02	11
ZYPREXA	ANTIPSYCHOTIC AGENTS	1,108	$ 516,615.55	19
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,580	$ 511,949.13	29
ABILIFY	ANTIPSYCHOTIC AGENTS	1,059	$ 450,197.96	24
PULMICORT*	ADRENALS	1,520	$ 351,036.91	73
ADDERALL XR*	AMPHETAMINES	2,767	$ 348,180.79	33
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,214	$ 340,962.12	20
ADVATE	HEMOSTATICS	14	$ 301,220.76	---------
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,261	$ 285,862.24	41
FEIBA VH IMMUNO	HEMOSTATICS	3	$ 276,680.56	---------
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,495	$ 262,487.36	4
AZITHROMYCIN	MACROLIDES	6,998	$ 248,580.68	3
OMNICEF*	CEPHALOSPORINS	2,558	$ 238,240.03	49
XOPENEX*	BETA-ADRENERGIC AGONISTS	1,460	$ 226,778.34	107
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	753	$ 222,248.65	26
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,182	$ 221,337.65	74
AMOX TR-POTASSIUM CL	PENICILLINS	4,263	$ 221,330.33	6
GEODON*	ANTIPSYCHOTIC AGENTS	752	$ 219,406.04	72
EXJADE	HEAVY METAL ANTAGONISTS	54	$ 210,853.32	---------
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,718	$ 201,364.19	5
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,254	$ 180,915.56	63
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	1,016	$ 180,814.62	69
TOTAL TOP 25		59,158	$ 8,642,685.86	

Total Rx Claims From 05/01/07-05/31/07	343,357

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

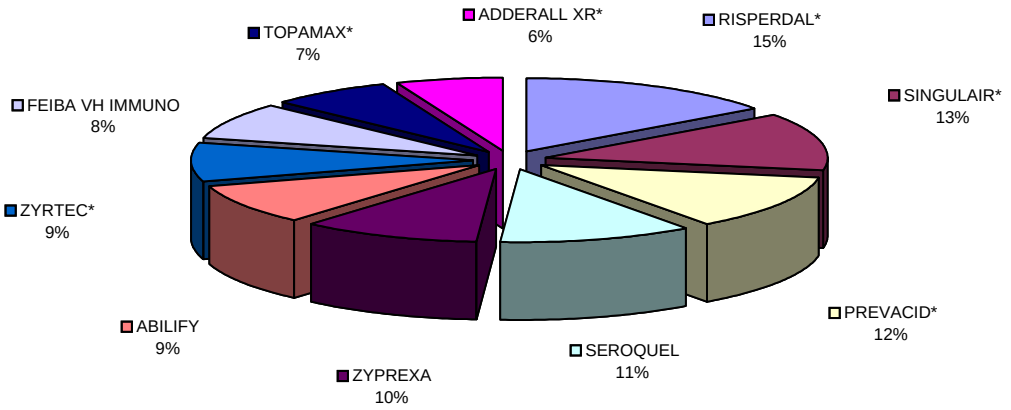
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 06/01/07-06/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,824	$ 731,482.24	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,178	$ 632,765.05	5
PREVACID*	PROTON-PUMP INHIBITORS	4,211	$ 598,410.12	3
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,812	$ 541,165.14	11
ZYPREXA	ANTIPSYCHOTIC AGENTS	1,053	$ 503,888.73	19
ABILIFY	ANTIPSYCHOTIC AGENTS	1,020	$ 443,713.95	24
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	7,839	$ 422,201.09	29
FEIBA VH IMMUNO	HEMOSTATICS	5	$ 388,447.47	---------
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,173	$ 352,022.05	20
ADDERALL XR*	AMPHETAMINES	2,311	$ 293,719.28	33
PULMICORT*	ADRENALS	1,134	$ 265,189.02	73
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,445	$ 256,286.83	4
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,873	$ 241,683.35	41
GEODON*	ANTIPSYCHOTIC AGENTS	754	$ 220,021.58	72
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,144	$ 218,010.65	74
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	728	$ 213,831.49	26
ADVATE	HEMOSTATICS	8	$ 206,386.62	---------
CEFDINIR	CEPHALOSPORINS	2,907	$ 205,577.93	---------
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,686	$ 196,531.34	5
EXJADE	HEAVY METAL ANTAGONISTS	48	$ 190,668.41	---------
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,807	$ 183,121.20	1
EFFEXOR XR*	ANTIDEPRESSANTS	1,220	$ 182,446.33	6
HELIXATE FS	HEMOSTATICS	9	$ 181,755.04	---------
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	741	$ 176,869.18	81
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	985	$ 171,164.41	69
TOTAL TOP 25		44,915	$ 8,017,358.50	

Total Rx Claims From 06/01/07-06/30/07	316,818

** Indicates preferred products on Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

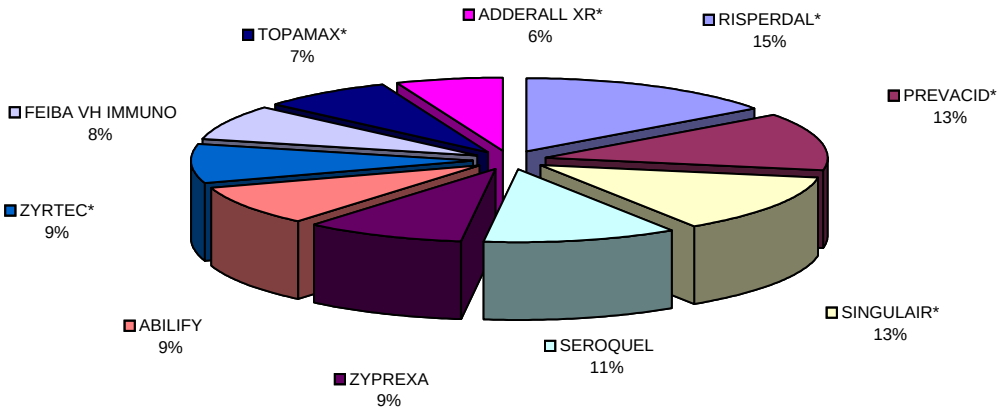
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 07/01/07-07/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	2,844	$ 730,280.72	18
PREVACID*	PROTON-PUMP INHIBITORS	4,382	$ 633,566.57	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,171	$ 631,214.36	5
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,738	$ 555,862.61	11
ZYPREXA	ANTIPSYCHOTIC AGENTS	911	$ 448,017.64	19
ABILIFY	ANTIPSYCHOTIC AGENTS	993	$ 435,014.02	24
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	7,524	$ 420,896.26	29
FEIBA VH IMMUNO	HEMOSTATICS	4	$ 379,463.01	---------
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,213	$ 363,045.13	20
ADDERALL XR*	AMPHETAMINES	2,384	$ 300,579.71	33
ADVATE	HEMOSTATICS	7	$ 282,183.87	---------
PULMICORT*	ADRENALS	1,146	$ 269,947.31	73
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,398	$ 247,550.25	4
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,932	$ 245,856.77	41
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	760	$ 227,543.81	26
CEFDINIR	CEPHALOSPORINS	3,112	$ 222,963.82	---------
GEODON*	ANTIPSYCHOTIC AGENTS	728	$ 217,424.95	72
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,131	$ 213,954.42	74
EXJADE	HEAVY METAL ANTAGONISTS	50	$ 209,352.25	---------
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,736	$ 201,328.41	5
AZITHROMYCIN	MACROLIDES	5,522	$ 197,073.62	3
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	754	$ 180,430.54	81
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,768	$ 180,150.84	1
EFFEXOR XR*	ANTIDEPRESSANTS	1,199	$ 177,781.57	6
AMOX TR-POTASSIUM CL	PENICILLINS	3,251	$ 176,305.58	6
TOTAL TOP 25		52,658	$ 8,147,788.04	

Total Rx Claims From 07/01/07-07/31/07	325,725

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

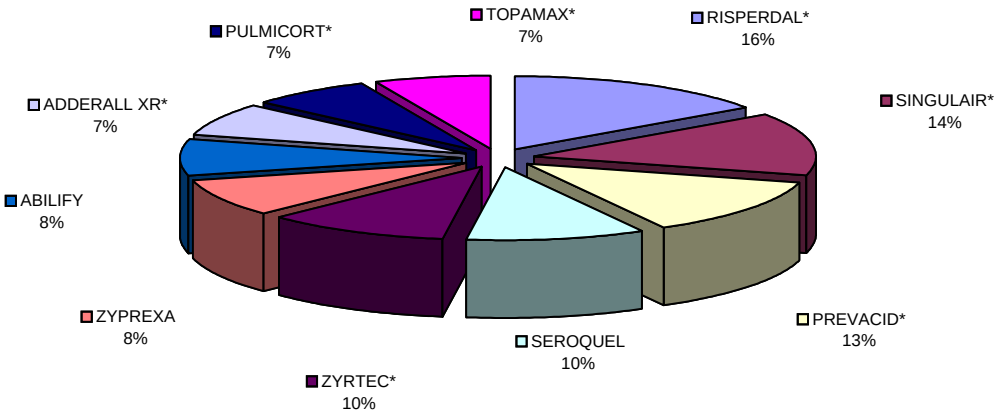
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 08/01/07-08/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,190	$ 838,727.02	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,549	$ 772,820.87	5
PREVACID*	PROTON-PUMP INHIBITORS	4,770	$ 699,259.38	3
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,807	$ 575,233.17	11
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,669	$ 572,569.60	29
ZYPREXA	ANTIPSYCHOTIC AGENTS	957	$ 468,292.10	19
ABILIFY	ANTIPSYCHOTIC AGENTS	1,020	$ 443,695.15	24
ADDERALL XR*	AMPHETAMINES	3,187	$ 396,453.10	33
PULMICORT*	ADRENALS	1,575	$ 376,293.34	73
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,270	$ 372,424.09	20
FEIBA VH IMMUNO	HEMOSTATICS	4	$ 340,685.32	----------
AZITHROMYCIN	MACROLIDES	9,116	$ 325,421.77	3
CEFDINIR	CEPHALOSPORINS	4,377	$ 321,946.58	----------
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,523	$ 317,519.58	41
ADVATE	HEMOSTATICS	5	$ 292,093.69	----------
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,601	$ 281,081.67	4
GEODON*	ANTIPSYCHOTIC AGENTS	845	$ 268,865.47	72
EXJADE	HEAVY METAL ANTAGONISTS	67	$ 263,799.38	----------
XOPENEX*	BETA-ADRENERGIC AGONISTS	1,461	$ 244,317.26	107
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	785	$ 243,410.66	26
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,225	$ 229,937.25	74
AMOX TR-POTASSIUM CL	PENICILLINS	4,145	$ 228,229.98	6
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,885	$ 219,666.59	5
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,398	$ 208,370.21	63
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	830	$ 200,873.49	81
TOTAL TOP 25		65,261	$ 9,501,986.72	

Total Rx Claims From 08/01/07-08/31/07	371,591

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



Potential Misuse of ADHD Agents

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a condition that becomes apparent in some children in the preschool and early school years, characterized by inattention, hyperactivity, and impulsivity. Although ADHD is considered to be a childhood disease, it often continues into adulthood, requiring treatment of this population as well.

Problem

At the May 17, 2007 DUR Board Meeting, there were some discussions about the potential misuse of agents that treat ADHD, particularly in the adult population. The following chart lists the medications used in the treatment of ADHD.

