Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

September 25, 2008

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

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

Laura Gray, M.D.
905 Garfield Street
Tupelo, MS 38801
Term Expires: June 30, 2009

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

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

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

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

Lee Merritt, R.Ph.
Medfusion
221 5th Street North
Columbus, MS 39705
Term expires: June 30, 2010

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

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

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

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

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

Upcoming Mississippi DUR Board Meeting Dates

November 20, 2008
February 19, 2009
May 21, 2009
August 20, 2009

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

September 25, 2008

Welcome	**Laura Gray, M.D.**
Old Business	**Laura Gray, M.D.**
Approval of Meeting Minutes and 1st / 2nd Quarter Criteria	
Cost Management Analysis	**Ashleigh Holeman, Pharm.D.**
Pharmacy Program Update	**Paige Clayton, Pharm.D.**
New Business	**Ashleigh Holeman, Pharm.D.**
FDA Updates	
DUR Overview	
Off-label Use of Atypical Antipsychotics for Children with ADHD/ODD	
Generalized Anxiety Disorder	
Carisoprodol Utilization Update	
Important Issues Surrounding Suboxone/Subutex	
Growth Suppression and ADHD Treatments	
Asthma	
Synagis: 2008-2009 Season Update	
Other Criteria Recommendations	
Next Meeting Information	**Laura Gray, M.D.**

In an effort to save time, please familiarize yourself with the following sets of minutes and criteria as the information included in this section has previously been clinically reviewed with the DUR Board but has yet to be implemented due to the lack of a voting quorum. While these items are important business to the DUR Board, it is believed that the time and efforts of the current Board would be better utilized on new business that has yet to be reviewed.

Accordingly, the Board will entertain a motion to accept all previously reviewed minutes and criteria in one vote rather than reading through all items individually.

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the November 15, 2007 Meeting

Members Attending: Billy Brown, PharmD.; Randy Calvert, R.Ph., Laura Gray, M.D.; Frank Marascalco, R.Ph., Chair; Andrea Phillips, M.D.; Lee Voulters, M.D.; Wallace Strickland

Members Absent: Roy Arnold, R.Ph.; Harold Blakely, R.Ph.; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, PharmD, DOM DUR Coordinator; Carlis Faler, DOM Program Integrity Director

HID Staff: Dennis Smith, R.Ph., Project Manager; Ashleigh Holeman, PharmD; Kathleen Burns, R.N.

Call to Order:
Frank Marascalco, Chairman of the Board, called the meeting to order at 2:10 p.m.

Dr. Clayton asked that the Board proceed with business not requiring a vote while awaiting arrival of enough members to constitute a quorum.

Updates:
Cost Management Analysis
Mr. Smith began by presenting reports reflecting several months of data. Antipsychotic agents continued to lead the top 15 therapeutic classes by total cost of claims throughout the five month period reported. The top drugs based on number of claims were led by hydrocodone-acetaminophen and followed by Zyrtec. Dr. Holeman added that the top 200 national ranking for each drug has been added to the report for reference. This report also designates by an asterisk those products classified as preferred on the preferred drug list. These additions were made to facilitate the understanding of the number of claims for these top medications. The top drugs based on total claims cost were led by Singulair® in April 2007. At this time, Mr. Smith and Dr. Holeman reviewed the findings of the analysis of Singulair® utilization that was presented during the previous DUR Board meeting. Of 4,500 patients not having a diagnosis of either asthma or allergic rhinitis, the majority were found to have had a non-specific upper respiratory diagnosis. The report further found that from May 2006 to May 2007, approximately 62 percent of patients receiving Singulair® had an asthma diagnosis, while approximately 65 percent of patients who received Singulair® had an allergic rhinitis diagnosis. According to this information, there did not appear to be gross over utilization of Singulair®. The Board agreed with these findings. Dr. Holeman continued with the top 25 drugs based on total claims cost by pointing out the remaining four months was led by Risperdal®.

Old Business:

Due to the lack of a quorum at the September 20, 2007 meeting, Mr. Smith briefly summarized several reports that were presented during the meeting.

Potential Misuse of ADHD Agents

The first of these reports was a review of the utilization of stimulants indicated for the treatment of ADHD. Although the study findings did not indicate extensive over-prescription of these agents among adults, a retrospective DUR criterion was recommended to identify adult patients who may be using these medications inappropriately. After discussion, Mr. Strickland made a motion to approve the criterion and Dr. Phillips offered a second. The motion was unanimously approved.

Inappropriate Use of Antibiotics

Mr. Smith next introduced the report which focused on the possible negative impact of the over-prescription of antibiotics to very young children. He reiterated that the Board had reached a consensus during the September meeting to not address this issue from a retrospective DUR perspective at this time.

HIV Criteria Report

Dr. Holeman presented a synopsis of the retrospective DUR activity that has resulted from the DUR Board's approval in May of a large group of criteria focusing on the encouragement of appropriate antiretroviral therapy. 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.

New Business:

Alprazolam and Lorazepam Utilization

Due to a high number of claims for alprazolam and lorazepam and at the request of the board during the September meeting, Mr. Smith presented a review of the utilization of these agents. Due to their anxiolytic effects, these medications tend to have a very high abuse potential. The results of this review were somewhat surprising in that the highest utilization occurred among beneficiaries in the 30 to 59 age range. Utilization was also determined in the long-term care population and found that there were a relatively small number of claims in this group. It was noted that while Medicare Part D provides the majority of drug coverage for dually-eligible patients, coverage of generic benzodiazepines such as alprazolam and lorazepam falls through to Medicaid. The board members recommended further study of this utilization by HID with the removal of the one time fills for all groups. Dr. Voulters also requested that HID review chronic users such as those with two or more refills. Dr. Gray suggested that HID identify patients on concurrent SSRI therapy. Mr. Strickland pointed out that, with the new wavier program allowing patients to receive long term care at home from a relative, this data might be skewed. It was suggested that HID include plan number and category of eligibility when the reports are re-run. Dr Voulters also requested that HID look at the long-acting benzodiazepines focusing on the LTC and elderly groups. Dr. Phillips continued with a

request to add diazepam to the review as she is seeing it used more frequently in her practice with patients requesting refills from other physicians. Carlis Faler, Program Integrity Director, added that it may be helpful for these reports to also reflect gender.

Hydrocodone Utilization
Hydrocodone remains consistently one of the top five drugs based on the number of claims. This has generated a concern with the DUR Board as to how Medicaid can address this over -utilization with its beneficiaries. While high rates of hydrocodone use are cause for concern both at the state and national level, it is difficult to identify the complexity of the problem as Medicaid has set a monthly dispensing limit of 62, or two doses per day per running 31 days. It was noted that in some cases, beneficiaries are paying cash for the remainder of the prescription. Medicaid is working with the State Pharmacy Board to gain access to available data on cash purchases by Medicaid beneficiaries. This is expected to add valuable input into the possible abuse of these products and other medications of interest. Dr. Voulters requested an age analysis be generated as was done on the benzodiazepines. In addition, he further requested that other medications with abuse potential have the same detailed reports run. Dr. Gray requested that HID continue to review carisoprodol and run a comparison on all three of these medications with their age, diagnosis and long term utilization. She also suggested that HID report on the effectiveness of the carisoprodol Medicaid Prescribing Update, or "one-pager" that was previously approved by the DUR Board.

Impact of Quinine Removal on Utilization of Gabapentin and Lyrica®
Dr. Holeman presented a review of the impact of FDA action in removing quinine products from the market. On December 11, 2006, the FDA ordered all manufacturers to stop marketing unapproved products containing quinine. Currently, Qualaquin® is the only FDA approved product that contains quinine. Quinine is approved for the treatment of malaria but is often used off-label for leg cramps. Because of the drug's risks, FDA believes that it should not be used to prevent and treat leg cramps. At the request of the DUR Board, utilization data was gathered by HID on the continued use of quinine after the FDA mandate. The searches performed by HID were for utilization of quinine, gabapentin and Lyrica® and attempted to identify trends based on the date that firms had to cease marketing quinine, February 13, 2007. While some increase was noted in utilization of gabapentin and Lyrica®, it was not as large as expected. HID generated a second chart reflecting the use of Requip® and Mirapex ® which are indicated for restless leg syndrome and concluded that physicians are possibly utilizing these medications in place of quinine products. The data presented was interpreted to indicate that appropriate therapy has generally been implemented by treating physicians in the wake of the change in the marketplace.

Duplicate Utilization of Risperdal Consta® and Oral Atypical Antipsychotic Agents
Mr. Smith next presented a review of the utilization of Risperdal Consta®, 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. According to the FDA-approved prescribing information, tolerability to oral Risperdal® should be established prior to initiating therapy with Risperdal Consta®. The labeling also stated

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. Mr. Smith continued by presenting findings of searches made by HID of the utilization from 1/1/2007 through 09/21/2007. The beneficiaries identified in these searches were intersected to determine those with utilization of Risperdal Consta® and one or more oral atypical antipsychotic agents. Beneficiaries with claims totaling less than 32 days of treatment with an oral agent were excluded from the study. The search resulted in 191 beneficiaries who received long-acting injectable risperidone and oral atypical antipsychotic therapy during the time period searched. According to this analysis, over 50 percent of the beneficiaries on Risperdal Consta® received greater than 31days of treatment with an oral atypical antipsychotic during the reviewed time. These findings indicate that many beneficiaries are receiving duplicate atypical antipsychotic treatment in addition to Risperdal Consta®. As a result, a retrospective DUR criterion was recommended to alert prescribers to the appropriate prescribing guidelines for this product. HID will bring such a criteria before the DUR Board at the next meeting for review and approval.

Approval of Minutes
Dr. Phillips voiced the need to be excused and requested that voting on appropriate matters take place due to the fact that when she left there would no longer be a quorum. The minutes of the previous two DUR board meetings on May 19, 2007 and September 20, 2007 were approved with a motion by Mr. Strickland and a second from Dr. Phillips. All members voted in favor of the motion.

Fourth Quarter Criteria Recommendations
In order to allow for voting on retrospective criteria recommendations, Mr. Smith presented the following criteria to the Board for approval.

- Elidel or Protopic/ Therapeutic Appropriateness - The topical calcineurin inhibitor, Elidel (pimecrolimus) or Protopic (tacrolimus), 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.
- Protopic or Elidel / Age Appropriateness - 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.
- Protopic 0.1% / Age Appropriateness - 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.

- Elidel or Protopic/ Immunocompromised Patients - Elidel (topical pimecrolimus) or 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 pimecrolimus or tacrolimus.
- Topical Immunomodulators / Therapeutic Duplication - Therapeutic duplication of topical immunomodulator agents may be occurring.
- Tizanidine / Ciprofloxacin - 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.
- Tizanidine / Fluvoxamine - 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.
- Pioglitazone / Therapeutic Appropriateness - 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.
- Rosiglitazone or pioglitazone/ Congestive Heart Failure & Fluid Retention – Rosiglitazone or 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.
- Codeine / Pregnancy - 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.
- Stimulants / Therapeutic Duplication - Therapeutic duplication of stimulants may be occurring (methylphenidate, dexmethylphenidate, amphetamine mixtures, methamphetamine, dextroamphetamine, lisdexamfetamine).
- Immediate Release Stimulants / Drug Abuse / Negating Agents - 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.

- Amphetamines / History of Drug Abuse - 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.
- Stimulants / Arrhythmias & Cardiac Conditions - 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.
- Stimulants /Bipolar Disorder - 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, and such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.
- Selzentry / Nonadherence - 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. Non-adherence 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.
- Selzentry /Therapeutic Appropriateness - 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.
- Selzentry /Cardiovascular Events - 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%).
- Selzentry /Liver Impairment - 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.
- Selzentry / High Dose - 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.
- Selzentry / High Dose - 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.

- Selzentry / Low Dose - 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.
- Selzentry / Renal Impairment - 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.
- Selzentry / Hypotension - 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.
- Selzentry /Therapeutic Appropriateness - 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-tropic and dual-tropic viruses. Tropism testing and treatment history should guide use of maraviroc.
- Viracept / Therapeutic Appropriateness - 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.
- Viracept / Therapeutic Appropriateness - 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.
- Haloperidol / Therapeutic Appropriateness - 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.
- Haloperidol / Over utilization - 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).

- Fentora / Therapeutic Appropriateness - 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.
- Quetiapine / Substance Abuse - 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.

Mr. Marascalco continued with a vote on the criteria presented by HID. Dr. Phillips made a motion to approve the criteria presented with the exceptions of the pioglitazone/therapeutic appropriateness criteria and the pioglitazone/congestive heart failure and fluid retention criteria. Dr. Gray seconded the motion and all voted in favor.

Appropriate Antibiotic Use

Dr. Holeman presented a review of the appropriate utilization of antibiotics by Medicaid prescribers. 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 seems to have been given credence by the spread of organisms, such as MRSA, all essentially untreatable with routinely available antibiotics. Dr. Holeman continued by stating that decreasing the inappropriate use of antimicrobials has been listed as a primary solution to address the threat that antimicrobial resistance poses. To help combat the risk, HID presented and recommended the use of a Medicaid Prescribing Information Update, or "one-pager", which outlines the importance of appropriate treatment of upper respiratory tract infections and of prudent prescribing of antibiotics. HID recommends distribution of this document to prescribers by the Academic Detailing Staff and availability from the Division of Medicaid's website. After discussion of this approach, the Board's consensus was to support the distribution of this information as recommended.

Dr. Holeman then addressed the use of Zyvox®. At present, this antibiotic is non-preferred and subject to manual prior authorization review. Several recent studies have shown that outpatient use of Zyvox® may lower costs and prevent or shorten hospitalizations. Dr. Brown asked about the turn-around time of the prior authorization process. Mr. Smith answered that DOM requires that requests be processed within 24 hours, although most are responded to in less time. After discussion, the clear consensus of the DUR Board was to recommend no change to the present status of this product, continuing to require prior authorization approval, while encouraging appropriate use of this product.

Other

Dr. Gray suggested that HID analyze the utilization trends of Provigil® for the next Board meeting.

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

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.

Next Meeting Information:
Mr. Marascalco reminded the Board of the next meeting scheduled for February 21, 2008.

Mr. Marascalco called for a motion of adjournment at 4:10 p.m. Mr. Strickland made the motion, which was seconded by Dr. Gray. 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 February 21, 2008 Meeting

Members Attending: Billy Brown, Pharm.D; Randy Calvert, R.Ph..; Laura Gray, M.D.; Frank Marascalso, R.Ph; Lee Montgomery, M.D.;

Members Absent: Roy Arnold, R.Ph; Harold Blakely, R.Ph; Wallace Strickland; Lee Voulters, M.D.; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, Pharm.D., DOM DUR Coordinator; Carlis Faler, DOM Program Integrity Director; Terri Kirby, R.Ph., Ella Holmes, Andrea McNeal,
HID Staff: Dennis Smith, R.Ph, Project Manager; Ashleigh Holeman, Pharm.D; Kathleen Burns, R.N.