Generic Name	Trade Name
Stimulants	
Amphetamine salt combination	Adderall®, Adderall XR®
Lisdexamfetamine	Vyvanse®
Dextroamphetamine	Dexedrine®, Dextrostat®
Dexmethylphenidate	Focalin®, Focalin XR®
Methylphenidate	Ritalin®
Methylphenidate (extended release)	Ritalin SR®, Ritalin LA®, Metadate CD®, Metadate ER®, Concerta®
Methylphenidate (transdermal)	Daytrana®
Selective Norepinephrine Reuptake Inhibitors	
Atomoxetine	Strattera®

Specific concerns were raised about the inappropriate use of these medications in the adult population for off-label indications such as decreased appetite and weight loss, which are common side effects of the ADHD treatment agents.

Method

Utilization data was gathered through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. Two unique searches were conducted covering the period from 7/1/06 through 5/25/07.

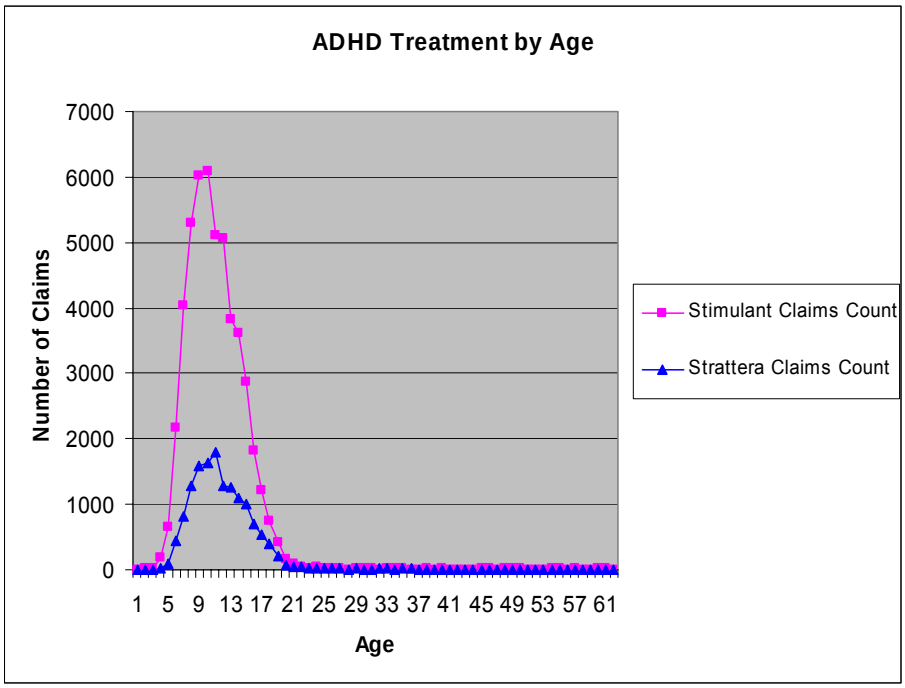
The search parameters were:

1. Stimulant utilization based on age
2. Strattera® utilization based on age

These searches were then compared to show any trends of utilization as a function of age.

Results

During the time period of July 1, 2006 to May 25, 2007, there were a total of 50,152 stimulant claims and 14,637 Strattera® claims. Utilization of both classes was highest for children and adolescents, from ages 5 to 21.



Summary

As the information above reveals, the majority of stimulant and Strattera® use is in children and adolescents. After the age of 21, utilization of both classes drops to insignificant levels, indicating that widespread misuse in adults is not occurring.

Recommendations

Although the above figures do not indicate extensive abuse of ADHD medications in the adult population, a retrospective DUR criterion is recommended to identify those adult patients (age ≥ 21) who may be using these medications inappropriately.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
ADHD RELATED CRITERIA
September 2007

Criteria Recommendations	*Approved*	*Rejected*

1. Stimulants / Appropriate use in Adults _____ _____

Alert Message: Our records do not indicate a supporting diagnosis for the use of the medication(s). Off label uses, diversion, and abuse are concerns with medications used for treating ADHA and/or narcolepsy. These agents have serious adverse effects and should only be used for FDA approved indications.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease:

Util A	Util B	Util C (Negating)
Dextroamphetamine		ADHD
Methamphetamine		ADD
Lisdexamfetamine		Narcolepsy
Amphetamine Mixtures		
Dexmethylphenidate		
Methylphenidate		
Atomoxetine		

Age Range: ≥ 21 years of age

References:
Facts & Comparisons, 2007 Updates.
Micromedex Healthcare Series, DRUGDEX Drug Evaluations, 2007.
Clinical Pharmacology, Gold Standard, 2007.

Inappropriate Use of Antibiotics

Data from the National Center for Health Statistics indicate that in recent years, approximately three fourths of all outpatient antibiotics have been prescribed for otitis media, sinusitis, bronchitis, pharyngitis, or nonspecific upper respiratory tract infection. Antimicrobial drug use rates are highest for children; therefore, the pediatric age group represents the focus of our attention for the following DUR suggestions.

The emergence of bacterial strains that are increasingly resistant to antimicrobial agents is a growing national and worldwide concern. This seems to have been given credence by the spread of organisms such as MRSA, vancomycin-resistant enterococci and multidrug-resistant tuberculosis, all essentially untreatable with routinely available antibiotics. In response to this growing problem, control of the spread of antimicrobial resistance has been identified as a priority by many organizations, including the Centers for Disease Control and Prevention, the American Society for Microbiology, the World Health Organization, the American Academy of Family Physicians, and the American Academy of Pediatrics.

Currently, millions of courses of unnecessary antibiotics are given each year. These courses may take the form of inappropriate diagnosis or inappropriate prescribing habits. There is little doubt that parental misunderstanding of appropriate antibiotic use plays a major role in physician prescribing. A well known study published in *JAMA* in 1995 found that from the time period of 1990 to 1992, almost one in six physician office visits resulted in an antimicrobial prescription. These included >17 million prescriptions for nonspecific upper respiratory infection, 16 million prescriptions for bronchitis, and 13 million prescriptions for pharyngitis. In a recent review of the Medicaid database in Kentucky, 60% of patients diagnosed with the common cold were treated with an antibiotic. These findings have prompted several Governmental agencies to launch national campaigns, such as the CDC's *Get Smart* program, to help educate both health care providers and the general public about the dangers of inappropriate antibiotic usage.

A recent study published in the April issue of *Pediatrics* set out to determine the impact of a community-wide educational intervention on parental misconceptions likely contributing to pediatric antibiotic overprescribing. The study found that although knowledge regarding appropriate use of antibiotics is improving without additional targeted intervention among more socially advantaged populations, parents of Medicaid-insured children may benefit from educational interventions to promote judicious antibiotic use.

Inappropriate antibiotic usage may have more implications than only multi-drug resistant microorganisms. A study recently published in the June issue of *Chest* found that children who were given antibiotics in the first year of life were significantly more likely to develop asthma by age 7. Risk of developing asthma increased with the number of antibiotic courses received: children who received 1-2 courses incurred a 21% increased risk, those who received 3-4 courses had an increased risk of 30%, and those children that were given > 4 courses within the first year of life had a 46% increased risk

of developing asthma. Increased risk of developing asthma was also associated with the prescribing of broad-spectrum antibiotics, particularly broad-spectrum cephalosporins. It is hypothesized by the author of this study that the broad-spectrum antibiotics may kill off too many of the good bacteria in the body, such as the natural microflora in the gut, that are necessary for proper development of the immune system in the first year of life.

Direct Impact on MS Medicaid

According to the American Lung Association, asthma is the most common chronic illness in childhood and is the leading cause of school absenteeism attributed to chronic conditions. Asthma is also the third leading cause of hospitalization among children under the age of 15, and is associated with an annual direct health care cost of approximately $11.5 billion. In Mississippi approximately 66,620 children (age < 18) and 156,117 adults (age ≥ 18) suffer from asthma. Since asthma cannot be cured, only controlled, researchers are now concentrating on factors that may play a role in initial development of the disease.

Upon review of the Cost Analysis reports for April 2007 and May 2007, it is clear that pharmaceutical treatment of asthma is a significant cost to the State. In those months four respiratory agents, Singulair®, Pulmicort®, Advair® and Xopenex®, were in the top 25 drugs based on total claims cost. Prevention of future asthma cases could present considerable cost savings to the State in drug expenditures alone.

Recommendations

In an effort to educate providers, a retrospective DUR criterion is recommended to identify those patients less than 1 year of age that may have been overutilizing antibiotic treatments.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
ASTHMA ANTIBIOTIC CRITERIA
September 2007

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

1. Antibiotics / Therapeutic Appropriateness _____ _____

Alert Message: The use of antibiotics during the first year of life has been associated with an increased risk of developing childhood asthma. The risk increases with the use of multiple courses of antibiotics and the use of broad-spectrum antibiotics. This risk may be reduced by the judicious and appropriate prescribing of antibiotics, particularly avoiding the use of broad-spectrum cephalosporins.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Disease:

Util A	Util B	Util C
Penicillins		
Cephalosporins		
Monobactams		
Quinolones		
Fluoroquinolones		
Tetracyclines		
Macrolides		
Ketolides		
Oxazolidinones		
Aminoglycosides Oral		
Sulfonamides		
Bacitracin		
Metronidazole		
Nitrofurans		
Methenamines		
Folate Antagonists		

Age Range: 0 – 1 year of age

References:

Kozyrskyj A, Ernst P, Becker AB, Increased risk of childhood asthma from antibiotic use in early life, Chest. 2007;131(6):1753-1759.

Marra F, Lynd L, Coombes M, et al., Does antibiotic exposure during infancy lead to development of asthma? Chest. 2006;126:610-618.

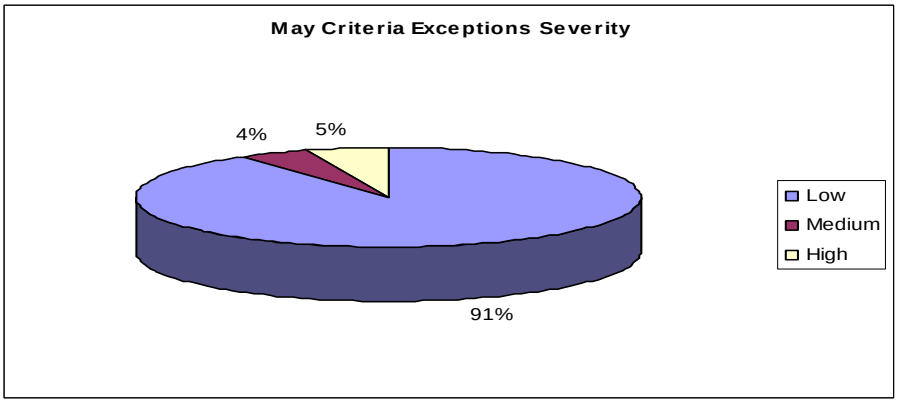
Johnson CC, Ownby DR, Alford SH, et al., Antibiotic exposure in early infancy and risk of childhood atopy. The Journal of Allergy and Clinical Immunology, June 2005. Vol. 115, Issue 6:1218-1224.

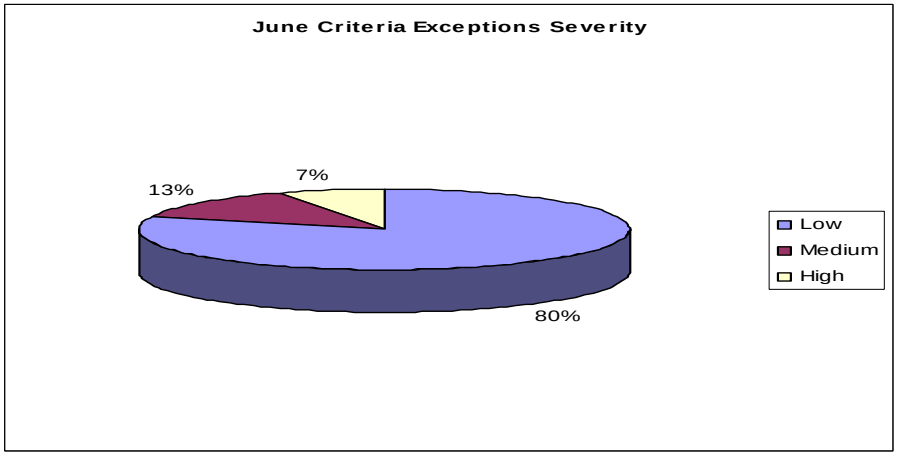
HIV Criteria Report

At the May 17, 2007 DUR Board Meeting there were several new criteria related to HIV therapy that were presented to the Board for consideration. Due to the very serious and complex nature of this disease and its treatment, there were some lengthy discussions related to concerns about the management of HIV patients. As a result HID has reviewed the activity of these criteria for May and June and compiled the results below.

Criteria Type (# of Criteria)	May Exceptions	June Exceptions
Impaired Antiviral Effect (4)	0	2
Protease Inhibitor Interaction (1)	1	1
Antiretroviral Drug Interaction (6)	7	6
Non-Adherence to Antiretroviral therapy (27)	124	86
Inappropriate HIV Drug Regimen (48)	73	63
Total HIV- Related Criteria Exceptions	205	158
Percentage of Total Criteria Exceptions	1.02%	0.88%`

HID has designed a system that accounts for individual patient factors that increase the risk for each criteria, as well as the documentation of the adverse event related to each criteria in the literature. A focused inquiry was made into the severity of the exceptions generated in May and June for the HIV- related criteria, and the charts below illustrate these findings.





Based on the information above, it appears that there is not a significant drug therapy problem in HIV patients enrolled in Mississippi Medicaid. Furthermore, of those identified as having a drug therapy problem, only a small percentage of those are considered to be high-risk. However, since appropriate use of HIV medications is imperative in *each* patient, retrospective DUR criteria are used to assist physicians in providing effective treatment for their HIV patients.

Proper Singulair Utilization

Singulair® (montelukast sodium) is a leukotriene receptor antagonist that is indicated for use in asthma and allergic rhinitis. Leukotriene-mediated effects are responsible for the signs and symptoms associated with asthma and allergic rhinitis. By inhibiting the physiologic activity of leukotrienes, Singulair® results in less airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process.

Singulair® is consistently one of the leaders in the monthly cost analysis reports. For example, in April 2007, it was the leading drug based on total claims cost for Medicaid, with a total of 7,434 prescriptions and $759,350.79 paid by DOM. Due to these consistently large numbers, there is some concern that Singulair® may be overutilized for allergic rhinitis when less expensive alternatives are available, such as generic antihistamines.

HID gathered utilization data for Singulair® through RxExlorer®, which searches through paid claims data submitted to HID by the fiscal agent. From 5/1/06 to 5/1/07 a total of 29,273 individual beneficiaries received Singulair®. The chart below illustrates the findings of Singulair® use based on diagnosis during this time frame.

Number of Patients	Diagnosis
18,149	Asthma
18,897	Allergic rhinitis
12,716	Asthma and allergic rhinitis

From May 2006 to May 2007, approximately 62% of patients who received Singulair® had an asthma diagnosis, while approximately 65% of patients who received Singulair® had an allergic rhinitis diagnosis. Approximately 43% of those patients who had a prescription for Singulair® filled during this time period had a diagnosis for both asthma and allergic rhinitis. According to this information, there doesn't appear to be gross overutilization of Singulair® outside of the asthma population.

While there are cheaper alternatives to Singulair® in the treatment of allergic rhinitis, it has a definite role in the management of this illness. It has been found to be as or more effective than antihistamines, with fewer side effects, such as dry mouth, drowsiness, constipation, etc. Also, a growing number of ENT physicians strongly oppose the use of antihistamines in patients with allergic rhinitis since they tend to make the mucus secretions more viscous and harder to clear. This can lead to build up of mucus in the sinus cavities and Eustachian tubes, setting up the ideal environment for recurrent otitis media and chronic sinusitis. Although the general consensus is that intranasal corticosteroids are more effective at treating allergic rhinitis than Singulair®, there are concerns with their use in young children due to the fear of growth suppression associated with corticosteroid use. All of these factors have led to increased use of Singulair® in allergic rhinitis patients.

Alprazolam and Lorazepam Utilization in Current MS Medicaid Population

Introduction

Alprazolam and lorazepam are benzodiazepines and are indicated for use in panic and anxiety disorders. Due to their anxiolytic effects, however, benzodiazepines have a very high abuse potential. It is not uncommon for patients who are given these medications for a valid medical purpose to become addicted to the calming effect they provide.

Problem

Alprazolam and lorazepam consistently appear in the cost analysis reports for DUR meetings. For the last five months, these medications have been in the Top 25 Drugs based on the number of claims. This is troublesome considering that the MS Medicaid population is now comprised mostly of children, and these medications are not considered a common treatment modality in the pediatric population. In addition, the misuse of alprazolam and lorazepam within the elderly population is another concern. While these medications are a valid treatment option in long-term care settings, their overuse within this population can cause many unwanted effects, such as falls, respiratory depression, and prolonged sedation.

Method

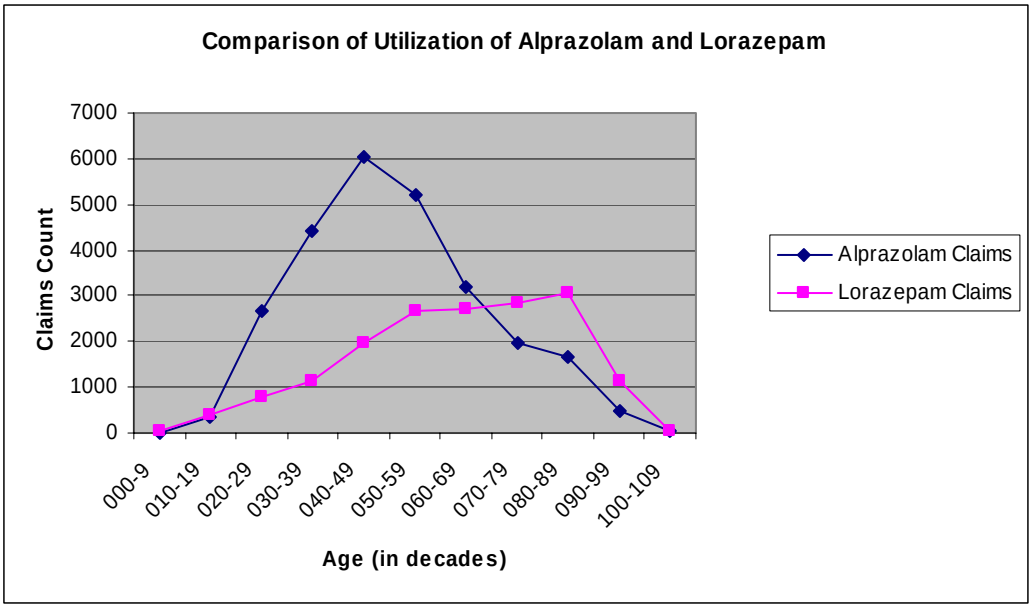
Utilization data was gathered through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. These searches were conducted covering the period from 8/25/06 through 8/24/07.

The search parameters were:

1. Alprazolam utilization based on age and LTC status
2. Lorazepam utilization based on age and LTC status

Results

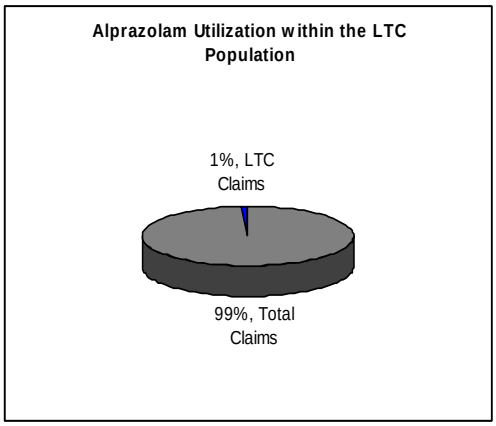
	Alprazolam			Lorazepam		
Age(decades)	**Total Claims**	**LTC Claims**	**Qty > 100**	**Total Claims**	**LTC Claims**	**Qty > 100**
000-9	19	5	0	34	0	0
010-19	329	2	13	374	170	17
020-29	2682	0	304	778	155	38
030-39	4412	31	549	1137	131	54
040-49	6016	50	729	1950	165	129
050-59	5217	79	636	2688	312	211
060-69	3174	77	275	2720	319	188
070-79	1951	25	90	2864	21	111
080-89	1664	1	28	3077	0	41
090-99	496	1	12	1153	9	9
100-109	38	1	0	57	0	0
Totals	**25998**	**272**	**2636**	**16832**	**1282**	**798**

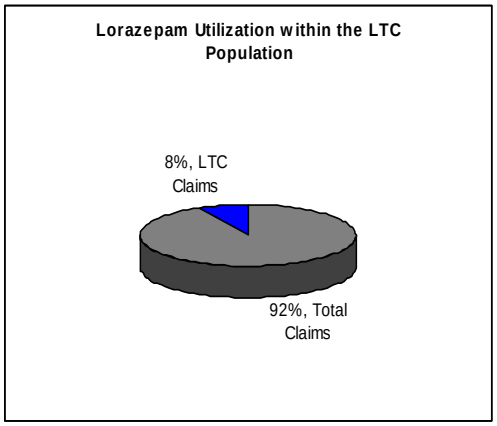


As the numbers above indicate, the majority of use of alprazolam and lorazepam occurs in the age range of 30-69 and 50-89, respectively. This shows that use of these medications is not rampant within the pediatric population, with 1.3% and 2.4% of alprazolam and lorazepam claims, respectively, within this time frame belonging to patients aged 0-19 years.

Utilization within the Long-Term Care Population

Alprazolam and lorazepam are often necessary treatment options in the long-term care setting for those patients who become agitated or experience anxiety. However, their misuse in this population is not uncommon, particularly in long-term care settings that face many challenges in the day-to-day care of these patients.