Call to Order:
Frank Marascalco, Chairman of the Board, called the meeting to order at 2:10 p.m.

Dr. Clayton asked that the Board proceed with business acknowledging that the Board would not have a quorum to vote on the issues presented today

Updates:
Cost Management Analysis:
Mr. Smith presented an overview of the reports to the Board reflecting several months of data. He continued noting that the same agents continue to top the 15 therapeutic classes by total cost of claims throughout the reports. Dr. Brown noted that the antibiotics continue to remain as one of the top agents and the Board still questions if this reflects an over utilization of antibiotics for unnecessary indications. Ms. Clark interjected the thoughts that HID might run reports on beneficiaries from birth to the age of 12 to determine misuse. She continued to recommend that the months of October plus a forward 6 month study could be done on individuals receiving more than one antibiotic with multiple prescribers. Dr. Montgomery questioned that the possibility of removing cold/cough preparations might have driven this over-use of antibiotics. He recommended that HID look at the previous year during the same timeframe and compare it with this year's data. Ms. Clark suggested that DOM might consider using HID's Newsletter for the educational purpose of informing the prescribers of this important antibiotic overuse. Dr. Brown suggested that DOM might utilize the different Regional Offices and Rural Health Clinics to post information for the parents to read.

Pharmacy Program Update:
Ms. Clark informed the Board that the Tamper-Proof prescription requirements go into effect April 1st, 2008. DOM will communicate with providers prior to this implementation date by faxes and other appropriate notices. The March 1st Bulletin will also have articles to address this April 1st deadline for Tamper-Proof prescription pads.

Dr. Clayton introduced at this time the pharmacy intern working with DOM, Eric Cornell. Eric was asked to present information regarding the abuse of promethazine with codeine syrup in MS. He informed the Board that this "street abuse" possibly started 10 years ago in Houston, Texas under many street names. The idea is to take 1 ounce of promethazine with codeine, mix it with Sprite and a piece of candy, turning it purple. He noted that 1 ounce is the entire daily dose allowance of codeine for an adult, which results in a person receiving 60mg of codeine in one drink. The DEA informed Eric that it is a growing concern in Jackson and they have noted an increase since September 2006. DOM elected to remove promethazine with codeine syrup from their approved OTC list as of November 1, 2007, without knowing about this method of abuse. When the OTC list for Medicaid patients was outsourced, this removal was recommended at that time from the respective vendor for other reasons. Mr. Smith continued by presenting an updated February 2008 report from the CDC on the prevalence of RSV in Mississippi. This graphic report indicated that Mississippi-specific occurrence was decreasing starting in January 2008. The Synagis® Season for MS Medicaid patients will end March 31st, 2008.

New Business:

Overview of rDur Process:

This was tabled per recommendation of Dr. Clayton until the next meeting of the Board

Utilization of Benzodiazepines, Carisoprodol, Hydrocodone, Ambien®, and Provigil®:

Dr. Holeman presented a lengthy requested study on these potential drugs of abuse. These medications have continued to concern the Board with the overuse and their continuation to remain on the Top 25 drug reports for the number of reported claims. Dr. Montgomery questioned how Medicare Part D entered into the number of reported claims. Dr. Holeman answered that Medicaid is the primary payer for the benzodiazepines for this group as Medicare Part D does not cover these medications. She continued that Medicare does cover hydrocodone, however, on the dual eligibles. In regard to the Ambien® overuse, Dr. Montgomery suggested informing the physician responsible, possibly with an education letter. This might alter the physician's prescribing habits on Ambien®. Dr. Brown suggested that HID look at these reports and see if there might be a pattern of the same physician prescribing all three of these medications per patient. Dr. Gray commented that the Board might recommend even further decreasing the limits on these medications for the Medicaid beneficiaries. However, Mr. Marascalco stated that in the pharmacy business, the beneficiary would just pay cash for the extra medication that Medicaid limited. He stated that it should start with the physician writing this excessive amount. HID will continue to monitor these medications and the physicians prescribing them.

Labeling Update for Desmopressin Acetate Nasal Spray

Dr. Holeman continued reporting on labeling updates on Desmopressin Acetate Nasal Spray. Based on gathered information, there was not extensive utilization for the nasal spray in children ages 5 to 15 in the Medicaid population. It was also noted that of those children receiving the nasal spray, a very small number received long-term treatment.

Retrospective DUR criteria are recommended to identify these patients receiving this medication in violation of the recent position of the FDA.

Pharmacy Coverage of Tobacco Cessation Products
The next topic covered by Dr. Holeman was the recent addition of Chantix® to the Tobacco Cessation products covered by MS Medicaid. Based on HID's reportings, the additional coverage of this medication has shown utilization of approximately 5 times that of the nicotine-replacement products also on the list. Approximately 15% of the beneficiaries have received a second prescription of either agent to continue their efforts to stop smoking. This indicates that MS Medicaid has made a positive step in the right direction to potentially lower health-care costs in the future by providing another option to support those beneficiaries who are making the effort to stop smoking.

New Criteria:
Mr. Smith reviewed these new recommendations with the Board but due to a lack of a quorum there was no voting.

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

Ortho Evra Contraceptive Transdermal Patch
1/19/2008: FDA modified the prescribing information for the Ortho Evra Contraceptive Transdermal (Skin) Patch to include the results of a new epidemiology study that found that users of the birth control patch were at higher risk of developing serious blood clots, also known as venous thromboembolism (VTE), than women using birth control pills. VTE can lead to pulmonary embolism. The label changes are based on a study conducted by the Boston Collaborative Drug Surveillance Program on behalf of Johnson and Johnson. The patch was studied in women aged 15-44. These findings support an earlier study that also said women in this group were at higher risk for VTE.

FDA believes that Ortho Evra is a safe and effective method of contraception when used according to the labeling, which recommends that women with concerns or risk factors for serious blood clots talk with their health care provider about using Ortho Evra versus other contraceptive options.

Cough and Cold Medications in Children Less Than Two Years of Age
1/17/2008: FDA informed consumers and healthcare professionals that the Agency has completed its review of information regarding the safety of over-the-counter (OTC) cough and cold medicines in children under 2 years of age and recommends that these drugs not be used to treat children in this age group because serious and potentially life-threatening side effects can occur. FDA's recommendation is based on both the review of the information the Agency received about serious side effects in children in the referenced age group and the discussion and recommendations made at the October 18 - 19, 2007, public advisory committee meeting at which this issue was discussed. FDA has not completed its review of information about the safety of OTC cough and cold

medicines in children 2 through 11 years of age. See the FDA Public Health Advisory for Agency recommendations regarding this issue.

Edetate Disodium (marketed as Endrate and generic products)
1/16/2008: FDA notified healthcare professionals and patients about important safety information concerning Edetate Disodium. There have been cases where children and adults have died when they were mistakenly given Edetate Disodium instead of Edetate Calcium Disodium (Calcium Disodium Versenate) or when Edetate Disodium was used for "chelation therapies" and other uses that are not approved by the FDA. Edetate Disodium was approved as an emergency treatment for certain patients with hypercalcemia (very high levels of calcium in the blood) or certain patients with heart rhythm problems as a result of very high amounts of digitalis in the blood. Edetate Calcium Disodium was approved to reduce dangerously high blood lead levels (severe lead poisoning).

The two drugs have very similar names and are commonly referred to only as EDTA. As a result, the two products are easily mistaken for each other when prescribing, dispensing, and administering them. Edetate Disodium and Edetate Calcium Disodium works by binding with heavy metals or minerals in the body allowing them to be passed out of the body through the urine. Read the FDA Public Health Advisory for recommended and important safety considerations for healthcare professionals until the FDA's ongoing evaluation of the risks and benefits of Edetate Disodium is complete.

Compounded Menopause Hormone Therapy Drugs
1/10/2008: FDA informed healthcare professionals and patients that the Agency sent letters warning seven pharmacy operations that the claims they make about the safety and effectiveness of their so-called "bio-identical hormone replacement therapy," or "BHRT" products are unsupported by medical evidence, and are considered false and misleading by the agency. The pharmacy operations improperly claim that their drugs, which contain hormones such as estrogen, progesterone, and estriol (which is not a component of an FDA-approved drug and has not been proven safe and effective for any use) are superior to FDA-approved menopausal hormone therapy drugs and prevent or treat serious diseases, including Alzheimer's disease, stroke, and various forms of cancer. FDA is concerned that the claims for safety, effectiveness, and superiority that these pharmacy operations are making mislead patients, as well as doctors and other healthcare professionals. Compounded drugs are not reviewed by the FDA for safety and effectiveness.

Patients who use compounded hormone therapy drugs should discuss menopausal hormone therapy options with their healthcare provider to determine if compounded drugs are the best option for their specific medical needs.

Bisphosphonates (marketed as Actonel, Actonel+Ca, Aredia, Boniva, Didronel, Fosamax, Fosamax+D, Reclast, Skelid, and Zometa)
1/07/2008: FDA informed healthcare professionals and patients of the possibility of severe and sometimes incapacitating bone, joint, and/or muscle (musculoskeletal) pain in

patients taking bisphosphonates. Although severe musculoskeletal pain is included in the prescribing information for all bisphosphonates, the association between bisphosphonates and severe musculoskeletal pain may be overlooked by healthcare professionals, delaying diagnosis, prolonging pain and/or impairment, and necessitating the use of analgesics. The severe musculoskeletal pain may occur within days, months, or years after starting a bisphosphonates. Some patients have reported complete relief of symptoms after discontinuing the bisphosphonate, whereas others have reported slow or incomplete resolution. The risk factors for and incidence of severe musculoskeletal pain associated with bisphosphonates are unknown.

Fentanyl Transdermal System (marketed as Duragesic and generics)
12/21/2007: FDA issued an update that highlights important information on appropriate prescribing, dose selection, and the safe use of the fentanyl transdermal system (patch). FDA previously issued a Public Health Advisory and Information for Healthcare Professionals in July 2005 regarding the appropriate and safe use of the transdermal system. However, the Agency continues to receive reports of death and life-threatening adverse events related to fentanyl overdose that have occurred when the fentanyl patch was used to treat pain in opioid-naive patients and when opioid-tolerant patients have applied more patches than prescribed, changed the patch too frequently, and exposed the patch to a heat source. The fentanyl patch is only indicated for use in patients with persistent, moderate to severe chronic pain who have been taking a regular, daily, around-the-clock narcotic pain medicine for longer than a week and are considered to be opioid-tolerant.

Patients must avoid exposing the patch to excessive heat as this promotes the release of fentanyl from the patch and increases the absorption of fentanyl through the skin which can result in fatal overdose. Directions for prescribing and using the fentanyl patch must be followed exactly to prevent death or other serious side effects from fentanyl overdose.

Carbamazepine (marketed as Carbatrol, Equetro, Tegretol and generics)
12/12/2007: FDA informed healthcare professionals that dangerous or even fatal skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis), that can be caused by carbamazepine therapy, are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians. Patients with ancestry from areas in which HLA-B*1502 is present should be screened for the HLA-B*1502 allele before starting treatment with carbamazepine. If these individuals test positive, carbamazepine should not be started unless the expected benefit clearly outweighs the increased risk of serious skin reactions. Patients who have been taking carbamazepine for more than a few months without developing skin reactions are at low risk of these events ever developing from carbamazepine. This is true for patients of any ethnicity or genotype, including patients positive for HLA-B*1502.

Desmopressin Acetate (marketed as DDAVP Nasal Spray, DDAVP Rhinal Tube, DDAVP, DDVP, Minirin, and Stimate Nasal Spray)

12/04/2007: FDA notified healthcare professionals and patients of the Agency's request that manufacturers update the prescribing information for desmopressin to include important new safety information about severe hyponatremia and seizures. Certain patients, including children treated with the intranasal formulation of the drug for primary nocturnal enuresis (PNE), are at risk for developing severe hyponatremia that can result in seizures and death. As such, desmopressin intranasal formulations are no longer indicated for the treatment of primary nocturnal enuresis and should not be used in hyponatremic patients or patients with a history of hyponatremia. PNE treatment with desmopressin tablets should be interrupted during acute illnesses that may lead to fluid and/or electrolyte imbalance. All desmopressin formulations should be used cautiously in patients at risk for water intoxication with hyponatremia.

Chantix (Varenicline)
11/20/2007: FDA informed healthcare professionals of reports of suicidal thoughts and aggressive and erratic behavior in patient who have taken Chantix, a smoking cessation product. There are also reports of patients experiencing drowsiness that affected their ability to drive or operate machinery. FDA is currently reviewing these cases, along with other recent reports. A preliminary assessment reveals that many of the cases reflect new-onset of depressed mood, suicidal ideation, and changes in emotion and behavior within days to weeks of initiating Chantix treatment. The role of Chantix in these cases is not clear because smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and has also been associated with the exacerbation of underlying psychiatric illness. However, not all patients described in the cases had preexisting psychiatric illness and not all had discontinued smoking.

Healthcare professionals should monitor patients taking Chantix for behavior and mood changes. Patients taking this product should report behavior or mood changes to their doctor and use caution when driving or operating machinery until they know how quitting smoking with Chantix may affect them.

Erythropoiesis Stimulating Agents: Aranesp (darbepoetin alfa), Epogen (epoetin alfa), and Procrit (epoetin alfa)
Updated 1/03/2008: FDA informed healthcare professionals of findings from two additional clinical studies, Preoperative Epirubicin Paclitaxel Aranesp Study (PREPARE), and the National Cancer Institute Gynecologic Oncology Group (COG-19), showing an increase in mortality and shorter time to tumor progression in patients with cancer receiving an Erythropoiesis-Stimulating Agent (ESA). Both the PREPARE study in breast cancer and the COG-19 study in cervical cancer showed higher rates of death and or tumor progression in patients who received an ESA compared to patients who did not receive an ESA. FDA strongly recommends that healthcare professionals discuss the risks of ESA-associated tumor progression and shortened survival in patients with cancer before starting or continuing ESA therapy.