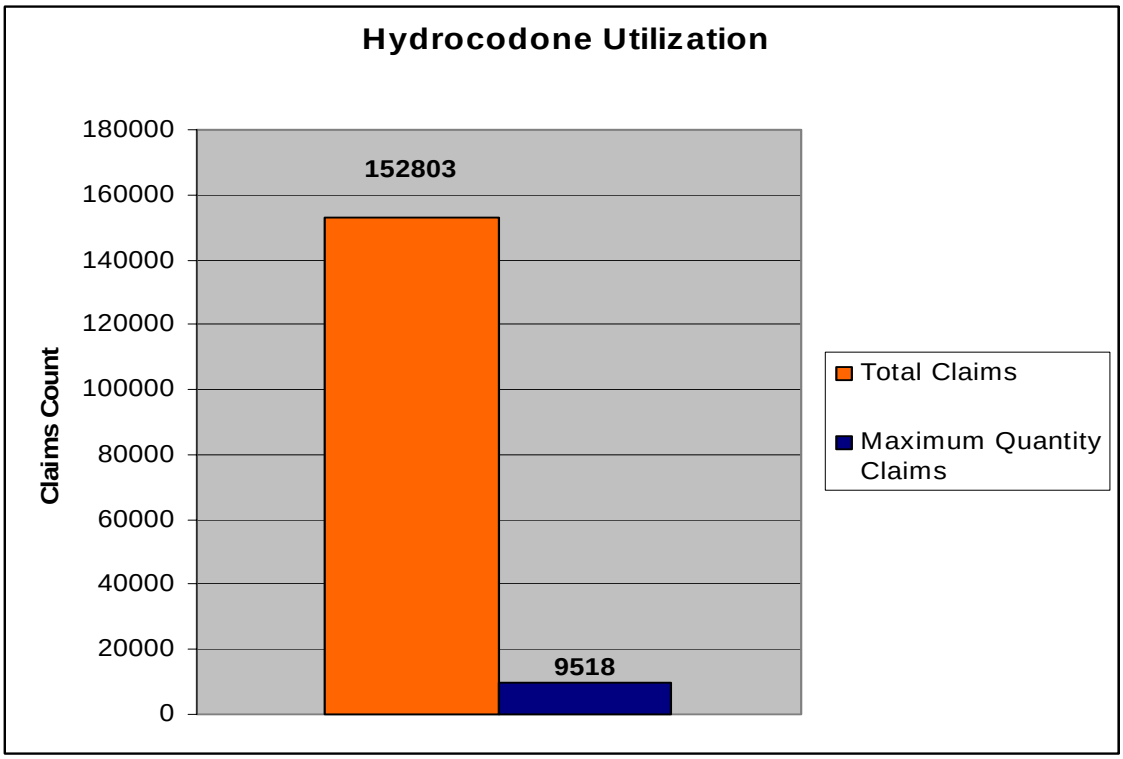
The graphs above illustrate that a relatively small number of claims for alprazolam and lorazepam are within the long-term care population. For alprazolam, the number of claims within this population is 272, representing approximately 1% of total claims for this medication. The number of claims for lorazepam within the long-term care population is 1282, which represents 7.6% of total claims for this medication.

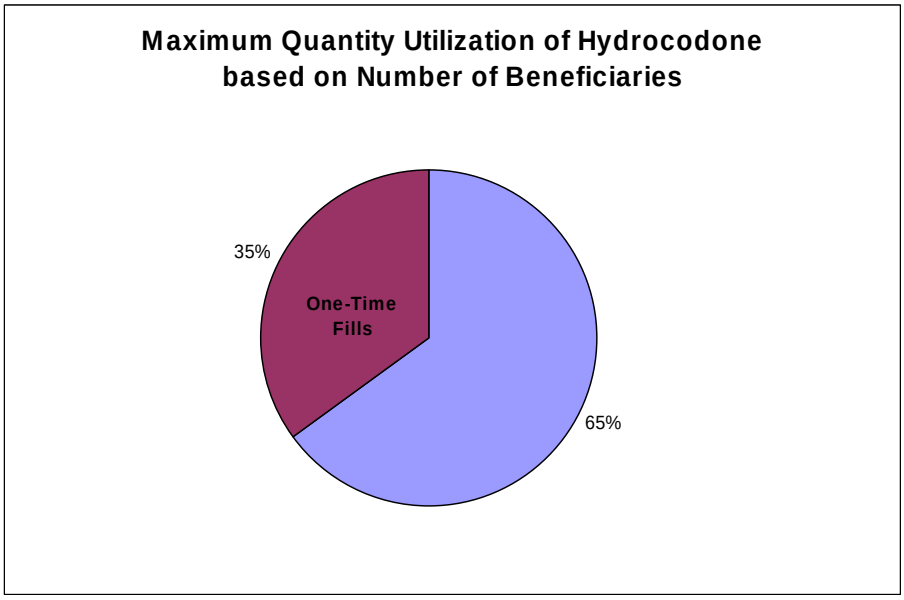
Another fact to consider when looking at the number of claims within the elderly population is that benzodiazepines are on the short list of medications covered by Medicaid for dual-eligible beneficiaries, i.e. those patients eligible for Medicare and Medicaid. While Medicare Part D provides the majority of drug coverage for these patients, generic benzodiazepines such as alprazolam and lorazepam are covered by Medicaid, contributing to the large number of claims to Medicaid for these medications each month.

Hydrocodone Utilization

Hydrocodone is consistently one of the Top 5 drugs based on the number of claims in the cost analysis reports for DUR meetings. This is not out of line with the national trends, with hydrocodone being the top generic drug dispensed nationwide. However, with the knowledge that this medication is the root of many substance-abuse cases, the fact that it represents such a large portion of Medicaid's drug claims is troubling.

HID gathered utilization data for hydrocodone through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. From 9/22/06 to 9/21/07, there were a total of 152,803 claims for hydrocodone. Of these claims, 9518 (~6%) were for the monthly maximum quantity of hydrocodone, which is 62 tablets.





Of the 2661 beneficiaries who received the maximum monthly quantity of hydrocodone, 935 received only one prescription, based on paid claims. Therefore, approximately 35% of the beneficiaries who received the maximum monthly quantity of hydrocodone did so for single incidents, such as surgery, sprains, etc.

While high rates of hydrocodone use are cause for concern both at the state and national level, based on the information above habitual use of the monthly maximum quantity of 62 tablets is not widespread within Mississippi Medicaid. And of those claims for the maximum quantity, approximately one-third are for one-time fills. From the information gathered, it appears measures that DOM has implemented, such as monthly quantity limits, have helped to curb abuse of hydrocodone.

Impact of Quinine Removal on Utilization of Gabapentin and Lyrica®

Introduction

On December 11, 2006, the FDA ordered all manufacturer's to stop marketing unapproved products containing quinine, citing serious safety concerns, including deaths, associated with these products. Currently, Qualaquin® is the only FDA-approved product that contains quinine. Quinine is a medication that is approved for the treatment of malaria, but it is often used for the off-label treatment of leg cramps and other similar conditions. As part of its recent action, the FDA also cautioned consumers about this off-label use of quinine to treat leg cramps. Because malaria is life-threatening, the risks associated with quinine use are justified for that condition. But because of the drug's risks, FDA believes it should not be used to prevent or treat leg cramps.

Problem

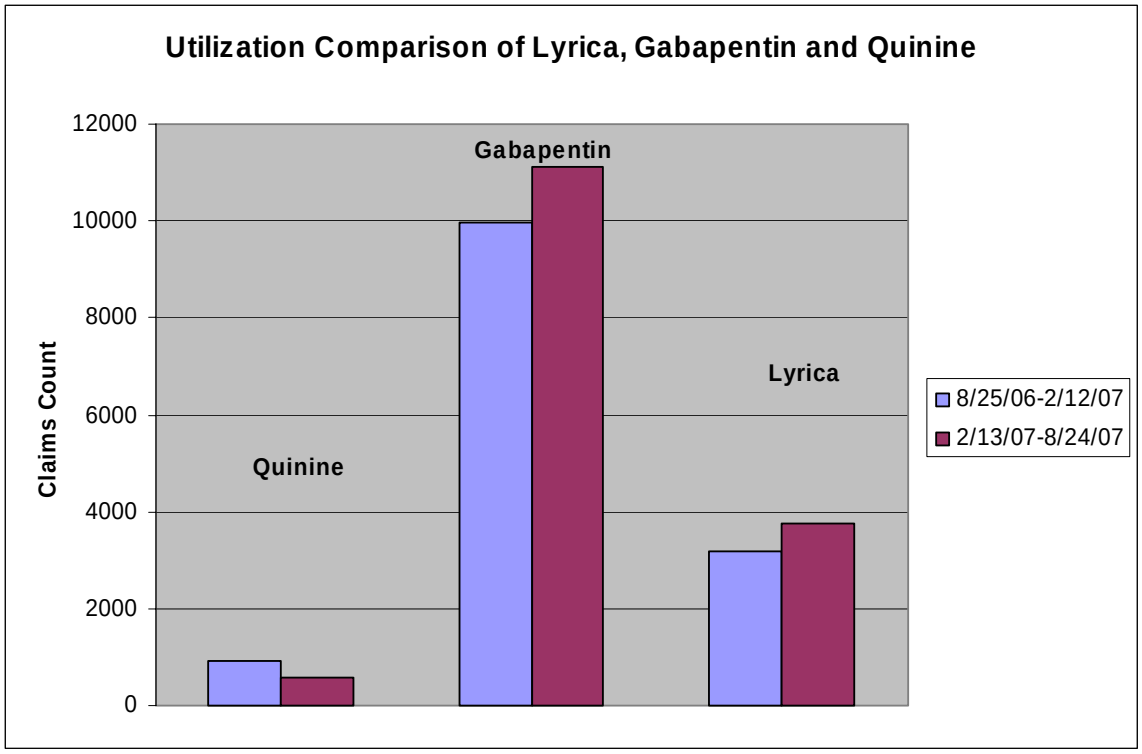
At the most recent DUR Board meeting in September, there was some discussion related to the removal of unapproved quinine products from the market. It was noted that as a result of this removal, some pharmacists had seen a significant increase in utilization of gabapentin and Lyrica® for the treatment of leg cramps and other similar conditions.

Method

Utilization data was gathered through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. Two unique searches were conducted covering the time periods from 8/25/06 through 2/12/07, and 2/13/07 through 8/24/07. These searches were for utilization of quinine, gabapentin, and Lyrica® for each time period and were compared to identify and trends based on the date that all firms had to cease marketing quinine, which was February 13, 2007.

Results

Drug	Claims from 8/25/06 – 2/12/07	Claims from 2/13/07 – 8/24/07
Quinine	914	585
Gabapentin	9959	11117
Lyrica®	3183	3747



Based on the information above, it appears that quinine utilization dropped approximately 36% within the year that the FDA announced its position. However, while there was some increase in utilization of gabapentin (~11%) and Lyrica® (~15%) after the withdrawal deadline for quinine, the increase was not as significant as initially anticipated.

Summary

Due to serious safety concerns associated with the use of quinine, the FDA ordered all manufacturer's to stop marketing unapproved products containing quinine by February 13, 2007. Since this medication was used off-label for the prevention and treatment of leg cramps and other associated disorders, it was expected to see a rise in the utilization of other medications, such as gabapentin and Lyrica®, used for these type conditions. While some increase was seen in their utilization, it was not as large of an increase as was expected.

Duplicate Utilization of Risperdal Consta and Oral Antipsychotic Agents

Risperdal Consta® is a long-acting atypical antipsychotic injection approved for the treatment of schizophrenia. This agent is well-suited for patients for whom medication compliance is a challenge. Risperdal Consta® is administered as an intramuscular injection every two weeks.

According to the FDA-approved prescribing information, tolerability to oral Risperdal® should be established prior to initiating therapy with Risperdal Consta®. The labeling also states that oral risperidone or another antipsychotic medication should be given with the first injection of Risperdal Consta® ,continued for three weeks, then discontinued to ensure that effective therapeutic plasma concentrations are reached and maintained prior to the main release phase of risperidone from the injection site.

Problem

From both therapeutic appropriateness and cost perspectives, there is concern about possible duplicate utilization of long-acting injectable risperidone and oral atypical antipsychotic agents. On October 9, 2007, the P&T Committee reviewed the antipsychotic agents and the discussion included a question about this very topic. During this meeting, a clinical representative for the manufacturer of Risperdal Consta® stated that beyond the initial three week transition period, he knew of no circumstance under which it would be appropriate to treat a patient concurrently with an oral atypical antipsychotic and Risperdal Consta®.

Method

Utilization data was gathered through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. Two unique searches were conducted covering the period from 1/1/07 through 9/21/07.

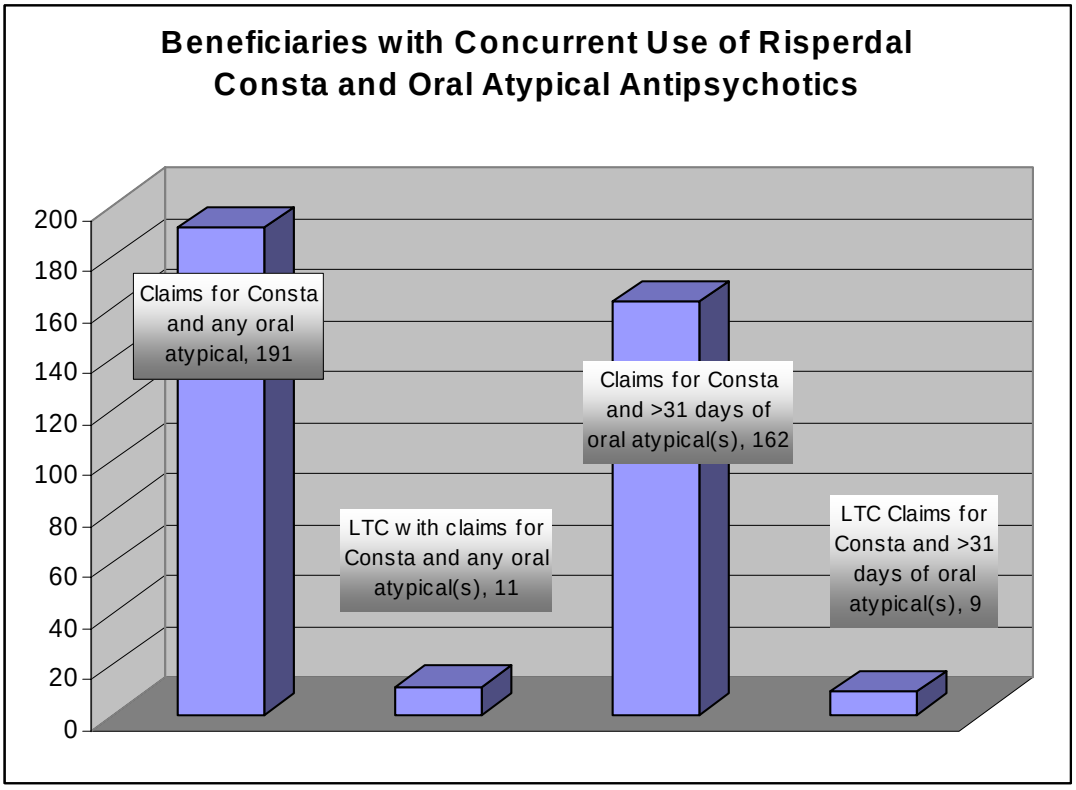
The search parameters were:

1. Total Risperdal Consta utilization
2. Total utilization of any oral atypical antipsychotic(s)
3. Risperdal Consta utilization among beneficiaries in long-term care settings
4. Utilization of any oral atypical antipsychotic(s) among beneficiaries in long-term care settings.

The beneficiaries identified in these searches were then intersected to determine those beneficiaries with utilization of Risperdal Consta® and one or more oral atypical antipsychotic agents. In order to control for the recommended initial three week transition with oral agents, beneficiaries with claims totaling less than 32 days of treatment with an oral agent were then subtracted from the search.

Results

The search resulted in 191 beneficiaries who received long-acting injectable risperidone and oral atypical antipsychotic therapy during the time period searched. Of these, 162 beneficiaries had oral agent claims totaling greater than 31 days. A very small number of these beneficiaries were determined to be residents of long-term care facilities.



LTC = Beneficiaries in long-term care facilities

The following search results are included to provide points of reference regarding general utilization of the atypical antipsychotic agents within the Mississippi Medicaid population.

Data Parameters:	# of Benes
One or more claims for Risperdal Consta	302
LTC one or more claims for Risperdal Consta	16
One or more claims for oral atypical antipsychotic(s)	13,373
LTC one or more claims for oral atypical antipsychotic(s)	1,542
Claims for oral atypical antipsychotic(s) totaling > 31 days supply	325
LTC claims for any oral atypical antipsychotic(s) totaling > 31 days supply	190

According to this analysis, over 50 percent (162/302) of beneficiaries on Risperdal Consta received greater than 31 days of treatment with an oral atypical antipsychotic during the time period reviewed.

Recommendations

Concurrent use of long-acting injectable risperidone and oral atypical antipsychotic agents clearly falls outside of treatment recommendations. A significant number of Medicaid beneficiaries have been identified as receiving this duplicate therapy. As a result, retrospective DUR criterion may be helpful in alerting prescribers to the appropriate prescribing guidelines for this product. In addition, appropriate therapy will be encouraged for specific beneficiaries.

Appropriate Antibiotic Use

Antimicrobial resistance among pathogens has become a common clinical problem, and the association of resistance with the use of antimicrobial drugs has been documented in both inpatient and outpatient settings. This emergence of bacterial strains that are increasingly resistant to antimicrobial agents is a growing national and worldwide concern. This seems to have been given credence by the spread of organisms such as MRSA, vancomycin-resistant enterococci and multidrug-resistant tuberculosis, all essentially untreatable with routinely available antibiotics. In fact, a fatal case of MRSA in a young girl from Vancleave, Mississippi has garnered national media attention in recent weeks. In response to this growing problem, control of the spread of antimicrobial resistance has been identified as a priority by many organizations, including the Centers for Disease Control and Prevention, the American Society for Microbiology, the World Health Organization, the American Academy of Family Physicians, and the American Academy of Pediatrics.

Decreasing the inappropriate use of antimicrobials has been listed as a primary solution to address the threat that antimicrobial resistance poses. Currently, millions of courses of unnecessary antibiotics are given each year. These courses may take the form of inappropriate diagnosis or inappropriate prescribing habits. A well known study published in *JAMA* in 1995 found that from the time period of 1990 to 1992, almost one in six physician office visits resulted in an antimicrobial prescription. These included >17 million prescriptions for nonspecific upper respiratory infection, 16 million prescriptions for bronchitis, and 13 million prescriptions for pharyngitis. In a recent review of the Medicaid database in Kentucky, 60% of patients diagnosed with the common cold were treated with an antibiotic.

There is little doubt that parental misunderstanding of appropriate antibiotic use plays a major role in physician prescribing. A recent study published in the April issue of *Pediatrics* set out to determine the impact of a community-wide educational intervention on parental misconceptions likely contributing to pediatric antibiotic overprescribing. The study found that although knowledge regarding appropriate use of antibiotics is improving without additional targeted intervention among more socially advantaged populations, parents of Medicaid-insured children may benefit from educational interventions to promote judicious antibiotic use.

To help combat the risk that antimicrobial resistance poses, HID recommends development of a Medicaid Prescriber Update, or “one-pager”, that outlines the importance of prudent prescribing of antibiotics, particularly in upper respiratory infection cases. HID recommends distribution of this document to prescribers by the Academic Detailing Staff, as well as availability by a link from the Division of Medicaid website.

Zyvox

Zyvox® (linezolid) is an oral oxazolidinone antibiotic that is used for the treatment of the following infections caused by susceptible strains of the designated microorganisms:

- Vancomycin-resistant enterococcal infections, including cases with concurrent bacteremia.
- Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains), or Streptococcus pneumoniae (penicillin-susceptible strains only)
- Complicated skin and skin structure infections: Complicated skin and skin structure infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains), Streptococcus pyogenes, or Streptococcus agalactiae.
- Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes.
- Community-acquired pneumonia caused by Streptococcus pneumoniae (penicillin-susceptible strains only), including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible strains only).

Currently, Zyvox® is a non-preferred product on the Preferred Drug List for Mississippi Medicaid. For the month of August, there were 63 RxPert® denials for Zyvox®. This represented 21 unique beneficiaries. While looking at more detailed data in an effort to streamline the electronic prior authorization process for Zyvox®, several recent studies were found showing that outpatient use of Zyvox® actually resulted in lower costs and prevented or shortened hospital stays. These studies were included in the *American Journal of Surgery*, the *Annals of Pharmacotherapy*, and *Clinical Therapeutics*, among others. In light of this valuable information, rather than streamlining the prior authorization process, the focus may now move to opening up access to Zyvox® as a product excluded from PDL status.

Prescribing Information Update

Upper Respiratory Infections

Mississippi Division of Medicaid

- *The common cold is caused by viral pathogens and resolves without antibiotic treatment.*
- *Symptoms may persist for 10-14 days*
- *First-generation antihistamines and decongestants may provide relief for cough associated with the common cold*
- *Antibiotic treatment may be needed if symptoms persist for longer than 10-14 days without improvement or if they are accompanied by fever, facial pain or swelling*

Upper respiratory infections are believed to be one of the most common diagnoses that result in improper antibiotic prescribing, since the source for most URIs is the common cold. The common cold is caused by viral pathogens, such as rhinovirus, parainfluenza, adenovirus, RSV, and influenza. Bacterial rhinosinusitis complicates only ~2% of cases. Symptoms may persist for 10-14 days, and purulent nasal secretions do not predict bacterial involvement unless other signs and symptoms of bacterial infection accompany these secretions. These may include:

- Fever
- Facial tenderness or pain
- Periorbital swelling

Treatment

The common cold resolves without antibiotic treatment, and treatment with an antibiotic does not shorten the duration of illness or prevent secondary bacterial infections. Acute cough associated with the common cold may be relieved by first-generation antihistamines and decongestants.

If symptoms persist for longer than 10-14 days without improvement or the patient experiences one or more of the symptoms listed above, antibiotic treatment may be warranted. In these cases, antibiotic treatment should target likely organisms, such as *S. pneumoniae* and *H. influenzae*. First-line drugs should be amoxicillin or amoxicillin/clavulanate. Patients should see improvement within 2-3 days; treatment should be continued for 7 days after symptoms improve or resolve (usually a 10-14 day course). In recurrent or unresponsive cases imaging studies of the sinuses should be considered.

Patients and Parents of Patients

- Tell patients (or parents) that antibiotic use increases the risk of an antibiotic-resistant infection.
- Recommend specific symptomatic therapy for cough, pain, sneezing, etc.
- Spend time answering questions and offer a contingency plan if symptoms worsen
- Provide patient education materials on antibiotic resistance.