Posted 11/08/2007: FDA notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs), which treat certain types of anemia. These new statements address the risks that

the drugs Aranesp, Epogen, and Procrit pose to patients with cancer and patients with chronic kidney failure. For patients with cancer, the new boxed warnings emphasize that ESAs caused tumor growth and shortened survival in patients with advanced breast, head and neck, lymphoid and non-small cell lung cancer when they received a dose that attempted to achieve a hemoglobin level of 12 grams per deciliter (g/dL) or greater. For patients with chronic kidney failure, the new boxed warning states that ESAs should be used to maintain a hemoglobin level between 10 g/dL to 12 g/dL. Maintaining higher hemoglobin levels in patients with chronic kidney failure increases the risk of death and other serious conditions. The new labeling provides specific instructions for dosage adjustments and hemoglobin monitoring for chronic kidney failure patients who do not respond to ESA treatment with an adequate increase in their hemoglobin levels. Additionally, the new boxed warnings clarify that ESAs should only be used in patients with cancer when treating anemia specifically caused by chemotherapy and not for other causes of anemia. Further, it states that ESAs should be discontinued once the patient's chemotherapy course has been completed.

CellCept (mycophenolate mofetil)

Updated 11/27/2007: Prescribing information for Mycophenolic Acid (marketed as Myfortic Delayed Released Tablets) revised to include information that use of drug during pregnancy is associated with increased risks of pregnancy loss and congenital malformations. See the MedWatch alert for Myfortic (mycophenolic acid).

[Posted 10/29/2007] 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

10/24/2007: FDA and Cephalon notified healthcare professionals of updates to the WARNINGS section of the 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 labeling 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. See revised labeling below.

Viagra (sildenafil), Cialis (tadalafil), Levitra (vardenafil), Revatio (sildenafil)
10/18/2007: FDA informed healthcare professionals of reports of sudden decreases or loss of hearing following the use of PDE5 inhibitors Viagra, Levitra, Cialis for the treatment of erectile dysfunction, and Revatio for the treatment of pulmonary arterial hypertension. In some cases, the sudden hearing loss was accompanied by tinnitus and dizziness. Medical follow-up on these reports was often limited which makes it difficult to determine if the loss of hearing was related to the use of one of the drugs, an underlying medical condition or other risk factors for hearing loss, a combination of these factors or other factors. The PRECAUTIONS and ADVERSE REACTIONS sections of the approved product labeling for Viagra, Levitra, and Cialis were revised. FDA is working with the manufacturer to revise the labeling for Revatio.

Byetta (exenatide)
10/16/2007: 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.

Next Meeting Information:
Mr. Marascalco reminded the Board of the next meeting scheduled for May 15th, 2008.

Mr. Marascalco called for adjournment at 3:45p.m.

Respectfully Submitted:
Health Information Designs

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the May 15, 2008 Meeting

Members Attending: Frank Marascalco, R.Ph., Chair; and Lee Voulters, M.D.

Members Absent: Roy Arnold, R.Ph.; Harold Blakely. R.Ph., Laura Gray, M.D.; Wallace Strickland; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, Pharm D, DOM DUR Coordinator; Terri Kirby, R.Ph., Andrea McNeal, Ella Holmes.

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

Call to Order:
Frank Marascalco, Chairman of the Board, called the meeting to order at 2:15 p.m.

Ms. Clark offered that the Board may choose to delay the meeting until June in light of the lack of quorum or continue with the present meeting. The Board members in attendance agreed to proceed, acknowledging that no voting would be possible.

Updates:

Cost Management Analysis:
Mr. Smith presented an overview of data covering several months, including top therapeutic classes by total cost of claims, top drugs based on the number of claims, and top drugs based on total cost of claims. Mr. Smith pointed out seasonal trends, such as increases in antibiotic use and Synagis.

Pharmacy Program Update:
Dr. Clayton reminded the Board that the new PDL will be available on the DOM website on or about June 1, 2008 with an effective date of July 1, 2008.

New Business:

FDA Updates:
Mr. Smith presented recent FDA labeling updates and other FDA healthcare provider communications. In past DUR Board meetings, this presentation was referred to as Box Warning Updates, but has been renamed and moved up in the agenda. This information is provided to assist in identifying drug products with potential for concern surrounding safety and appropriate utilization. He stated that 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 the FDA.

CellCept (mycophenolate mofetil)
Myfortic (mycophenolate acid)
4/10/2008: FDA informed healthcare professionals that the Agency is investigating a potential association between the use of CellCept and Myfortic, medicines used to prevent organ rejection, and the development of progressive multifocal leukoencephalopathy (PML), a life-threatening disease. PML is a rare disorder that affects the central nervous system usually occurring in patients with immune systems suppressed by disease or medicines. FDA is reviewing data submitted by Roche, including postmarketing reports it has received of PML in patients who took CellCept or Myfortic, and the proposed revisions to the CellCept prescribing information. FDA has asked Novartis, the maker of Myfortic, for data on PML cases and to revise the Myfortic prescribing information to include the same information about PML included in the CellCept prescribing information. FDA anticipates it may take about 2 months to complete its review of the postmarketing reports and the proposed revisions to the prescribing information. As soon as the review is completed, FDA will communicate the conclusions and recommendations to the public.
Until further information is available, patients and healthcare professionals should be aware of the possibility of PML, such as localized neurologic signs and symptoms in the setting of a suppressed immune system, including during therapy with CellCept and Myfortic.

Neupro (rotigotine transdermal system)
4/09/2008: Schwarz Pharma informed healthcare professionals and patients of the recall of Neupro, a transdermal delivery system worn on the skin and used to treat early stage Parkinson's disease, at the end of April 2008, because of the formation of rotigotine crystals in the patches. When the drug crystallizes, less drug is available to be absorbed through the skin and the efficacy of the product may vary. Healthcare professionals should not initiate any new patients on Neupro and should begin to down-titrate all patients currently using the product per the guidelines in the product labeling. Patients should NOT abruptly discontinue therapy. Abrupt withdrawal of dopamine agonists has been associated with a syndrome resembling neuroleptic malignant syndrome or akinetic crises.

Exubera (insulin human rDNA origin) Inhalation Powder
4/09/2008: Pfizer informed healthcare professionals and patients of updated safety information in the WARNINGS section of prescribing information for Exubera, a short-acting insulin you breathe in through your mouth using the Exubera inhaler that helps to control high blood sugar in adults with diabetes. There have been 6 newly diagnosed cases of primary lung malignancies in clinical trials among Exubera-treated patients, and 1 newly diagnosed case among comparator treated patients. There has also been 1 post-marketing report of a primary lung malignancy in an Exubera-treated patient. There were too few cases to determine whether the emergence of these events is related to Exubera. All patients who were diagnosed with lung cancer had a prior history of cigarette smoking. Because of limited availability of Exubera, healthcare professionals should seek alternative treatment options to maintain patients' glycemic control.
Relenza (zanamivir)

4/01/2008: GlaxoSmithKline informed healthcare professionals of changes to the WARNINGS AND PRECAUTIONS sections of prescribing information for Relenza regarding information from postmarketing reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of Relenza to these events has not been established. Influenza can be associated with a variety of neurologic and behavioral symptoms which can include seizures, hallucinations, delirium, and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease.

Patients with influenza should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.

Ziagen (abacavir)
Videx (didanosine)
3/27/2008: The FDA issued an Early Communication about recent findings of The Data Collection on Adverse Events of Anti-HIV Drugs Study. Data analyses from this study indicate a higher risk of heart attack in patients infected with HIV-1 who were taking Ziagen (abacavir) or Videx (didanosine) as part of their drug therapy. The study is a large observational study of 33,347 HIV-1 infected patients living in North America, Europe and Australia. Patients in this study are being followed to evaluate the short and long term adverse effects of treatment with anti-HIV drugs. FDA continues to evaluate the overall risks and benefits of abacavir and didanosine. This evaluation may result in the need to revise labeling for the products. Until the FDA's review is complete, health care professionals should evaluate the potential risks and benefits of each HIV-1 antiretroviral drug their patients are taking.

Regranex (becaplermin) Gel
3/27/2008: The FDA is conducting a safety review based on study data suggesting there may be an increased risk of death from cancer in diabetic patients using Regranex (becaplermin) Gel, a skin product used to heal leg and foot ulcers. While the review is ongoing, the FDA recommends health care professionals discuss the potential risks and benefits of using Regranex with their patients.

Singulair (montelukast)
3/27/2008: FDA informed healthcare professionals and patients of the Agency's investigation of the possible association between the use of Singulair and behavior/mood changes, suicidality (suicidal thinking and behavior) and suicide. Singulair is a leukotriene receptor antagonist used to treat asthma and the symptoms of allergic rhinitis, and to prevent exercise-induced asthma. Patients should not stop taking Singulair before talking to their doctor if they have questions about the new information. Healthcare professionals and caregivers should monitor patients taking Singulair for suicidality (suicidal thinking and behavior) and changes in behavior and mood.

Tiotropium (marketed as Spiriva HandiHaler)
3/18/2008: Boehringer Ingelheim and FDA notified healthcare professionals that ongoing safety monitoring has identified a possible increased risk of stroke in patients who take Spiriva. This product contains tiotropium bromide and is used to treat bronchospasm associated with chronic obstructive pulmonary disease. Boehringer Ingelheim reported to the FDA that it has conducted an analysis of the safety data from 29 placebo controlled clinical studies ("pooled analysis"). Based on data from these studies, the preliminary estimates of the risk of stroke are 8 patients per 1000 patients treated for one year with Spiriva, and 6 patients per 1000 patients treated for one year with placebo. This means that the estimated excess risk of any type of stroke due to Spiriva is 2 patients for each 1000 patients using Spiriva over a one year period.

It is important to interpret these preliminary results with caution. FDA is working with Boehringer Ingelheim to further evaluate the potential association between Spiriva and stroke. FDA has not confirmed these analyses and while pooled analyses can provide early information about potential safety issues, these analyses have inherent limitations and uncertainty that require further investigation using other data sources. Patients should not stop taking Spiriva HandiHaler before talking to their doctor, if they have questions about this new information. This early communication is in keeping with FDA's commitment to inform the public about its ongoing safety reviews of drugs.

Erythropoiesis Stimulating Agents: Aranesp (darbepoetin alfa), Epogen (epoetin alfa), and Procrit (epoetin alfa)
3/12/2008: Amgen and FDA notified healthcare professionals of changes to the Boxed Warnings/WARNINGS: Increased Mortality and/or Tumor Progression section of the Aranesp and EPOGEN/PROCRIT labeling to update information describing the results of two additional studies showing increased mortality and more rapid tumor progression in patients with cancer receiving ESAs. Based on the results of these studies, the prescribing information has been revised as follows: ESAs shortened overall survival and/or time to tumor progression in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers when dosed to target a hemoglobin of ≥ 12 g/dL.

Prezista (darunavir)

3/21/2008: FDA issued a new "Information for Healthcare Professionals" sheet highlighting the addition of hepatotoxicity information to the WARNINGS section of prescribing information for Prezista.

3/12/2008: FDA and Tibotec Therapeutics notified healthcare professionals of changes to the WARNINGS section of the prescribing information for Prezista (darunavir) tablets regarding the risk of hepatotoxicity. In clinical trials and postmarketing experience, drug induced hepatitis has been reported in patients receiving combination therapy with Prezista/ritonavir. Appropriate laboratory testing should be conducted prior to initiating therapy with Prezista/ritonavir and patients should be monitored during treatment. Increased AST/ALT monitoring should be considered in patients with underlying chronic

hepatitis, cirrhosis, or in patients who have pretreatment elevations of transaminases, especially during the first several months of Prezista/ritonavir treatment.

Long-Acting Hydrocodone-Containing Cough Product (marketed as Tussionex Pennkinetic Extended-Release Suspension)
3/11/2008: FDA informed healthcare professionals of life-threatening adverse events and death in patients, including children, who have received Tussionex Pennkinetic Extended-Release Suspension (Tussionex). The reports indicate that healthcare professionals have prescribed Tussionex for patients younger than the approved age group of 6 years old and older, and more frequently than the labeled dosing interval of every 12 hours. Tussionex is contraindicated for use in patients less than 6 years of age because of their susceptibility to life-threatening and fatal respiratory depression.

Patients have administered the incorrect dose due to misinterpretation of the dosing directions, and have used inappropriate devices to measure the suspension. Overdose of Tussionex in older children, adolescents, and adults has also been associated with life-threatening and fatal respiratory depression. Prescribers should be familiar with the dosing recommendations of Tussionex before prescribing. In addition, patients and caregivers should use a properly marked measuring device to measure Tussionex to prevent overdose.

Tamiflu (oseltamivir phosphate)
3/04/2008, updated 3/04/2008: Roche and FDA informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu, in patients with influenza. The label has been revised as follows: Influenza can be associated with a variety of neurologic and behavioral symptoms which can include events such as hallucinations, delirium, and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease. There have been postmarketing reports (mostly from Japan) of delirium and abnormal behavior leading to injury, and in some cases resulting in fatal outcomes, in patients with influenza who were receiving Tamiflu. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made but they appear to be uncommon based on Tamiflu usage data. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of Tamiflu to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.

Spiriva (tiotropium bromide inhalation powder) Capsules
Foradil (formoterol fumarate inhalation powder) Capsules
2/29/2008: FDA informed healthcare professionals and consumers of the correct way to use Spiriva and Foradil inhalation powder capsules. FDA and the American Association of Poison Control Center's (AAPCC) National Poison Data System have received many reports of patients swallowing Spiriva and Foradil capsules rather than placing the capsules in the inhalation devices. Both products are to be used in the HandiHaler

(Spiriva) and Aerolizer (Foradil) devices to deliver the medicine to the lungs to improve breathing in patients with asthma, and in individuals affected by chronic obstructive lung disease and bronchitis. Both products will not treat a patient's breathing condition if the contents of a capsule are swallowed rather than inhaled. Healthcare professionals should discuss with patients how to correctly use the Spiriva HandiHaler or Foradil Aerolizer. See the Public Health Advisory for important information on the correct use of both products.

Tysabri (natalizumab)
2/27/2008: Biogen Idec, Elan and FDA notified healthcare professionals of reports of clinically significant liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose of Tysabri. The combination of transaminase elevations and elevated bilirubin without evidence of obstruction is recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients. Tysabri should be discontinued in patients with jaundice or other evidence of significant liver injury. Physicians should inform patients that Tysabri may cause liver injury.

Avandia (rosiglitazone maleate)
2/26/2008: FDA and GlaxoSmithKline notified pharmacists and physicians of a new Medication Guide for Avandia (rosiglitazone maleate). The FDA regulation 21CFR 208 requires a Medication Guide to be provided with each prescription that is dispensed for products that FDA determines pose a serious and significant public health concern. A list of currently approved Medication Guides are available at http://www.fda.gov/cder/Offices/ODS/medication_guides.htm. The Medication Guide and current Prescribing Information for Avandia are provided below.

Fentanyl transdermal system CII Patches
3/03/2008: Actavis Inc. has voluntarily recalled of all lots of Fentanyl Transdermal System CII patches sold in the United States.