Go to www.cdc.gov/getsmart or contact your local health department for more information and patient education materials.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
4th QUARTER 2007

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

1. Elidel / Therapeutic Appropriateness #2804 _____ _____

Alert Message: The topical calcineurin inhibitor, Elidel (pimecrolimus), is indicated as second-line therapy for the short-term, non-continuous chronic treatment of mild to moderate atopic dermatitis in patients who are unresponsive or intolerant to other agents. Rare cases of malignancy (i.e., skin cancer and lymphoma) have been reported in patients treated with topical pimecrolimus. Application should be limited to the areas affected with atopic dermatitis.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C (Negating)
Pimecrolimus		High to Very High Potency Topical Corticosteroids
		Augmented Betamethasone
		Clobetasol
		Diflorasone
		Halobetasol
		Amcinonide
		Betamethasone
		Desoximetasone
		Fluocinolone
		Fluocinonide
		Halcinonide
		Triamcinolone

Day Supply: 20 days in current 90 days
Age Range: 0 – 999 years of age
References:
Facts & Comparisons, 2006 Updates.
Elidel Prescribing Information, Jan. 2006. Novartis Pharmaceuticals Corp.

2. Protopic / Therapeutic Appropriateness #2805 _____ _____

Alert Message: The topical calcineurin inhibitor, Protopic (tacrolimus), is indicated as second-line therapy for the short-term, non-continuous chronic treatment of moderate to severe atopic dermatitis in patients who are unresponsive or intolerant to other agents. Rare cases of malignancy (i.e., skin cancer and lymphoma) have been reported in patients treated with topical tacrolimus. Application should be limited to the areas affected with atopic dermatitis.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C (Negating)
Tacrolimus		Very High Potency Topical Corticosteroids
		Augmented Betamethasone
		Clobetasol
		Diflorasone
		Halobetasol
		Amcinonide
		Betamethasone
		Desoximetasone
		Fluocinolone
		Fluocinonide
		Halcinonide
		Triamcinolone

Day Supply: 20 days in current 90 days
Age Range: 0 – 999 years of age
References:
Facts & Comparisons, 2006 Updates.
Protopic Prescribing Information, Jan. 2006, Astellas Pharma Inc.

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

3. Protopic & Elidel / Therapeutic Appropriateness (AGE) #2806 _____ _____

Alert Message: The topical calcineurin inhibitors, Protopic (tacrolimus) and Elidel (pimecrolimus), are not recommended for use in children less than 2 years of age. The long-term safety and effects of these agents on the developing immune system are unknown.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Tacrolimus		
Pimecrolimus		

Age Range: 0 – 1 years of age
References:
Facts & Comparisons, 2006 Updates.
Protopic Prescribing Information, Jan. 2006, Astellas Pharma Inc.
Elidel Prescribing Information, Jan. 2006, Novartis Pharmaceuticals, Inc.

4. Protopic / Therapeutic Appropriateness (AGE) #2807 _____ _____

Alert Message: The use of Protopic 0.1% ointment (topical tacrolimus) is not recommended in children less than 15 years of age. The 0.03% tacrolimus ointment is approved for use in children ages 2 to 15. Application should be limited to areas affected with atopic dermatitis. If signs and symptoms have not resolved within 6 weeks patient should be re-examined to confirm diagnosis.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Tacrolimus 0.1%		

Age Range: 2-15 years of age
References:
Facts & Comparisons, 2006 Updates.
Protopic Prescribing Information, Jan. 2006, Astellas Pharma Inc.

5. Elidel / Immunocompromised Patients #2808 _____ _____

Alert Message: Elidel (topical pimecrolimus) should not be used in immunocompromised adults and children. These patients are at risk for increased systemic exposure and adverse effects of pimecrolimus.
Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Pimecrolimus	HIV Diagnosis	
	Antiretrovirals	
	Transplant Diagnoses	
	Immunosuppressive Agents	

Age Range: 0-999 years of age
References:
Facts & Comparisons, 2006 Updates.
Elidel Prescribing Information, Jan. 2006, Novartis Pharmaceuticals, Inc.

Criteria Recommendations *Approved* *Rejected*

6. Protopic / Immunocompromised Patients #2809 _____ _____

Alert Message: Protopic (topical tacrolimus) should not be used in immunocompromised adults and children. These patients are at risk for increased systemic exposure and adverse effects of tacrolimus.
Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Drug/Disease:

Util A	Util B	Util C
Tacrolimus	HIV Diagnosis	
	Antiretrovirals	
	Transplant Diagnosis	
	Immunosuppressive Agents	

Age Range: 0-999 years of age
References:
Facts & Comparisons, 2006 Updates.
Elidel Prescribing Information, Jan. 2006, Novartis Pharmaceuticals, Inc.

7. Topical Immunomodulators / Therapeutic Duplications #2964 _____ _____

Alert Message: Therapeutic duplication of topical immunomodulator agents may be occurring.
Conflict Code:
Drug/Disease:

Util A	Util B	Util C
Tacrolimus		
Pimecrolimus		

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DRUGDEX Drug Evaluations, 2007.

8. Tizanidine / Ciprofloxacin #2982 _____ _____

Alert Message: Concurrent use of tizanidine and ciprofloxacin, a potent CYP 1A2 inhibitor, is contraindicated. Co-administration of these agents has been shown to cause significant increases in the AUC and Cmax of tizanidine resulting in hypotension, excessive sedation, and psychomotor impairment.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Tizanidine	Ciprofloxacin	

References:
Zanaflex Prescribing Information, June 2006, Acorda Therapeutics.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.
MedWatch – The FDA Safety Information and Adverse Event Reporting Program, 2007.

9. Tizanidine / Fluvoxamine #2414 _____ _____

Alert Message: Concurrent use of tizanidine and fluvoxamine, a potent CYP 1A2 inhibitor, is contraindicated. Significant alterations of pharmacokinetic parameters of tizanidine, including AUC, t1/2, Cmax, increased oral bioavailability and decreased plasma clearance, have been observed with concomitant fluvoxamine administration. Coadministration of these agents has resulted in profound hypotension, bradycardia and excessive drowsiness.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Tizanidine	Fluvoxamine	

References:
Zanaflex Prescribing Information, June 2006, Acorda Therapeutics.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.
MedWatch – The FDA Safety Information and Adverse Event Reporting Program, 2007.

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

10. Pioglitazone / Therapeutic Appropriateness #2965 _____ _____

Alert Message: Pioglitazone-containing products (Actos/ActoPlusMet/Duetact) may increase the risk of fractures in female patients. Analysis of clinical trial data revealed an increased incidence of fractures in female patients taking long-term pioglitazone therapy as compared to females taking a comparator (placebo or active). Consider the risk of fractures when initiating or treating female, type 2 diabetic patients with pioglitazone.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease:

Util A	Util B	Util C
Pioglitazone		

Gender: Female
References:
MedWatch – The FDA Safety Information and Adverse Event Reporting Program, 2007.

11. Rosiglitazone / Congestive Heart Failure & Fluid Retention #2947 _____ _____

Alert Message: Rosiglitazone-containing products may cause or exacerbate congestive heart failure. Their use is contraindicated in patients with NYHA class 3 or 4 heart failure and not recommended in patients with symptomatic heart failure. Patients should be observed for signs and symptoms of heart failure (rapid weight gain, dyspnea, and /or edema). If heart failure develops initiate appropriate therapy and consider alternative antidiabetic therapy.
Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Rosiglitazone	Heart Failure	
	Fluid Retention	

References:
Avandia Prescribing Information, September 2006, GlaxoSmtihKline.
Avandamet Prescribing Information, Feb. 2007, GlaxoSmithKline.
Avandaryl Prescribing Information, Oct. 2006, GlaxoSmithKline.

12. Pioglitazone / Congestive Heart Failure & Fluid Retention #1053 _____ _____

Alert Message: Pioglitazone-containing products may cause or exacerbate congestive heart failure. Their use is contraindicated in patients with NYHA class 3 or 4 heart failure and not recommended in patients with symptomatic heart failure. Patients should be observed for signs and symptoms of heart failure (rapid weight gain, dyspnea, and/or edema). If heart failure develops initiate appropriate therapy and consider alternative antidiabetic therapy.
Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Pioglitazone	Heart Failure	
	Fluid Retention	

References:
Facts & Comparisons, 2006 Updates.
Actos Prescribing Information, Nov. 2006, Takeda Pharmaceuticals American, Inc.
ActoPlus Met Prescribing Information, Nov. 2006, Takeda Pharmaceuticals American, Inc.
DuetAct Met Prescribing Information, Nov. 2006, Takeda Pharmaceuticals American, Inc.

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

13. Codeine / Pregnancy _____ _____

Alert Message: Nursing infants may be at an increased risk of morphine overdose if their mothers are taking codeine-containing products and are ultra-rapid metabolizers of codeine. If codeine use is necessary in the nursing mothers prescribe the lowest effective dose for the shortest amount of time. Inform mothers receiving codeine of the potential risks and signs of morphine overdose in themselves and their infants.
Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Disease

Util A	Util B	Util C (Negating)
Codeine	Pregnancy	Miscarriage
	Lactation	Abortion

References:
FDA Public Health Advisory: Use of Codeine by some Breastfeeding Mothers may lead to Life-threatening Side Effect in Nursing Babies. August 17, 2007. Available at: http://www.fda.gov/cder/drug/advisory/codeine.htm

14. Stimulants / Therapeutic Duplication _____ _____

Alert Message: Therapeutic duplication of stimulants may be occurring.
Conflict Code: TD – Therapeutic Duplication
Drugs/Disease

Util A	Util B	Util C
Methylphenidate		
Dexmethylphenidate		
Amphetamine Mixtures		
Methamphetamine		
Dextroamphetamine		
Lisdexamfetamine		

References:
Facts & Comparisons, 2007 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.
Clinical Pharmacology, Gold Standard, 2007.

15. Immediate Release Stimulants / Drug Abuse / Negating Agents _____ _____

Alert Message: The patient has a diagnosis of substance use disorder (SUD) and is receiving immediate-release stimulant medication. Treatment recommendations for patients with the dual diagnosis of ADHD and SUD suggest that ADHD be treated with non-stimulant agents, extended-release stimulants or transdermal stimulant formulations to reduce the potential for misuse, abuse and/or diversion.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C (Negating)
Methylphenidate IR	Drug Abuse	Extended-release Methylphenidate
Dexmethylphenidate IR		Extended-release Dexmethylphenidate
		Non-stimulant ADHD Med
		Transdermal Stimulant

References:
Upadhyaya HP, Managing Attention-Deficit/Hyperactivity Disorder in the Presence of Substance Use Disorder. J Clin Psychiatry 2007;68[suppl 11]:23-30.
Mariani JJ, Levin FR, Treatment Strategies for Co-Occurring ADHD and Substance Use Disorders. Am J Addict. 2007, 16[suppl 1]:45-54.
Wilens TE, Impact of AHDA and Its Treatment on Substance Abuse in Adults. J Clin Psychiatry 2004;65[supple 3]:28-45.

Criteria Recommendations	*Approved*	*Rejected*

16. Amphetamines / History of Drug Abuse _____ _____

Alert Message: Amphetamines are contraindicated in patients with a history of drug abuse. Chronic, abusive use can lead to tolerance, extreme psychological dependence, and severe social disability.
Conflict Code: MC – Drug (Actual) Disease Contraindication
Drugs/Diseases

Util A	Util B	Util C
Dextroamphetamine	Drug Abuse	
Amphetamine Mixtures		
Methamphetamine		
Lisdexamfetamine		

References:
Facts & Comparisons, 2006 Updates.
Dexedrine Prescribing Information, June 2006, GlaxoSmithKline.
Desoxyn Prescribing Information, February 2003, Abbott Laboratories.
Adderall Prescribing Information, June 2006, Shire US, Inc.