2/19/2008: Actavis Inc. announced a nationwide recall of certain lots of Fentanyl transdermal system CII Patches sold in the United States and labelled with an Abrika or Actavis label. The product may have a fold-over defect which can cause the patch to leak and expose patients or caregivers directly to the fentanyl gel. Exposure to fentanyl gel may lead to serious adverse events, including respiratory depression and possible overdose, which may be fatal. The lots covered by this recall include doses of 25, 50, 75, and 100 mcg/hr and are listed in the firm's press release.

Duragesic 25 mcg/hr (fentanyl transdermal system) CII Pain Patches
2/15/2008: PriCara and Sandoz Inc. announced a nationwide recall of all lots of 25 mcg/hr Duragesic Patches sold in the United States. The product is being recalled because the patches may have a cut along one side of the drug reservoir within the patch which may result in the possible release of fentanyl gel that may expose patients or caregivers directly to fentanyl gel on the skin. Fentanyl is a potent Schedule II opioid medication and exposure to the gel may lead to serious adverse events, including

respiratory depression and possible overdose, that may be fatal. Patches with a cut edge should not be used. These recalled patches have expiration dates on or before December 2009 and are all manufactured by ALZA Corporation.

Heparin Sodium Injection (Baxter)
2/28/2008: Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection, and their heparin lock flush solutions.
2/11/2008: FDA informed healthcare professionals of important warnings and instructions for Heparin Sodium Injection use. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension. Most events developed within minutes of heparin initiation although the possibility for a delayed response has not been excluded. The reports have largely involved use of multiple-dose vials. However, there have been several cases in which product from multiple, single-dose vials have been combined to administer a bolus dose. Heparin sodium is an anticoagulant (blood thinner) that is used in patients undergoing kidney dialysis, certain types of cardiac surgery, and treatment or prevention of other serious medical conditions, including deep venous thrombosis and pulmonary emboli. Heparin treatment is initiated using high doses (5000-50,000 units) given directly into the blood stream (intravenously) as a bolus. Serious adverse events have recently been reported in patients who received these higher bolus doses.

The manufacture of multiple-dose vials of heparin sodium has been suspended pending the completion of an extensive ongoing investigation to determine the root cause of the problem. Because heparin sodium is a medically necessary product and serious public health consequences would result if there were a sudden shortage of the drug, the multiple-dose vials of heparin sodium manufactured by Baxter that are currently in distribution will not be recalled. See the FDA Public Health Advisory for Agency recommendations to healthcare professionals on the use of heparin sodium for injection.

Botox, Botox Cosmetic (Botulinum toxin Type A), Myobloc (Botulinum toxin Type B)
2/07/2008: FDA issued an early communication about an ongoing safety review regarding Botox and Botox Cosmetic. FDA has received reports of systemic adverse reactions including respiratory compromise and death following the use of botulinum toxins types A and B for both FDA-approved and unapproved uses. The reactions reported are suggestive of botulism, which occurs when botulinum toxin spreads in the body beyond the site where it was injected. The most serious cases had outcomes that included hospitalization and death, and occurred mostly in children treated for cerebral palsy-associated limb spasticity. Use of botulinum toxins for treatment of limb spasticity (severe arm and leg muscle spasms) in children or adults is not an approved use in the U.S. See the FDA's "Early Communication about an Ongoing Safety Review" for Agency recommendations and additional information for healthcare professionals.

Injectable Colchicine (including drugs containing colchicine)

2/06/2008: FDA announced its intention to take enforcement action against companies marketing unapproved, injectable colchicine, a drug used to treat gout. Colchicine is a highly toxic drug that can easily be administered in excessive doses, especially when given intravenously. There is a narrow margin between an effective dose of the drug and a toxic dose that can result in serious health risks, including death. The FDA is aware of 50 reports of adverse events associated with the use of intravenous colchicine, including 23 deaths. Potentially fatal effects include low blood cell counts, cardiac events, and organ failure. This action does not affect colchicine products that are dispensed in tablet form.

Individuals and companies must stop making these products within 30 days and stop shipping the product within 180 days or face regulatory action. After these dates, all injectable colchicine drug products must have FDA approval to be manufactured or shipped interstate.

Varenicline (marketed as Chantix)
2/01/2008: FDA informed healthcare professionals and consumers of important revisions to the WARNINGS and PRECAUTIONS sections of the prescribing information for Chantix regarding serious neuropsychiatric symptoms experienced in patients taking Chantix. These symptoms include changes in behavior, agitation, depressed mood, suicidal ideation, and attempted and completed suicide. While some patients may have experienced these types of symptoms and events as a result of nicotine withdrawal, some patients taking Chantix who experienced serious neuropsychiatric symptoms and events had not yet discontinued smoking. In most cases, neuropsychiatric symptoms developed during Chantix treatment, but in others, symptoms developed following withdrawal of Chantix therapy. See the FDA Information for Healthcare Professionals Sheet for recommendations and considerations for healthcare professionals on using Chantix therapy for patients.

Antiepileptic Drugs
1/31/2008: FDA informed healthcare professionals that the Agency has analyzed reports of suicidality (suicidal behavior or ideation) from placebo-controlled clinical studies of eleven drugs used to treat epilepsy as well as psychiatric disorders, and other conditions. In the FDA's analysis, patients receiving antiepileptic drugs had approximately twice the risk of suicidal behavior or ideation (0.43%) compared to patients receiving placebo (0.22%). The increased risk of suicidal behavior and suicidal ideation was observed as early as one week after starting the antiepileptic drug and continued through 24 weeks. The results were generally consistent among the eleven drugs. The relative risk for suicidality was higher in patients with epilepsy compared to patients who were given one of the drugs in the class for psychiatric or other conditions.

Healthcare professionals should closely monitor all patients currently taking or starting any antiepileptic drug for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior or depression.

The drugs included in the analyses include (some of these drugs are also available in generic form):
Carbamazepine (marketed as Carbatrol, Equetro, Tegretol, Tegretol XR)
Felbamate (marketed as Felbatol)
Gabapentin (marketed as Neurontin)
Lamotrigine (marketed as Lamictal)
Levetiracetam (marketed as Keppra)
Oxcarbazepine (marketed as Trileptal)
Pregabalin (marketed as Lyrica)
Tiagabine (marketed as Gabitril)
Topiramate (marketed as Topamax)
Valproate (marketed as Depakote, Depakote ER, Depakene, Depacon)
Zonisamide (marketed as Zonegran)

Although the 11 drugs listed above were the ones included in the analysis, FDA expects that the increased risk of suicidality is shared by all antiepileptic drugs and anticipates that the class labeling changes will be applied broadly.

NuCel Labs Eye Drops and Eye/Ear Wash Products
1/31/2008: NuCel Labs and FDA informed consumers and healthcare professionals of a voluntary nationwide recall of all Eye Drops and Eye/Ear Wash Products. The products were recalled after testing indicated the presence of bacteria and particulate matter, deeming these products non-sterile. Non-sterile eye drops pose an unacceptable risk of causing eye infections, which in rare cases could lead to blindness. No illnesses or injuries have been reported to date. There are no lot numbers or expiration dates on the products. Consumers who have the product should discontinue use of the product and return it to NuCel Labs. See the manufacturer's press release for return shipping information.

Ezetimibe/Simvastatin (marketed as Vytorin), Ezetimibe (marketed as Zetia), and Simvastatin (marketed as Zocor): Early Communication about an Ongoing Data Review
1/25/2008: FDA provided healthcare professionals with an early communication about an ongoing data review for Ezetimibe/Simvastatin (marketed as Vytorin), Ezetimibe (marketed as Zetia), and Simvastatin (marketed as Zocor). This early communication is in keeping with FDA's commitment to inform the public about ongoing postmarketing drug issues.

Merck/Schering Plough Pharmaceuticals reported preliminary results from the Effect of Combination Ezetimibe and High-Dose Simvastatin vs. Simvastatin Alone on the Atherosclerotic Process in Patients with Heterozygous Familial Hypercholesterolemia (ENHANCE) trial. This trial was designed to evaluate the amount of atherosclerotic plaque in blood vessels located in the neck based on images obtained through ultrasound in patients treated with Vytorin (ezetimibe plus simvastatin) or simvastatin alone. Merck/Schering Plough stated that there was no significant difference between Vytorin and simvastatin in the amount of atherosclerotic plaque in the inner walls of the carotid

(neck) arteries despite greater lowering of LDL-cholesterol (bad cholesterol) with Vytorin compared to simvastatin. Once Merck/Schering Plough completes the analysis of the unblinded data from ENHANCE, it will submit a final study report to FDA. Once FDA receives the final study report, FDA estimates it will take approximately 6 months to fully evaluate the data. After reviewing the data from the ENHANCE study, and considering all other available information about the link between LDL lowering and reduction of cardiovascular events, FDA will determine whether any further regulatory action is warranted with regard to Zetia and Vytorin and also whether any changes to FDA's current approach to drugs that lower LDL cholesterol are warranted.

Patients should talk to their doctors if they have any questions about the information from the ENHANCE trial.

Leukine (sargramostim)
1/24/2008 Bayer and FDA informed healthcare professionals of the market withdrawal of the current liquid formulation of Leukine, a growth factor that helps fight infection and disease in appropriate patients by enhancing immune cell function. The product was withdrawn because of an upward trend in spontaneous reports of adverse reactions, including syncope (fainting), which are temporally correlated with a change in the formulation of liquid Leukine to include edetate disodium (EDTA). The upward trend in adverse reaction reporting rates has not been observed with the use of lyophilized Leukine. Healthcare professionals should immediately stop using liquid Leukine and return unused vials to the manufacturer.

Review of 1st Quarter Meeting Materials:
The members present were briefed on the prior meeting information and agreed to continue with other business.

Carisoprodol Prior Authorization Update:
Mr. Smith began by reporting that the P& T Committee concurred with the recommendation of the DUR Board to require a PA for all carisoprodol products. He continued by pointing out that with quantity limits and distribution of the prescribing information update and tapering schedule to physicians, this medication continues to show high utilization. Dr. Clayton interjected that she had requested input from several states and heard similar concerns and approaches throughout the country. The new carisoprodol prior authorization form to be implemented July 1, 2008 was presented for review.

Off-label Use of Atypical Antipsychotics for Children with ADHD/ODD:
Dr. Holeman noted that HID receives prior authorization requests regularly for atypical antipsychotics in pediatric patients with the only diagnosis provided being ADHD or ODD, neither of which is an approved indication. The youngest age for which any of the atypical antipsychotics is approved is five years. This indication is approved for Risperdal® in children with irritability associated with autistic disorder. Abilify ® is approved for adolescents from 13 years of age for Schizophrenia. The remaining atypical antipsychotics (Geodon®, Invega®, Zyprexa®, and Seroquel®) are not approved for use

in children or adolescents under the age of 18. This information, coupled with the large number of prior authorization requests seen for these medications in the pediatric population, raised concerns about the off-label use of these medications in children with ADHD and/or ODD. Dr. Holeman presented a chart depicting the use of these medications in pediatric Medicaid beneficiaries. While the largest number of beneficiaries range between the ages of 13 and 16 years, the chart also showed substantial use of atypical antipsychotics in children as young as six for ADHD and/or ODD.
In an effort to encourage appropriate use of these agents among this young population, a retrospective DUR criterion is recommended to identify these beneficiaries who do not have an FDA-approved diagnosis. The criterion will be presented at the next meeting due to the lack of a quorum at this meeting.

Synagis® trending Report:
HID has compiled seasonal information on Synagis utilization with emphasis on year-to-year trending of this costly medication. The intent of DOM policies regarding this agent is to ensure that the medication is available to all children who meet the criteria and that the medication is delivered to the appropriate beneficiary. The information presented illustrates that, while maintaining and encouraging appropriate utilization of this medication, the criteria and dose limits have resulted in a leveling of the average number of claims per beneficiary over the past three seasons. The outcome of the trending study showed that although 2007-2008 had more approved beneficiaries and the cost of the medication had increased, significant cost avoidance can be attributed to the policies implemented by DOM and HID.

Generalized Anxiety Disorder (GAD):
Dr. Holeman reviewed the prevalence of GAD, stating that it affects about 6.8million adult Americans and about twice as many women as men. With SSRI antidepressants being the preferred class for the treatment of GAD, once treatment at optimal dosing with one or more of the SSRIs has been tried and failed, second line treatment with Effexor XR® or Cymbalta® should be considered. Dr. Holeman mentioned that while benzodiazepines do have a place in the treatment of GAD, treatment guidelines recommend that their use be short-term, not to exceed two to four weeks. Due to apparent inappropriate use of benzodiazepines, the DUR Board has recommended that DOM distribute information to prescribers to encourage appropriate use. As a result, a Medicaid Prescribing Update was created by HID highlighting current GAD treatment guidelines. This update will be distributed by the Academic Detailers to all prescribers and will also be available by a link from the Division of Medicaid website.

Risperdal Consta:
Mr. Smith and Dr. Holeman presented a review of the impact of subjecting Risperdal Consta® to the prior authorization process. Risperdal Consta® is well-suited for patients for whom medication compliance is a challenge. According to the FDA-approved prescribing information, tolerability to oral risperidone 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. In October 2007, HID was given the responsibility for supervising the prior authorization of Risperdal Consta®. Utilization data was gathered by searching the paid claims submitted to HID by the fiscal agent. The six month period prior to HID involvement in this PA saw 138 beneficiaries on duplicate therapy with Risperdal Consta® and an oral atypical antipsychotic, compared to 124 beneficiaries during the subsequent six month period. In this analysis, indicating a ten percent decrease in duplicate therapy, DOM realized a decrease of approximately $900,000 in oral atypical antipsychotic expenditures in this short time. Based on the information presented, this effort has been successful. Dr. Holeman mentioned HID's efforts to educate prescribers on the Risperdal Consta® prescribing information, monitoring claims data and following up with those patients who are supposed to be tapered off oral medication. Dr Voulters suggested that HID contact the American Psychiatric Association for guidelines or treatment recommendations for the above mentioned disease states reviewed today.

Criteria Recommendations:
Unable to present at this time due to a lack of quorum

Frank Marascalco reminded the Board of the next meeting August 21, 2008 and adjourned the meeting at 3:15 p.m.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1ST and 2ND Quarter 2008

Criteria Recommendations ***Accepted*** ***Rejected***

1. Nebivolol / High Dose _____ _____

Alert Message: Bystolic (nebivolol) may be over-utilized. The recommended maximum dose is 40 mg per day.
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C
Nebivolol		

Max Dose: 40 mg/day
References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

2. Nebivolol / Contraindications _____ _____

Alert Message: Bystolic (nebivolol) is contraindicated in patients with severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (no permanent pacemaker in place), hypersensitivity to the product, or severe hepatic impairment (Child-Pugh >B).
Conflict Code: MC – Drug Actual Disease Problem
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Bradycardia	
	Heart Block	
	Cardiogenic Shock	
	Cardiac failure	
	Sick Sinus Syndrome	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

3. Nebivolol / Hepatic Impairment _____ _____

Alert Message: Bystolic (nebivolol) is contraindicated in patients with severe hepatic impairment and should be used with caution in patients with moderate impairment. Studies have shown patients with moderate hepatic impairment have an 86% decrease in nebivolol clearance. The recommended initial dose of nebivolol in patients with moderate impairment is 2.5 mg once daily with upward titration performed cautiously if needed.
Conflict Code: DB – Drug/Drug or Drug Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Hepatic Impairment	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

Criteria Recommendations	*Accepted*	*Rejected*

4. Nebivolol / Renal Impairment _____ _____

Alert Message: Bystolic (nebivolol) should be used with caution in patient with severe renal impairment. Studies have shown a 53% decrease in the renal clearance of nebivolol in patients with a CrCl < 30 mL/min. The recommended initial dose of nebivolol in this population is 2.5 mg once daily with upward titration performed cautiously if needed.
Conflict Code: DB – Drug/Drug or Drug Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Severe Renal Impairment	
	Lanthanum	
	Sevelamer	
	Doxercalciferol	
	Paricalcitol	
	Calcitriol	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

5. Nebivolol / CYP2D6 Inhibitors _____ _____

Alert Message: The concurrent administration of Bystolic (nebivolol) and a CYP2D6 inhibitor (e.g., paroxetine, fluoxetine, quinidine, and bupropion) is expected to result in elevated nebivolol plasma concentrations. Patients receiving concurrent therapy with these agents should be monitored closely and the nebivolol dose adjusted according to blood pressure response.
Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Paroxetine	
	Fluoxetine	
	Quinidine	
	Bupropion	
	Duloxetine	
	Amiodarone	
	Cimetidine	
	Propafenone	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

6. Nebivolol / CYP2D6 Inducers _____ _____

Alert Message: The concurrent administration of Bystolic (nebivolol) and a CYP2D6 inducer (e.g., rifampin and dexamethasone) is expected to result in decreased nebivolol plasma concentrations. Patients receiving concurrent therapy with these agents should be monitored closely and the nebivolol dose adjusted according to blood pressure response.
Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Dexamethasone	
	Rifampin	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

Criteria Recommendations ***Accepted*** ***Rejected***

7. Atypical Antipsychotics / Therapeutic Duplication _____ _____
Alert Message: Therapeutic duplication of atypical antipsychotic agents may be occurring.
Conflict Code: TD – Therapeutic Duplication
Drugs/Disease

Util A	Util B	Util C
Clozapine		
Risperidone		
Olanzapine		
Quetiapine		
Ziprasidone		
Aripiprazole		
Paliperidone		

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

8. Risperdal Consta / Oral Atypical Antipsychotics _____ _____
Alert Message: Patients prescribed Risperdal Consta (risperidone injection) should receive oral antipsychotic supplementation until risperidone has achieved steady-state plasma concentrations, typically after 4 injections. The use of oral antipsychotics with risperidone injection beyond the recommended transition time period may represent an unnecessary and costly duplication of therapy.
Conflict Code: TD – Therapeutic Duplication (DD-100P)
Drugs/Disease

Util A	Util B	Util C
Risperdal Consta	Clozapine	
	Risperidone (except Consta)	
	Olanzapine	
	Quetiapine	
	Ziprasidone	
	Aripiprazole	
	Paliperidone	

References:
Risperdal Consta Prescribing Information, Sept 2007, Janssen Pharmaceuticals, Ltd.
Facts & Comparisons, 2007 Updates.
Clinical Pharmacology, Gold Standard, 2007.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.

9. Clopidogrel / Non-adherence _____ _____
Alert Message: Non-adherence to clopidogrel therapy may result in a sub-therapeutic effect increasing mortality, morbidity and healthcare cost.
Conflict Code: LR - Non-Adherence
Drug/Diseases:

Util A	Util B	Util C
Clopidogrel		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. Aug. 2005;353(5):487-497.
Munger MA, Van Tassell BW, La Fleur J. Medication nonadherence: an unrecognized cardiovascular risk factor. MedGenMed. Sep. 2007;19;9(3): 58.

Criteria Recommendations	***Accepted***	***Rejected***

10. Clopidogrel / Over-utilization _____ _____

Aler Message: The recommended daily dose of clopidogrel is 75 mg. Exceeding the recommended dose may put the patient at increased risk of bleeding and other adverse effects.
Conflict Code: HD – High Dose
Drug/Diseases:

Util A	Util B	Util C
Clopidogrel		

Maximum Dose: 75 mg/day
References:
Facts & Comparisons, 2008 Updates.
Plavix Prescribing Information, Oct. 2007, Bristol-Myers Squibb Company.

11. Tussionex / Warning _____ _____

Alert Message: The FDA has received reports of death and life-threatening side effects in patients who have received Tussionex (hydrocodone/chlorpheniramine). The reports indicate that healthcare professionals have prescribed Tussionex for patients younger than the approved aged group of 6 years old and older, more frequently than the labeled dosing interval of every 12 hours, and that patients have administered the incorrect dose due to misinterpretation of the dosing directions and use of inappropriate devices to measure the suspension. Carefully counsel patients concerning the use of this medication.
Conflict Code: TA – Therapeutic Appropriateness (Public Health Advisory)
Drug/Diseases:

Util A	Util B	Util C
Tussionex		

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Tussionex Prescribing Information, Jan. 2008, UCB, Inc.
FDA Public Health Advisory: Important Information for the Safe Use of Tussionex Pennkinetic Extended-Release Suspension. March 2008.

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

12. Tussionex / Contraindication _____ _____

Alert Message: The use of Tussionex suspension (hydrocodone/chlorpheniramine) is contraindicated in children less then 6 years of age due to the risk of fatal respiratory depression.
Conflict Code: TA – Therapeutic Appropriateness
Drug/Diseases:

Util A	Util B	Util C
Tussionex		

Age Range: 0 – 5 years of age
References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Tussionex Prescribing Information, Jan. 2008, UCB, Inc.

13. Erythropoiesis Stimulating Agents / Black Box Warning _____ _____

Alert Message: In clinical trials erythropoiesis stimulating agents (ESAs) have been shown to shorten the overall survival and/or time to tumor progression in patients with breast cancer, non-small cell lung, head and neck, lymphoid and cervical cancers when dosed to target a hemoglobin of ≥ 12g/dL. To minimize this risk, use the lowest dose needed to avoid red blood cell transfusions.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Diseases:

Util A	Util B	Util C
Aranesp	Breast Cancer	
Epogen/Procrit	Non-small Cell Lung Cancer	
	Head and Neck Cancer	
	Lymphoid Cancers	
	Cervical Cancer	

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Procrit Prescribing Information, March 2008. Ortho Biotech Products, L.P.
Epogen Prescribing Information, March 2008, Amgen.
Aranesp Prescribing Information, March 2008, Amgen.

14. Desmopressin / Therapeutic Appropriateness _____ _____

Alert Message: Desmopressin may cause severe hyponatremia which may put patients at risk for seizures and death. Intranasal desmopressin is no longer indicated for the treatment of primary nocturnal enuresis (PNE). The agent should not be used in patients with hyponatremia or a history of hyponatremia. Desmopressin tablets are still indicted for the treatment of PNE but therapy should be interrupted during acute illness that may lead to fluid or electrolyte imbalance.
Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Desmopressin		

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2007.
DDAVP Prescribing Information, October 2007, Sanofi-Aventis.

15. Desmopressin / Pressor Agents _____ _____

Alert Message: The concomitant administration of drugs that may increase the risk of water intoxication with hyponatremia (e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics, NSAIDS, lamotrigine, and carbamazepine) should be performed with caution.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Desmopressin	Tricyclic Antidepressants	
	Selective Serotonin Re-uptake Inhibitors	
	Chlorpromazine	
	Opiate Analgesics	
	NSAIDS	
	Lamotrigine	
	Carbamazepine	

References:
DDAVP Prescribing Information, October 2007, Sanofi-Aventis.
Facts & Comparisons, 2007 Updates.

Criteria Recommendations ***Accepted*** ***Rejected***

16. Atypical Antipsychotics / Metabolic Syndrome _____ _____

Alert Message: The use of second-generation antipsychotics (SGAs) has been associated with the development of serious health risks (e.g., cardiovascular disease, diabetes, dramatic weight gain, and atherogenic lipid profiles). All patients should receive baseline screenings for risk factors associated with metabolic syndrome before receiving a SGA and regular monitoring of metabolic parameters throughout therapy. If metabolic risk factors cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable metabolic risk profile.
Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Disease

Util A	Util B	Util C (Negating)
Clozapine		
Olanzapine		
Risperidone		
Quetiapine		

Age Range: > 18 years of age
References:

Lieberman JA, Stroup S., McEvoy JP, et al, Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIE Trial). N Engl J Med 2005;353(12):1209-1223.
Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.
Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.
Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.

17. Atypical Antipsychotics / Pediatric Patients _____ _____

Alert Message: The effects of prolonged use of atypical antipsychotics in pediatric patients are unknown. Preliminary evidence suggests that pediatric patients experience more prevalent and severe adverse effects than those reported in adults (e.g., weight gain, extrapyramidal side effects, and insulin resistance). If therapy with these agents is clinically necessary use the lowest effective dose and observe patients closely for adverse events. If adverse effects cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable adverse effect profile.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases:

Util A	Util B	Util C
Clozapine		
Risperidone		
Olanzapine		
Quetiapine		
Ziprasidone		
Aripiprazole		
Paliperidone		

Age Range: < 19 years of age
References:

Kumra S, Oberstar JV, Sikich L et al., Efficacy and Tolerability of Second Generation Antipsychotics in Children and Adolescents with Schizophrenia. Schizophrenia Bulletin. 2008;34(1):61-70.
Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994.Arch Pediatr Adolesc Med 2003, 157:821-827.
Correll CU, Carlson HE, Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents, J Am Acad Child Adolesc Psychiatry (2006)45:771-791.
Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.
Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.
Cada DJ, Baker DE, Levien T, Formulary Drug Reviews: Paliperidone, Hospital Pharmacy, 2007;42(7):637-647.

[TODAY]

[adrs1]
[adrs2]
[adrs3]
[adrs4]

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to institute Retrospective Drug Utilization Review Programs (RDUR). The program's goal is to ensure that Medicaid patients receive optimal drug therapy at the lowest reasonable cost. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This RDUR program is informational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, it was noted that your patient, **[t1d0-recip-fst-nm] [t1d0-recip-lst-nm]**, *is receiving* **[drug_a_name].** *The use of second-generation antipsychotics (SGAs) has been associated with the development of serious health risks (e.g., cardiovascular disease, diabetes, dramatic weight gain, and atherogenic lipid profiles). All patients should receive baseline screenings for risk factors associated with metabolic syndrome before receiving a SGA and regular monitoring of metabolic parameters throughout therapy. If metabolic risk factors cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable metabolic risk profile.* In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

The success of the DUR program is enhanced by effective two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although your participation in this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please use the enclosed response to note your comments and return it in the enclosed envelope or fax it to the number below.

At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information. Thank you for your professional consideration.

RX #(s): [rx_no_a]

Sincerely,

W. Murray Yarbrough M.D.

W. Murray Yarbrough, M.D.
Medical Director

Case#: [case_no]
Enclosures

PRESCRIBER RESPONSE

All information used to generate the enclosed letter, including Prescriber identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

1. This patient **is** under my care:

_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s)_____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy, however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___.(Please provide a fax number if available_____-_____-_____.)

Comments: _____
_____
_____
_____

[adrs1] Case# [case_no]
Letter Type [letter_type]
[alert_msg]
[criteria]

METABOLIC SYNDROME AND SECOND GENERATION ANTIPSYCHOTICS

Metabolic syndrome is the simultaneous occurrence of at least three of five clinical and laboratory risk factors: central obesity (defined by waist circumference), hypertension, hyperglycemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein cholesterol.[1]

Risk Factors for Metabolic Syndrome[1]	Clinical Identification[1]
Abdominal Obesity	Waist circumference: Males > 40 in Females > 35 in
Atherogenic Dyslipidemia	Low HDL-C Males <40 mg /dL Females < 50 mg/ dL
Hypertriglyceridemia	≥ 150 mg/dL
Hypertension	Blood Pressure (BP) ≥ 130 /80 mmHg
Impaired Glucose Tolerance/Type II Diabetes/ Insulin Resistance/Hyperinsulinemia	Fasting Glucose (FBD) ≥ 110 mg/dL

MANAGEMENT OF PATIENTS WITH METABOLIC SYNDROME ON SGA THERAPY[2]

1. Prescreen all patients for presence of risk factors for metabolic syndrome
2. Select SGA based on risks vs. benefits
3. Monitor patients throughout therapy for adverse effects of SGA therapy
4. Educate and monitor for healthy lifestyle (e.g., diet and exercise)
5. Treat underlying metabolic disorder(s) with lifestyle changes and medication if necessary
6. If adverse effects or metabolic disorders worsen consider switching, if clinically possible, to an alternative SGA with a lower risk profile

EFFECTS OF SGAs ON METABOLIC PARAMETERS[2, 3, 4, 5]

Second Generation Antipsychotics	Weight Gain	Dyslipidemia	Insulin resistance / Glucose Abnormalities	Hypertension
Clozapine	+++	+++	+++	+++
Olanzapine	+++	+++	+++	+
Quetiapine	++	+	+	-
Risperidone	++	+	+	++
Ziprasidone	+	-/+	-/+	++
Aripiprazole	+	-/+	-/+	+
Paliperidone	+	-	-	-

+++ = Highest incidence, ++ = Moderate incidence, + = Low incidence, - = No incidence

1. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.

2. Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

3. Lieberman JA, Stroup S., McEvoy JP, et al, Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIR Trial). N Engl J Med 2005;353(12):1209-1223.

4. Newcomer JW, Metabolic Considerations in the use of Antipsychotic Medications: A Review of Recent Evidence, J Clin Psychiatry 2007;68[Suppl 1]:20-27.