17. Stimulants / Arrhythmias & Cardiac Conditions _____ _____

Alert Message: Stimulant products generally should not be used in children or adolescents with known structural cardiac abnormalities, cardiomyopathy, serious rhythm abnormalities or other serious cardiac problems. Sudden death has been reported in association with CNS stimulant treatment at usual doses in this population. All patients treated with stimulant medications should have a careful history (including family history of sudden death or ventricular arrhythmia) and physical exam to assess presence of cardiac disease.
Conflict Code: MC – Drug (Actual) Disease Contraindication
Drugs/Diseases

Util A	Util B	Util C
Dextroamphetamine		
Amphetamine Mixtures		
Methamphetamine		
Lisdexamfetamine		
Methylphenidate		
Dexmethylphenidate		

Age Range: 0 – 18 Years of age
References:
Dexedrine Prescribing Information, June 2006, GlaxoSmithKline.
Desoxyn Prescribing Information, February 2003, Abbott Laboratories.
Adderall Prescribing Information, June 2006, Shire US, Inc.
Ritalin Prescribing Information, Oct. 2006 Novartis Pharmaceuticals Corporation.
Focalin Prescribing Information, Oct. 2006. Novartis Pharmaceuticals Corporation.
Facts & Comparisons, 2007 Updates.

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

18. Stimulants /Bipolar Disorder _____ _____

Alert Message: Particular care should be taken when using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder, such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.
Conflict Code: MC – Drug (Actual) Disease Contraindication
Drugs/Diseases

Util A	Util B	Util C
Dextroamphetamine	Bipolar Disorder	
Amphetamine Mixtures		
Methamphetamine		
Lisdexamfetamine		
Methylphenidate		
Dexmethylphenidate		

References:
Dexedrine Prescribing Information, June 2006, GlaxoSmithKline.
Desoxyn Prescribing Information, February 2003, Abbott Laboratories.
Adderall Prescribing Information, June 2006, Shire US, Inc.
Ritalin Prescribing Information, Oct. 2006 Novartis Pharmaceuticals Corporation.
Focalin Prescribing Information, Oct. 2006. Novartis Pharmaceuticals Corporation.
Facts & Comparisons, 2007 Updates.

19. Selzentry / Nonadherence _____ _____

Alert Message: A review of the patient's prescription refill history suggests that the patient may not be taking the drug in the manner it was prescribed. Nonadherence to antiretroviral therapy may result in insufficient drug plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.
Conflict Code: LR - Nonadherence
Drugs/Disease

Util A	Util B	Util C
Maraviroc		

References:
Hoffman C, Mulcahy F, Goals and Principles of Therapy, Eradication, Cost, Prevention and Adherence. In: Hoffman C, Rockstroh J, Kamps BS, eds. HIV Medicine, Flying Publishers-Paris, Cagliari, Wuppertal, Sevilla, 2005:167-173.

Cheever LW, Chapter V: Adherence to HIV Therapies. In: A Guide to Clinical Care of Women with HIV/AIDS, 2005 Edition, HIV/AIDS Bureau, US Department of Health and Human Services.
http://hab.hrsa.gov/publications/womencare05/WG05chap5.htm

20. Selzentry /Therapeutic Appropriateness _____ _____

Alert Message: Selzentry (maraviroc) is FDA approved to be used in combination with other antiretroviral agents to treat adult patients infected with only CCR5-tropic HIV-1 detectable virus, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents. There is insufficient data to recommend monotherapy with this agent.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C (Negating)
Maraviroc		All other Antiretrovirals

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

Criteria Recommendations	*Approved*	*Rejected*

21. Selzentry /Cardiovascular Events _____ _____

Alert Message: Selzentry (maraviroc) should be used with caution in patients at increased risk for cardiovascular events. In clinical studies, more cardiovascular events, including myocardial ischemia and/or infarction, were observed in patients who received maraviroc as compared to placebo (1.3% vs. 0%).
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C
Maraviroc	Cardiovascular Problems	

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

22. Selzentry /Liver Impairment _____ _____

Alert Message: Selzentry (maraviroc) has been linked to hepatotoxicity that may be preceded by a systemic allergic reaction (e.g., pruritic rash, eosinophilia, or elevated IgE). Discontinuation of maraviroc should be considered in any patient with signs and symptoms of hepatitis, or with increased liver transaminases combined with rash or other systemic symptoms. Caution is advised if maraviroc is used in patients with pre-existing liver dysfunction or who are co-infected with hepatitis B or C.
Conflict Code: TA – Therapeutic Appropriateness **(Black Box Warning)**
Drugs/Disease

Util A	Util B	Util C
Maraviroc		

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

23. Selzentry / High Dose _____ _____

Alert Message: The recommended dose of Selzentry (maraviroc) for patients receiving concomitant therapy with NRTIs, tipranavir/ritonavir, nevirapine, and other drugs that are **not** strong CYP3A inhibitors or CYP3A inducers is 300 mg twice daily.
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C (Negating)
Maraviroc		Strong CYP3A Inhibitors Ritonavir, Atazanavir, Indinavir, Saquinavir, Nelfinavir, Clarithromycin, Telithromycin, Ketoconazole, Itraconazole, Nefazodone Strong CYP3A Inducers Carbamazepine, Rifampin, Phenobarbital, Phenytoin, Efavirenz

Max Dose: 600mg/day
References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.
FDA Center for Drug Evaluation and Research, Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/CDER/drug/drugInteractions/tableSubstrates.htm

Criteria Recommendations	*Approved*	*Rejected*

24. Selzentry / High Dose _____ _____

Alert Message: Selzentry (maraviroc) is metabolized by the CYP3A isoenzyme and patients receiving concomitant therapy with protease inhibitors (except tipranavir/ritonavir), delavirdine, ketoconazole, itraconazole, clarithromycin, or other strong CYP3A inhibitors (e.g., nefazodone and telithromycin) should receive a reduced dose of 150 mg of maraviroc twice daily.
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C (Inclusive)
Maraviroc		Protease Inhibitors (except tipranavir/ritonavir)
		Delavirdine
		Ketoconazole
		Itraconazole
		Clarithromycin
		Nefazodone
		Telithromycin

Max Dose: 300 mg/day
References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

25. Selzentry / High Dose _____ _____

Alert Message: Selzentry (maraviroc) is metabolized by the CYP3A isoenzyme and patients receiving concomitant treatment with CYP3A inducers (e.g., efavirenz, rifampin, carbamazepine, phenobarbital, and phenytoin), without a strong inhibitor, should receive a dose of 600 mg of maraviroc twice daily.
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C (Inclusive)
Maraviroc		Efavirenz
		Rifampin
		Carbamazepine
		Phenobarbital
		Phenytoin

Max Dose: 1200 mg/day
References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

26. Selzentry / Renal Impairment _____ _____

Alert Message: Selzentry (maraviroc) should be used with caution in patients with renal impairment, particularly in those with concurrent use of a CYP3A inhibitor and a CrCl < 50 mg/mL. Approximately 25% of maraviroc is renally eliminated and impairment may lead to increased drug concentrations and risk of dose-related adverse effects (e.g., dizziness and postural hypotension). Patients should be monitored for adverse effects.
Conflict Code: DB – Drug/Drug Marker and/or Diagnosis
Drugs/Disease

Util A	Util B	Util C
Maraviroc	Renal Impairment	
	Lanthanum	
	Sevelamer	
	Doxercalciferol	
	Paricalcitol	
	Calcitriol	

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

Criteria Recommendations	*Approved*	*Rejected*

27. Selzentry / Hypotension

Alert Message: Selzentry (maraviroc) should be used with caution in patients with a history of postural hypotension or who are on concomitant medication known to lower blood pressure. The frequency of postural hypotension is increased at higher than recommended doses of maraviroc.
Conflict Code: DB – Drug/Drug Marker and/or Diagnosis
Drugs/Disease

Util A	Util B	Util C
Maraviroc	Postural Hypotension	
	Beta Blockers	
	Calcium Channel Blockers	
	ACE Inhibitors	
	ARBs	
	Anti-adrenergic Agents	
	Vasodilator Antihypertensives	
	Diuretics	

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

28. Selzentry /Therapeutic Appropriateness

Alert Message: Selzentry (maraviroc) should only be used in combination with other antiretroviral agents in adult treatment-experienced patients infected with CCR5-tropic HIV-1 detectable virus, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents. The agent is not active against CXCR4-topic and dual-topic viruses. Tropism testing and treatment history should guide use of maraviroc.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C
Maraviroc		

References:
Selzentry Prescribing Information, August 2007, Pfizer Labs.

29. Viracept / Therapeutic Appropriateness

Alert Message: Viracept (nelfinavir) has been found to contain the process-related impurity ethyl methanesulfonate (EMS), a potential human carcinogen. The FDA states that pediatric patients stable on nelfinavir therapy may continue therapy due to a favorable benefit-risk ratio. Pediatric patients who need to begin HIV treatment should not start on a regimen containing nelfinavir until further notice.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C
Nelfinavir		

Age range: 0 – 12 years of age
References:
MedWatch The FDA Safety Information and Adverse Event Reporting Program, 2007.

30. Viracept / Therapeutic Appropriateness

Alert Message: Viracept (nelfinavir) has been found to contain the process-related impurity ethyl methanesulfonate (EMS), a potential human carcinogen. The FDA has recommended that pregnant patients currently receiving nelfinavir be switched to an alternative agent if possible and that those needing to begin HIV treatment not be offered nelfinavir until further notice. Pregnant women with no alternative treatment options may continue to receive nelfinavir because the benefit-risk ratio remains favorable.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C (Negating)
Nelfinavir	Pregnancy	Miscarriage
		Abortion
		Delivery

References:
MedWatch The FDA Safety Information and Adverse Event Reporting Program, 2007.

Criteria Recommendations *Approved* *Rejected*

31. Haloperidol / Therapeutic Appropriateness _____ _____

Alert Message: Higher doses and intravenous administration of haloperidol appear to be associated with an increased risk of QT prolongation, torsades de pointes and even sudden death. Particular caution is advised when prescribing haloperidol to patients with predisposing factors (e.g., cardiac abnormalities, hypothyroidism and electrolyte imbalance) that could cause an even greater risk of these serious adverse effects.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C
Haloperidol		

Criterion will hit on patients receiving higher doses (8mg/day or above).

References:
MedWatch The FDA Safety Information and Adverse Event Reporting Program, 2007.

32. Haloperidol / Over utilization _____ _____

Alert Message: Haloperidol may be over-utilized. The recommended maximum dose is 100 mg per day. Exceeding this dose may enhance the risk of adverse effects (e.g., QT prolongation, torsades de pointes, extrapyramidal symptoms, seizures, and hypertension).
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C
Haloperidol		

Max Dose: 100 mg/day

References:
Facts & Comparisons, 2007 Updates.
Clinical Pharmacology, Gold Standard, 2007.
MedWatch: The FDA Safety Information and Adverse Event Reporting Program, 2007.