5. Casey DE, Dyslipidemia and Atypical Antipsychotic Drugs, J Clini Psychiatry;65[Suppl 18]:27-35.

[TODAY]

[adrs1]
[adrs2]
[adrs3]
[adrs4]

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to institute Retrospective Drug Utilization Review Programs (RDUR). The program's goal is to ensure that Medicaid patients receive optimal drug therapy at the lowest reasonable cost. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This RDUR program is informational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, it was noted that your patient, **[t1d0-recip-fst-nm] [t1d0-recip-lst-nm]**, *is receiving* **[drug_a_name].** *The effects of prolonged use of atypical antipsychotics in pediatric and adolescent patients are unknown. Preliminary evidence suggests that these patients experience more prevalent and severe adverse effects than those reported in adults (e.g., weight gain, extrapyramidal side effects, and insulin resistance). If therapy with these agents is clinically necessary use the lowest effective dose and observe patients closely for adverse events. If adverse effects cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable adverse effect profile.* In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

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RX #(s): [rx_no_a]

Sincerely,

W. Murray Yarbrough M.D.

W. Murray Yarbrough, M.D.
Medical Director

Case#: [case_no]
Enclosures

PRESCRIBER RESPONSE

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_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s)_____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy, however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___.(Please provide a fax number if available_____-_____-_____.)

Comments: _____
_____
_____
_____

[adrs1] Case# [case_no]
Letter Type [letter_type]
[alert_msg]
[criteria]

SECOND GENERATION ANTIPSYCHOTIC (SGA) USE IN PEDIATRIC AND ADOLESCENT PATIENTS

MANAGEMENT OF PEDIATRIC AND ADOLSECENT PATIENTS ON SGA THERAPY[2,3]

1. Prescreen all patients for presence of risk factors for metabolic syndrome
2. Select SGA based on risks vs. benefits
3. Educate and monitor for healthy lifestyle (e.g., diet and exercise)
4. Monitor patients throughout therapy for adverse effects of SGA therapy
5. Treat underlying metabolic disorder(s) with lifestyle changes and medication if necessary
6. If adverse effects or metabolic disorders worsen consider switching, if clinically possible, to an alternative SGA with a lower risk profile

Risk Factors for Metabolic Syndrome[1]	Clinical Identification[1]
Abdominal Obesity	Waist circumference: ≥ 90th percentile or BMI 95th percentile (i.e. overweight)
Atherogenic Dyslipidemia	Low HDL-C <40 mg /dL in males and females
Hypertriglyceridemia	≥ 110 mg/dL
Hypertension	Blood Pressure ≥ 90th Percentile for sex and age
Impaired Glucose Tolerance/Type II Diabetes/ Insulin Resistance/Hyperinsulinemia	Fasting glucose (FBG) ≥ 110 mg/dL

Metabolic syndrome is the simultaneous occurrence of at least three of five clinical and laboratory risk factors: central obesity (defined by waist circumference), hypertension, hyperglycemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein cholesterol.[6]

EFFECTS OF SGAs OF METABOLIC PARAMETERS[4,5]

Second Generation Antipsychotics	Weight Gain	Dyslipidemia	Insulin resistance / Glucose Abnormalities	Hyperprolactinemia	EPS
Clozapine	+++	+++	+++	+	-
Olanzapine	+++	+++	+++	++	+
Quetiapine	++	++	++	+	-
Risperidone	++	++	+	+++	++
Ziprasidone	+	+	+	++	++
Aripiprazole	+	+	+	-	+
Paliperidone	+	-	-	+++	+

+++ = High Incidence, ++ = Moderate incidence, + = Low incidence, - = No effect

1. Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994.Arch Pediatr Adolesc Med 2003, 157:821-827.

2 Correll CU, Carlson HE, Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents, J Am Acad Child Adolesc Psychiatry (2006)45:771-791.

3. Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

4. Rosack J, Better Monitoring Urged for Youth Taking Newer Antipsychotics, Psychiatr News Aug 4, 2006, Vo. 41, No, 15, 1.

5. Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.

6. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.

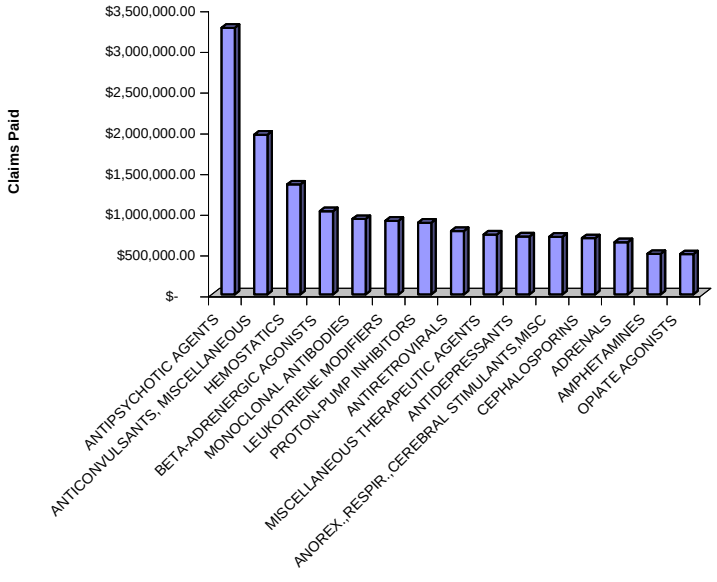
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 03/01/08-03/31/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	10,160	$ 3,273,804.54	$ 322.22	2.68%
ANTICONVULSANTS, MISCELLANEOUS	10,847	$ 1,960,773.91	$ 180.77	2.86%
HEMOSTATICS	57	$ 1,349,821.48	$23,681.08	0.02%
BETA-ADRENERGIC AGONISTS	12,900	$ 1,022,055.40	$ 79.23	3.40%
MONOCLONAL ANTIBODIES	667	$ 924,274.69	$ 1,385.72	0.18%
LEUKOTRIENE MODIFIERS	8,347	$ 902,907.70	$ 108.17	2.20%
PROTON-PUMP INHIBITORS	5,663	$ 878,689.82	$ 155.16	1.49%
ANTIRETROVIRALS	1,074	$ 777,869.33	$ 724.27	0.28%
MISCELLANEOUS THERAPEUTIC AGENTS	2,346	$ 733,646.77	$ 312.72	0.62%
ANTIDEPRESSANTS	13,505	$ 710,180.98	$ 52.59	3.56%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,782	$ 707,597.02	$ 122.38	1.52%
CEPHALOSPORINS	12,338	$ 688,749.29	$ 55.82	3.25%
ADRENALS	9,454	$ 640,459.94	$ 67.74	2.49%
AMPHETAMINES	4,237	$ 496,850.65	$ 117.26	1.12%
OPIATE AGONISTS	24,972	$ 492,630.76	$ 19.73	6.58%
TOTAL TOP 15	122,349	$ 15,560,312.28	$ 127.18	32.25%

Total Rx Claims	379,408
From 03/01/08-03/31/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



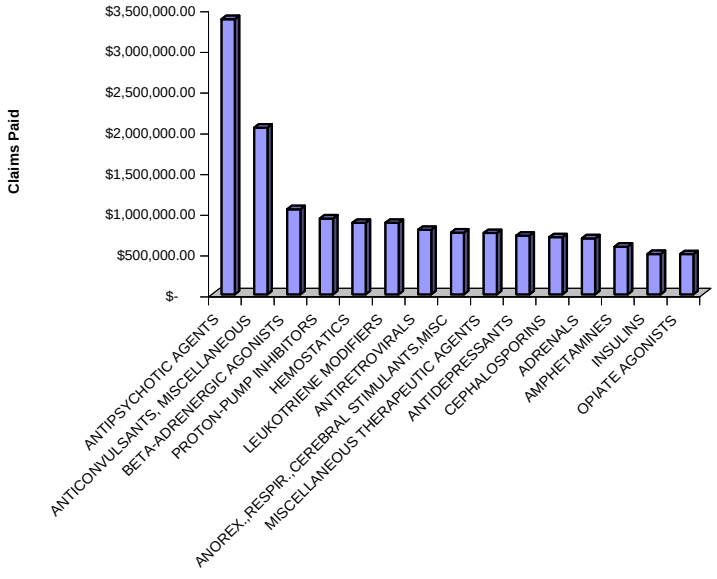
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 04/01/08-04/30/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	10,550	$ 3,378,091.50	$ 320.20	2.71%
ANTICONVULSANTS, MISCELLANEOUS	11,217	$ 2,047,873.60	$ 182.57	2.88%
BETA-ADRENERGIC AGONISTS	13,342	$ 1,043,580.97	$ 78.22	3.42%
PROTON-PUMP INHIBITORS	5,965	$ 930,490.67	$ 155.99	1.53%
HEMOSTATICS	38	$ 878,189.34	$23,110.25	0.01%
LEUKOTRIENE MODIFIERS	8,114	$ 877,680.44	$ 108.17	2.08%
ANTIRETROVIRALS	1,095	$ 791,452.52	$ 722.79	0.28%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,160	$ 757,006.83	$ 122.89	1.58%
MISCELLANEOUS THERAPEUTIC AGENTS	2,299	$ 751,777.79	$ 327.00	0.59%
ANTIDEPRESSANTS	13,949	$ 719,668.86	$ 51.59	3.58%
CEPHALOSPORINS	12,658	$ 699,907.68	$ 55.29	3.25%
ADRENALS	10,203	$ 685,911.81	$ 67.23	2.62%
AMPHETAMINES	4,600	$ 585,561.43	$ 127.30	1.18%
INSULINS	3,572	$ 493,258.07	$ 138.09	0.92%
OPIATE AGONISTS	25,809	$ 491,613.52	$ 19.05	6.62%
TOTAL TOP 15	129,571	$ 15,132,065.03	$ 116.79	33.25%

Total Rx Claims	389,724
From 04/01/08-04/30/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



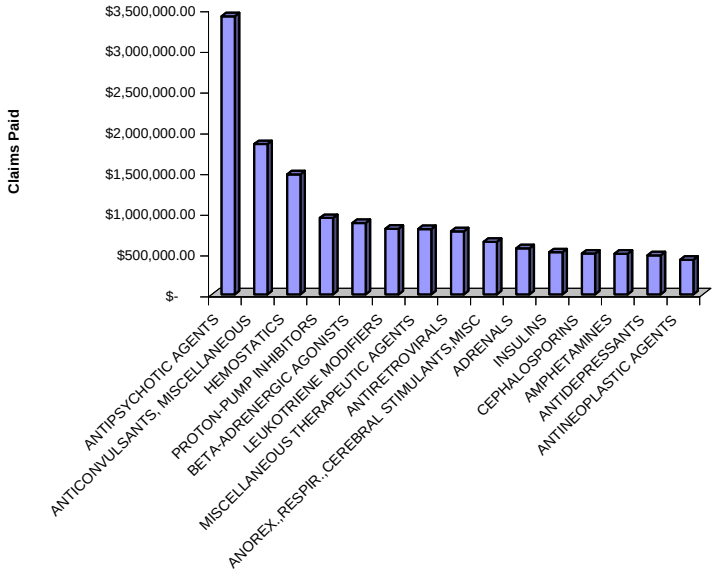
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 05/01/08-05/31/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	10,589	$ 3,414,813.47	$ 322.49	2.91%
ANTICONVULSANTS, MISCELLANEOUS	11,197	$ 1,843,678.16	$ 164.66	3.08%
HEMOSTATICS	47	$ 1,472,952.28	$31,339.41	0.01%
PROTON-PUMP INHIBITORS	5,918	$ 936,478.30	$ 158.24	1.63%
BETA-ADRENERGIC AGONISTS	11,597	$ 875,288.23	$ 75.48	3.19%
LEUKOTRIENE MODIFIERS	7,461	$ 805,604.67	$ 107.98	2.05%
MISCELLANEOUS THERAPEUTIC AGENTS	2,337	$ 801,644.47	$ 343.02	0.64%
ANTIRETROVIRALS	1,081	$ 773,274.07	$ 715.33	0.30%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,218	$ 644,748.71	$ 123.56	1.43%
ADRENALS	9,025	$ 565,606.57	$ 62.67	2.48%
INSULINS	3,763	$ 516,582.37	$ 137.28	1.03%
CEPHALOSPORINS	10,415	$ 500,821.29	$ 48.09	2.86%
AMPHETAMINES	4,087	$ 498,692.85	$ 122.02	1.12%
ANTIDEPRESSANTS	13,845	$ 478,861.70	$ 34.59	3.80%
ANTINEOPLASTIC AGENTS	876	$ 422,703.54	$ 482.54	0.24%
TOTAL TOP 15	97,456	$ 14,551,750.68	$ 149.32	26.77%

Total Rx Claims	363,982
From 05/01/08-05/31/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



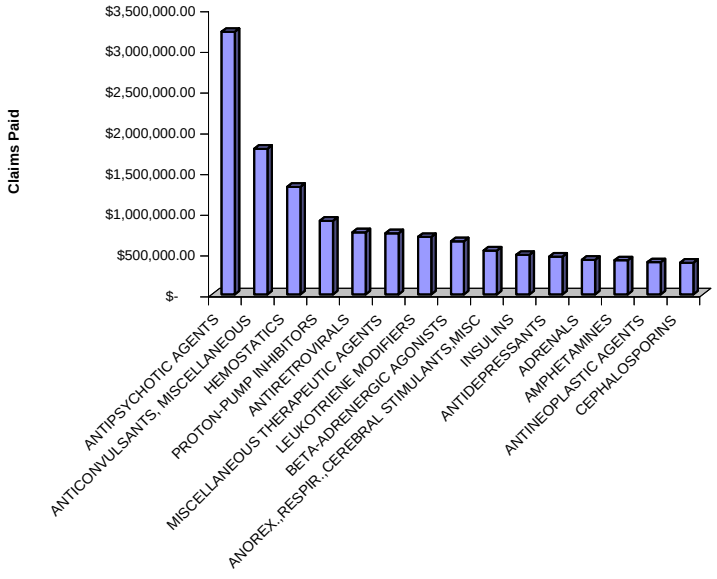
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 06/01/08-06/30/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	9,944	$ 3,224,183.06	$ 324.23	2.99%
ANTICONVULSANTS, MISCELLANEOUS	10,907	$ 1,787,659.44	$ 163.90	3.28%
HEMOSTATICS	41	$ 1,319,217.39	$32,176.03	0.01%
PROTON-PUMP INHIBITORS	5,743	$ 903,578.73	$ 157.34	1.73%
ANTIRETROVIRALS	1,062	$ 762,407.80	$ 717.90	0.32%
MISCELLANEOUS THERAPEUTIC AGENTS	2,355	$ 750,865.26	$ 318.84	0.71%
LEUKOTRIENE MODIFIERS	6,507	$ 705,104.63	$ 108.36	1.96%
BETA-ADRENERGIC AGONISTS	9,356	$ 650,661.75	$ 69.54	2.81%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,320	$ 537,994.61	$ 124.54	1.30%
INSULINS	3,522	$ 485,133.47	$ 137.74	1.06%
ANTIDEPRESSANTS	13,120	$ 463,121.07	$ 35.30	3.94%
ADRENALS	6,872	$ 424,596.19	$ 61.79	2.07%
AMPHETAMINES	3,401	$ 417,740.22	$ 122.83	1.02%
ANTINEOPLASTIC AGENTS	828	$ 394,685.44	$ 476.67	0.25%
CEPHALOSPORINS	8,445	$ 389,185.19	$ 46.08	2.54%
TOTAL TOP 15	86,423	$ 13,216,134.25	$ 152.92	25.98%

Total Rx Claims	332,702
From 06/01/08-06/30/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

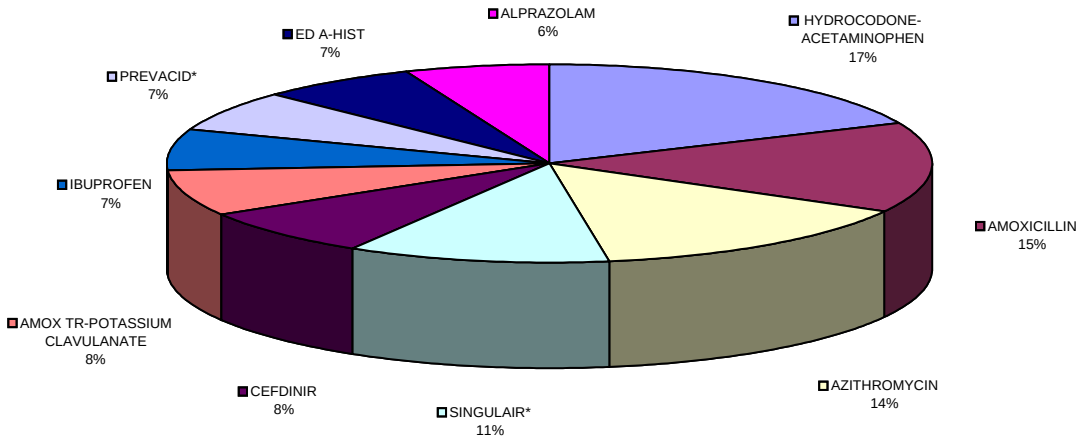
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 03/01/08-03/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	13,838	$ 147,398.60	1
AMOXICILLIN	PENICILLINS	11,144	$ 104,738.04	3
AZITHROMYCIN	MACROLIDES	10,951	$ 391,819.97	6
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,343	$ 902,165.94	2
CEFDINIR	CEPHALOSPORINS	6,028	$ 441,440.56	105
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	5,678	$ 306,366.84	26
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,097	$ 42,415.60	14
PREVACID*	PROTON-PUMP INHIBITORS	5,032	$ 788,704.49	8
ED A-HIST	PROPYLAMINE DERIVATIVES	4,949	$ 43,576.97	~
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,633	$ 38,394.50	9
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,105	$ 48,027.65	62
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	3,804	$ 102,792.48	67
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,502	$ 40,468.75	55
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,453	$ 66,388.34	25
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,303	$ 959,625.95	46
CEPHALEXIN	CEPHALOSPORINS	3,292	$ 51,720.23	18
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,180	$ 25,761.99	41
ADDERALL XR*	AMPHETAMINES	3,046	$ 412,756.57	36
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	2,892	$ 218,789.22	100
FERROUS SULFATE	IRON PREPARATIONS	2,767	$ 9,715.37	113
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,737	$ 73,169.62	23
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,655	$ 83,337.91	47
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,586	$ 66,835.14	27
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,576	$ 341,169.77	44
NYSTATIN	POLYENES	2,485	$ 32,687.90	145
TOTAL TOP 25		122,076	$ 5,740,268.40	

Total Rx Claims From 03/01/08-03/31/08	379,408

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

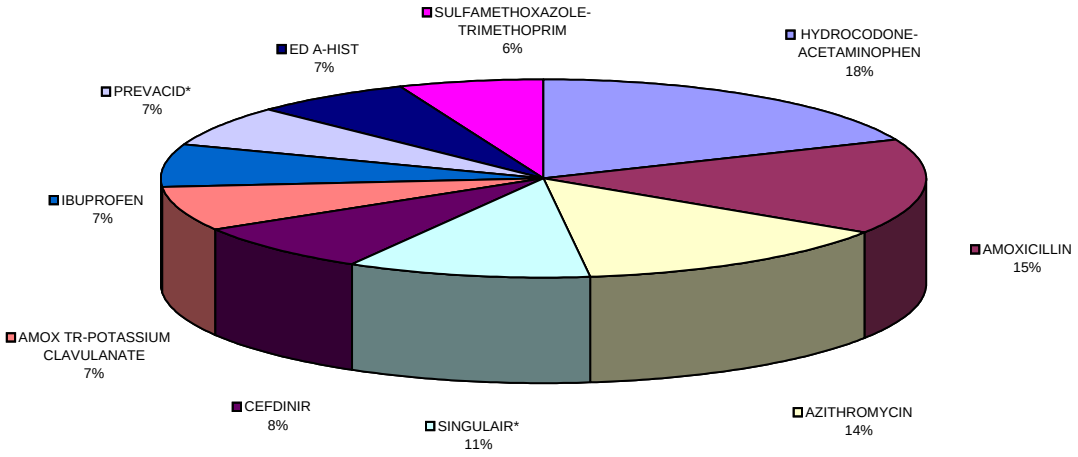
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/08-04/30/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	14,368	$ 152,140.25	1
AMOXICILLIN	PENICILLINS	11,958	$ 113,030.74	3
AZITHROMYCIN	MACROLIDES	10,693	$ 381,333.14	6
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,110	$ 876,935.68	2
CEFDINIR	CEPHALOSPORINS	6,059	$ 444,398.71	105
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	5,574	$ 294,787.88	26
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,362	$ 43,672.22	14
PREVACID*	PROTON-PUMP INHIBITORS	5,329	$ 837,187.14	8
ED A-HIST	PROPYLAMINE DERIVATIVES	5,062	$ 44,687.82	~
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,701	$ 55,866.51	62
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,589	$ 38,000.35	9
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	4,286	$ 310,801.90	100
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	3,844	$ 103,109.57	67
CEPHALEXIN	CEPHALOSPORINS	3,552	$ 56,233.60	18
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,508	$ 66,609.49	25
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,402	$ 962,541.63	46
ADDERALL XR*	AMPHETAMINES	3,318	$ 494,452.91	36
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,286	$ 26,295.08	41
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,153	$ 37,492.46	55
FERROUS SULFATE	IRON PREPARATIONS	2,822	$ 9,914.78	113
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,787	$ 72,398.01	27
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,787	$ 72,971.47	23
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,730	$ 361,375.41	44
NYSTATIN	POLYENES	2,703	$ 36,597.88	145
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,699	$ 84,944.26	47
TOTAL TOP 25		126,682	$ 5,977,778.89	

Total Rx Claims From 04/01/08-04/30/08	389,724

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

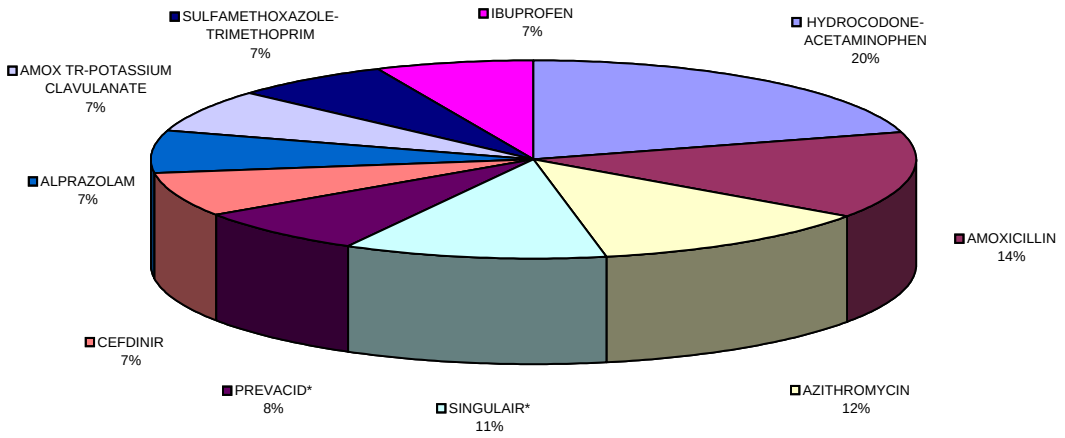
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 05/01/08-05/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	14,060	$ 90,104.28	1
AMOXICILLIN	PENICILLINS	9,573	$ 77,541.21	3
AZITHROMYCIN	MACROLIDES	8,397	$ 238,492.07	6
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,457	$ 805,048.93	2
PREVACID*	PROTON-PUMP INHIBITORS	5,235	$ 827,104.34	8
CEFDINIR	CEPHALOSPORINS	4,959	$ 357,573.83	105
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,723	$ 30,452.05	9
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	4,654	$ 159,556.73	26
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,589	$ 34,385.36	62
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,487	$ 34,436.77	14
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	3,659	$ 269,738.01	100
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,599	$ 21,502.10	25
ED A-HIST	PROPYLAMINE DERIVATIVES	3,521	$ 32,682.93	~
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,407	$ 992,617.05	46
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	3,245	$ 53,444.66	67
CEPHALEXIN	CEPHALOSPORINS	3,152	$ 33,802.51	18
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,022	$ 18,479.94	41
ADDERALL XR*	AMPHETAMINES	2,923	$ 437,612.67	36
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,870	$ 16,503.46	23
FERROUS SULFATE	IRON PREPARATIONS	2,757	$ 9,585.54	113
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,751	$ 29,149.36	55
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,696	$ 48,209.97	108
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,616	$ 75,003.65	47
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,512	$ 66,161.18	27
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,462	$ 12,074.65	2
TOTAL TOP 25		113,326	$ 4,771,263.25	

Total Rx Claims From 05/01/08-05/31/08	363,982

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

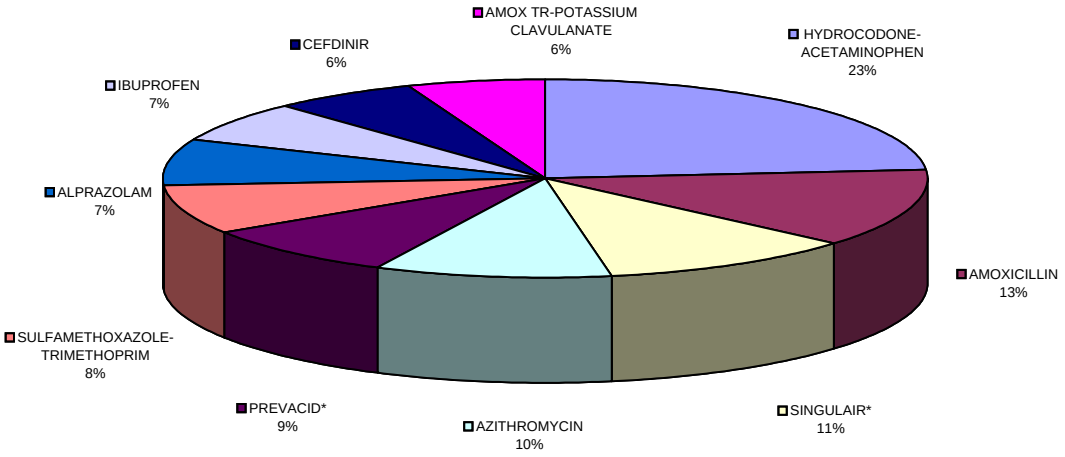
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 06/01/08-06/30/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	13,955	$ 90,292.76	1
AMOXICILLIN	PENICILLINS	7,636	$ 61,462.68	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,503	$ 704,369.95	2
AZITHROMYCIN	MACROLIDES	5,937	$ 167,123.46	6
PREVACID*	PROTON-PUMP INHIBITORS	5,107	$ 806,017.10	8
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,719	$ 35,581.92	62
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,430	$ 28,624.04	9
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	3,959	$ 29,029.83	14
CEFDINIR	CEPHALOSPORINS	3,621	$ 263,173.95	105
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	3,489	$ 119,940.32	26
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,380	$ 20,644.29	25
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,160	$ 914,731.87	46
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	3,080	$ 55,898.41	108
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	2,995	$ 18,475.35	41
CEPHALEXIN	CEPHALOSPORINS	2,965	$ 31,782.79	18
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,778	$ 16,987.76	23
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	2,758	$ 211,739.60	100
FERROUS SULFATE	IRON PREPARATIONS	2,682	$ 9,153.19	113
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,634	$ 46,648.92	67
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,477	$ 68,714.97	47
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,476	$ 26,578.26	55
ADDERALL XR*	AMPHETAMINES	2,392	$ 365,224.87	36
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,341	$ 13,012.12	2
ED A-HIST	PROPYLAMINE DERIVATIVES	2,313	$ 21,241.88	~
AMLODIPINE BESYLATE	DIHYDROPYRIDINES	2,295	$ 13,493.33	15
TOTAL TOP 25		100,082	$ 4,139,943.62	