33. Fentora / Therapeutic Appropriateness

Alert Message: Fentora (buccal fentanyl) is only approved for the treatment of breakthrough pain in patients with cancer who are already receiving and are tolerant to opioid therapy. Buccal fentanyl must not be used in opioid non-tolerant patients. The improper selection of patients, incorrect dosing and improper product substitution may result in a fatal overdose with this agent.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C (Negating)
Fentora		Cancer ICD-9s
		Antineoplastic Agents

References:
Fentora Prescribing Information, April 2007, Cephalon, Inc.
FDA News: FDA Warns of Potential Serious Side Effects with Breakthrough Cancer Pain Drug. September 26, 2007.

34. Fentora / Therapeutic Appropriateness

Alert Message: Fentora (buccal fentanyl) is only approved for the treatment of breakthrough pain in patients with cancer who are already receiving and are tolerant to opioid therapy. Buccal fentanyl must not be used in opioid non-tolerant patients. The improper selection of patients, incorrect dosing and improper product substitution may result in a fatal overdose with this agent.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Disease

Util A	Util B	Util C (Negating)	
Fentora		Meperidine	Levorphanol
		Morphine	Methadone
		Fentanyl Transdermal	Oxycodone
		Fentanyl Lozenges	Oxymorphone
		Hydrocodone	Propoxyphene
		Hydromorphone	

References:
Fentora Prescribing Information, April 2007, Cephalon, Inc.
Facts & Comparisons, 2007 Updates.

35. Quetiapine / Substance Abuse

Alert Message: Seroquel (quetiapine) should be prescribed with caution to patients with a history of substance abuse. The agent has sedative and anxiolytic properties and may be misused by some patients. Closely observe patients for signs of misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior). Inappropriate use of quetiapine may put patients at risk for arrhythmias, hypotension, weight gain, and diabetes.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Disease

Util A	Util B	Util C
Quetiapine	Substance Abuse	

References:
Seroquel Prescribing Information, July 2007, AstraZeneca. Pharmaceuticals LP.
Pharmacist's Letter, Seroquel (Quetiapine) Abuse, October 2007 #ISSN #0883-0371.
Pierre JM, Shnayder I, Wirshing DA, et al., Intranasal Quetiapine Abuse, Am J Psychiatry Sept 2004, 161(9):1718.
Reeves RR, Brister JC. Additional Evidence of the Abuse of Potential of Quetiapine, South Med J 2007;100(8):834-6.

Boxed Warning Update

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.

Avandia (rosiglitazone)
FDA informed healthcare professionals of a potential safety issue related to Avandia (rosiglitazone). An on-going analysis of safety data for the treatment of type 2 diabetes mellitus using Avandia showed differing rates of ischemic cardiovascular events including heart attack or heart-related adverse events, some fatal, relative to other drugs used to treat diabetes mellitus. The clinical studies reviewed to date vary with respect to their populations, treatment regimens, and length of follow-up. Based on these data, the risk of ischemic cardiovascular events due to Avandia remain unclear. Prescribers should continue to carefully make individualized treatment decisions for patients with diabetes mellitus.

Exjade (deferasirox) Tablets For Oral Suspension
Novartis and FDA notified healthcare professionals of changes to the WARNINGS and ADVERSE REACTIONS sections of the product labeling for Exjade, a drug used to treat chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients

2 years of age and older. Cases of acute renal failure, some with a fatal outcome, have been reported following the post marketing use of Exjade. Most of the fatalities occurred in patients with multiple co-morbidities and who were in advanced stages of their hematological disorders. Additionally, there were post marketing reports of cytopenias, including agranulocytosis, neutropenia and thrombocytopenia in patients treated with Exjade where some of the patients died. The relationship of these episodes to treatment with Exjade is uncertain. Most of these patients had preexisting hematologic disorders that are frequently associated with bone marrow failure. Further, cases of leukocytoclastic vasculitis, urticaria, and hypersensitivity reactions (including anaphylaxis and angioedema) were reported.

Healthcare professionals should monitor serum creatinine in patients who are at increased risk of complications, having preexisting renal conditions, are elderly, have co-morbid conditions, or are receiving medicinal products that depress renal function. Blood counts should also be monitored regularly and treatment should be interrupted in patients who develop unexplained cytopenia.

Propofol (marketed as Diprivan and generic products)
FDA informed healthcare professionals about several clusters of patients who experienced chills, fever, and body aches shortly after receiving propofol for sedation or general anesthesia. Multiple vials and several lots of propofol used in patients who experienced these symptoms were tested and there was no evidence that the propofol vials or prefilled syringes used were contaminated with bacteria or endotoxins. Propofol is an intravenous sedative-hypnotic agent for use in the induction and maintenance of anesthesia or sedation. To minimize the potential for bacterial contamination, propofol vials and prefilled syringes should be used within six hours of opening and one vial should be used for one patient only. Patients who develop fever, chills, body aches or other symptoms of acute febrile reactions shortly after receiving propofol should be evaluated for bacterial sepsis. Healthcare professionals who administer propofol for sedation or general anesthesia should carefully follow the recommendations for handling and use in the product's full prescribing information.

Rocephin (ceftriaxone sodium) for Injection
Roche and FDA informed healthcare professionals of revisions to the CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections of the prescribing information for Rocephin for Injection. The revisions are based on new information that describes the potential risk associated with concomitant use of Rocephin with calcium or calcium containing solutions or products. Cases of fatal reactions with calcium-ceftriaxone precipitates in the lungs and kidneys in both term and premature neonates were reported. Hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin. The drug must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines. Additionally, calcium-containing solutions or products must not be administered within 48-hours of the last administration of ceftriaxone.

Use of CellCept (mycophenolate mofetil) associated with increased pregnancy loss and congenital malformations

Roche and FDA notified healthcare providers that use of CellCept (mycophenolate mofetil) is associated with increased risk of first trimester pregnancy loss and increased risk of congenital malformations, especially external ear and facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney.

Based on postmarketing data from the United States National Transplantation Pregnancy Registry and additional postmarketing data collected in women exposed to systemic mycophenolate mofetil during pregnancy, the pregnancy category for CellCept has been changed from Category C (risk of fetal harm cannot be ruled out) to Category D (positive evidence of fetal risk). Labeling changes include the following sections: BOXED WARNING, WARNINGS/Pregnancy and Pregnancy Exposure Prevention, PRECAUTIONS/Information for Patients, and ADVERSE REACTIONS/Postmarketing Experience.

Within one week of beginning CellCept therapy, women of childbearing potential should have a negative serum or urine pregnancy test. In addition, women of childbearing potential (including pubertal girls and peri-menopausal woman) taking CellCept must receive contraceptive counseling and use effective contraception. Healthcare professionals and patients should be aware that CellCept reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness. See the Dear Healthcare Professional Letter for additional recommendations for women of childbearing potential.

Provigil (modafinil) Tablets- WARNINGS Added To Prescribing Information Regarding Serious Rash And Hypersensitivity Reactions, And Psychiatric Symptoms

FDA and Cephalon notified healthcare professionals of Warnings added to prescribing information for Provigil (modafinil). Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. The revised prescribing information updates safety information to include warnings regarding serious rash, including Stevens-Johnson Syndrome (SJS) and hypersensitivity reactions, and psychiatric symptoms. Rare cases of serious or life-threatening rash, including Toxic Epidermal Necrolysis, and Drug Rash with Eosinophilia and Systemic Symptoms have been reported in adults and children in worldwide postmarketing experience. Angioedema and multi-organ hypersensitivity reactions have also been reported in postmarketing experience.

Physicians should instruct their patients to immediately discontinue the use of Provigil and contact them if a rash or other hypersensitivity reaction occurs. Healthcare professionals and consumers should also be aware that Provigil is not approved for use in pediatric patients for any indication. In addition, psychiatric adverse experiences (including anxiety, mania, hallucinations, and suicidal ideation) have been reported in

patients treated with Provigil. Caution should be exercised when Provigil is given to patients with a history of psychosis, depression, or mania.

Additional labeling revisions were made to the CLINICAL PHARMACOLOGY, PRECAUTIONS, and PATIENT PACKAGE INSERT sections.

Byetta (exenatide) and postmarketing reports of acute pancreatitis
FDA has reviewed 30 postmarketing reports of acute pancreatitis in patients taking Byetta (exenatide), a drug used to treat adults with type 2 diabetes. An association between Byetta and acute pancreatitis is suspected in some of these cases. Amylin Pharmaceuticals, Inc. has agreed to include information about acute pancreatitis in the PRECAUTIONS section of the product label.

Healthcare professionals should be alert to the signs and symptoms of acute pancreatitis and instruct patients taking Byetta to seek prompt medical care if they experience unexplained, persistent, severe abdominal pain which may or may not be accompanied by vomiting. If pancreatitis is suspected, Byetta should be discontinued. If pancreatitis is confirmed, Byetta should not be restarted unless an alternative etiology is identified.

Early Communication Issued Regarding Atrial Fibrillation With Oral And Intravenous Bisphosphonates
FDA issued an early communication about the ongoing review of new safety data regarding the association of atrial fibrillation with the use of bisphosphonates. Bisphosphonates are a class of drugs used primarily to increase bone mass and reduce the risk for fracture in patients with osteoporosis, slow bone turnover in patients with Paget's disease of the bone, treat bone metastases, and lower elevated levels of blood calcium in patients with cancer.

FDA reviewed spontaneous postmarketing reports of atrial fibrillation reported in association with oral and intravenous bisphosphonates and did not identify a population of bisphosphonate users at increased risk of atrial fibrillation. In addition, as part of the data review for the recent approval of once-yearly Reclast for the treatment of postmenopausal osteoporosis, FDA evaluated the possible association between atrial fibrillation and the use of Reclast. Most cases of atrial fibrillation occurred more than a month after drug infusion. Also, in a subset of patients monitored by electrocardiogram up to the 11th day following infusion, there was no significant difference in the prevalence of atrial fibrillation between patients who received Reclast and patients who received placebo.

Upon initial review, it is unclear how these data on serious atrial fibrillation should be interpreted. Therefore, FDA does not believe that healthcare providers or patients should change either their prescribing practices or their use of bisphosphonates at this time.

Haloperidol Marketed As Haldol, Haldol Decanoate, And Haldol Lactate Get New Warnings And Revised Prescription Information

Johnson and Johnson and FDA informed healthcare professionals that the WARNINGS section of the prescribing information for haloperidol has been revised to include a new Cardiovascular subsection regarding cases of sudden death, QT prolongation and Torsades de Pointes(TdP) in patients treated with haloperidol, especially when given intravenously, or at doses higher than recommended. Although injectable haloperidol is only approved by the FDA for intramuscular injection, there is considerable evidence that the intravenous administration of haloperidol is a relatively common off-label clinical practice.

There are at least 28 case reports of QT prolongation and TdP, some with fatal outcome in the context of off-label intravenous haloperidol.
Healthcare professionals should consider this new risk information when making individual treatment decisions for their patients.

Fentora (fentanyl buccal tablet) and the occurrence of serious adverse events, including deaths as a result of improper patient selection, improper dosing, and/or improper product substitution

Cephalon issued two Dear Healthcare Professional Letters to inform prescribers and other healthcare providers of important safety information regarding Fentora. Fentora is indicated only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Serious adverse events, including deaths, have occurred in patients treated with Fentora. These deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients), improper dosing, and/or improper product substitution. The healthcare professional letters provide key points regarding appropriate patient selection and proper dosing and administration of Fentora to reduce the risk of respiratory depression.