Total Rx Claims From 06/01/08-06/30/08	332,702

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

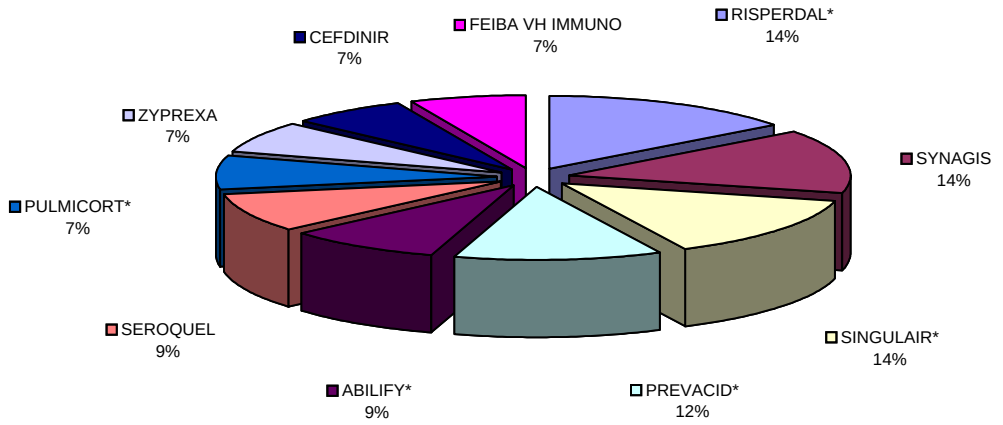
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 03/01/08-03/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,303	$ 959,625.95	14
SYNAGIS	MONOCLONAL ANTIBODIES	667	$ 924,274.69	~
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,343	$ 902,165.94	6
PREVACID*	PROTON-PUMP INHIBITORS	5,032	$ 788,704.49	4
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,215	$ 567,524.50	15
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,628	$ 565,293.93	7
PULMICORT*	ADRENALS	1,836	$ 483,020.57	64
ZYPREXA	ANTIPSYCHOTIC AGENTS	864	$ 458,625.02	18
CEFDINIR	CEPHALOSPORINS	6,028	$ 441,440.56	31
FEIBA VH IMMUNO	HEMOSTATICS	10	$ 428,591.54	~
ADDERALL XR*	AMPHETAMINES	3,046	$ 412,756.57	27
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,271	$ 395,965.86	13
AZITHROMYCIN	MACROLIDES	10,951	$ 391,819.97	2
XOPENEX*	BETA-ADRENERGIC AGONISTS	2,194	$ 391,018.66	104
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,576	$ 341,169.77	34
NOVOSEVEN	HEMOSTATICS	13	$ 313,643.83	~
AMOX TR-POTASSIUM CL	PENICILLINS	5,678	$ 306,366.84	9
ADVATE	HEMOSTATICS	6	$ 298,167.49	~
GEODON*	ANTIPSYCHOTIC AGENTS	832	$ 289,323.82	58
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,557	$ 288,074.70	3
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	852	$ 275,877.76	17
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	854	$ 233,264.41	57
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	2,892	$ 218,789.22	117
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,850	$ 206,201.01	11
EFFEXOR XR*	ANTIDEPRESSANTS	1,212	$ 199,927.61	8
TOTAL TOP 25		64,710	$ 11,081,634.71	

Total Rx Claims From 03/01/08-03/31/08	379,408

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

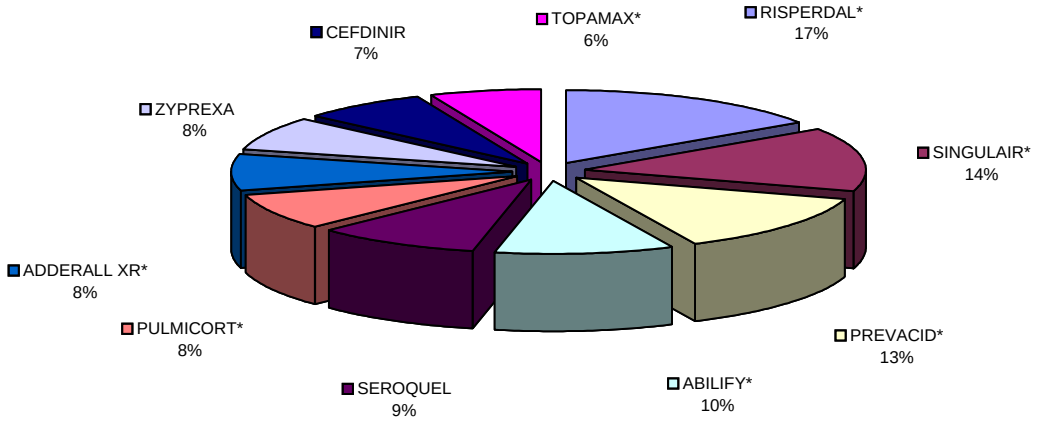
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/08-04/30/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,402	$ 962,541.63	14
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,110	$ 876,935.68	6
PREVACID*	PROTON-PUMP INHIBITORS	5,329	$ 837,187.14	4
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,346	$ 626,304.20	15
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,715	$ 585,770.01	7
PULMICORT*	ADRENALS	1,902	$ 506,306.47	64
ADDERALL XR*	AMPHETAMINES	3,318	$ 494,452.91	27
ZYPREXA	ANTIPSYCHOTIC AGENTS	885	$ 471,443.55	18
CEFDINIR	CEPHALOSPORINS	6,059	$ 444,398.71	31
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,301	$ 401,280.39	13
XOPENEX*	BETA-ADRENERGIC AGONISTS	2,171	$ 386,057.08	104
AZITHROMYCIN	MACROLIDES	10,693	$ 381,333.14	2
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,730	$ 361,375.41	34
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	4,286	$ 310,801.90	117
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,630	$ 303,786.22	3
AMOX TR-POTASSIUM CL	PENICILLINS	5,574	$ 294,787.88	9
GEODON*	ANTIPSYCHOTIC AGENTS	831	$ 291,702.93	58
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	892	$ 284,179.03	17
FEIBA VH IMMUNO	HEMOSTATICS	4	$ 263,462.04	~
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	912	$ 251,976.08	57
ADVATE	HEMOSTATICS	7	$ 247,667.43	~
NASONEX*	CORTICOSTEROIDS (EENT)	2,513	$ 216,901.57	43
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,915	$ 216,252.36	11
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,600	$ 202,825.45	133
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,351	$ 199,948.95	73
TOTAL TOP 25		70,476	$ 10,419,678.16	

Total Rx Claims From 04/01/08-04/30/08	389,724

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

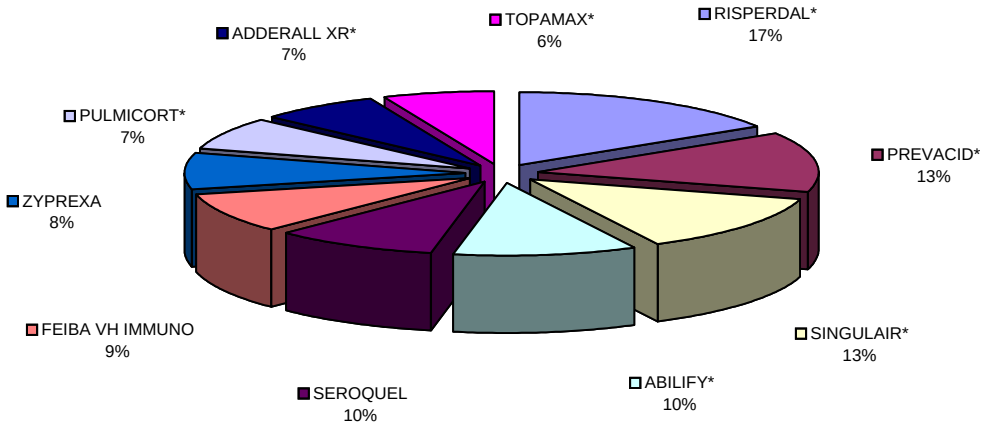
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 05/01/08-05/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,407	$ 992,617.05	14
PREVACID*	PROTON-PUMP INHIBITORS	5,235	$ 827,104.34	4
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,457	$ 805,048.93	6
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,385	$ 646,201.56	15
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,708	$ 589,948.97	7
FEIBA VH IMMUNO	HEMOSTATICS	8	$ 559,992.26	~
ZYPREXA	ANTIPSYCHOTIC AGENTS	924	$ 485,852.17	18
PULMICORT*	ADRENALS	1,655	$ 442,193.51	64
ADDERALL XR*	AMPHETAMINES	2,923	$ 437,612.67	27
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,296	$ 394,378.16	13
CEFDINIR	CEPHALOSPORINS	4,959	$ 357,573.83	31
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,335	$ 310,305.97	34
XOPENEX*	BETA-ADRENERGIC AGONISTS	1,697	$ 301,553.80	104
LAMICTAL	ANTICONVULSANTS, MISCELLANEOUS	893	$ 292,451.96	17
GEODON*	ANTIPSYCHOTIC AGENTS	841	$ 288,963.43	58
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,535	$ 287,164.40	3
ADVATE	HEMOSTATICS	5	$ 275,744.83	~
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	3,659	$ 269,738.01	117
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	965	$ 268,653.53	57
AZITHROMYCIN	MACROLIDES	8,397	$ 238,492.07	2
NOVOSEVEN	HEMOSTATICS	8	$ 222,234.32	~
EFFEXOR XR*	ANTIDEPRESSANTS	1,229	$ 198,533.28	8
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	941	$ 196,028.42	67
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,789	$ 193,802.04	1
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,397	$ 188,793.07	5
TOTAL TOP 25		56,648	$ 10,070,982.58	

Total Rx Claims From 05/01/08-05/31/08	363,982

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

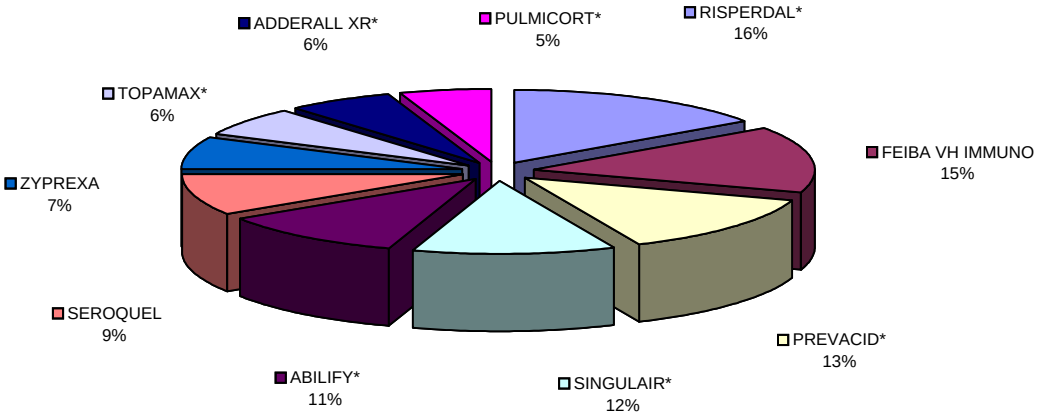
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 06/01/08-06/30/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTIC AGENTS	3,160	$ 914,731.87	14
FEIBA VH IMMUNO	HEMOSTATICS	12	$ 890,549.37	~
PREVACID*	PROTON-PUMP INHIBITORS	5,107	$ 806,017.10	4
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,503	$ 704,369.95	6
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,397	$ 643,332.84	15
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,580	$ 559,553.50	7
ZYPREXA	ANTIPSYCHOTIC AGENTS	815	$ 433,090.86	18
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,249	$ 380,756.43	13
ADDERALL XR*	AMPHETAMINES	2,392	$ 365,224.87	27
PULMICORT*	ADRENALS	1,212	$ 321,477.48	64
GEODON*	ANTIPSYCHOTIC AGENTS	789	$ 277,013.46	58
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,469	$ 274,977.92	3
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	837	$ 267,766.56	17
CEFDINIR	CEPHALOSPORINS	3,621	$ 263,173.95	31
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	925	$ 257,431.96	57
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,930	$ 256,413.36	34
CLARINEX*	SECOND GENERATION ANTIHISTAMINES	2,758	$ 211,739.60	117
EFFEXOR XR*	ANTIDEPRESSANTS	1,192	$ 197,020.78	8
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	925	$ 196,029.47	67
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,382	$ 186,651.86	5
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,649	$ 177,844.04	1
EXJADE	HEAVY METAL ANTAGONISTS	39	$ 169,851.71	~
DEPAKOTE ER*	ANTICONVULSANTS, MISCELLANEOUS	920	$ 167,302.59	66
AZITHROMYCIN	MACROLIDES	5,937	$ 167,123.46	2
RISPERDAL CONSTA	ANTIPSYCHOTIC AGENTS	208	$ 166,328.17	160
TOTAL TOP 25		48,008	$ 9,255,773.16	

Total Rx Claims From 06/01/08-06/30/08	332,702

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



FDA Updates

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

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

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

Vivitrol (naltrexone)

8/12/2008: FDA informed healthcare professionals of the risk of adverse injection site reactions in patients receiving naltrexone. Naltrexone is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment. Naltrexone is administered as an intramuscular gluteal injection and should not be administered intravenously, subcutaneously, or inadvertently into fatty tissue. Physicians should instruct patients to monitor the injection site and contact them if they develop pain, swelling, tenderness, induration, bruising, pruritus, or redness at the injection site that does not improve or worsens within two weeks. Physicians should promptly refer patients with worsening injection site reactions to a surgeon. Read the FDA recommendations for healthcare professionals to consider regarding the use of Naltrexone injection.

Simvastatin Used With Amiodarone

8/08/2008: FDA notified healthcare professionals of the risk of muscle injury, rhabdomyolysis, which can lead to kidney failure or death, when simvastatin is used with amiodarone. This risk is dose-related and increases when a dose of simvastatin greater than 20 mg per day is given with amiodarone. Although a revision of the simvastatin labeling in 2002 described an increased risk of rhabdomyolysis when amiodarone is taken with simvastatin doses greater than 20 mg daily, FDA continues to receive reports of rhabdomyolysis in patients treated concurrently with amiodarone and simvastatin. Prescribers should be aware of the increased risk of rhabdomyolysis when simvastatin is prescribed with amiodarone, and they should avoid doses of simvastatin greater than 20 mg per day in patients taking amiodarone.

Erythropoiesis Stimulating Agents (ESAs) - Epoetin alfa (marketed as Procrit, Epogen), Darbepoetin alfa (marketed as Aranesp)

7/31/2008: FDA informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated. Additional revisions to prescribing information regarding ESAs use in patients receiving myelosuppressive therapy when the expected outcome is cure and when to initiate and discontinue ESA dosing will be forthcoming. FDA continues to encourage healthcare professionals to discuss with their patients before starting or continuing therapy with ESAs, the benefits of treatment with ESAs and the potential and demonstrated risks of ESAs for thrombovascular events, shortened time to tumor progression or recurrence, and shortened survival time.

Mitoxantrone Hydrochloride (marketed as Novantrone and generics)

7/29/2008: FDA reminded health care professionals who treat patients with mitoxantrone about recommendations that left ventricular ejection fraction (LVEF) be evaluated before initiating treatment and prior to administering each dose of mitoxantrone. FDA offered additional recommendations for cardiac monitoring to detect late-occurring cardiac toxicity, and provided information for patients with multiple sclerosis who receive the drug.

These recommendations were established in 2005 in response to post-marketing reports and case reports in the medical literature that described decreases in LVEF or frank congestive heart failure in patients with MS who had received cumulative doses of mitoxantrone that were lower than 100 mg/m^2. Since that time, FDA has received information from a post-marketing safety study that demonstrated there is poor adherence to these recommendations in clinical practice. FDA is working with the manufacturers to educate healthcare providers

to adhere to cardiac monitoring recommendations for patients with MS.

Abacavir (marketed as Ziagen) and Abacavir-containing Medications

7/24/2008] FDA informed healthcare professionals that serious and sometimes fatal hypersensitivity reactions (HSR) caused by abacavir therapy are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*5701. FDA reviewed data from two studies that support a recommendation for pre-therapy screening for the presence of the HLA-B*5701 allele and the selection of alternative therapy in positive subjects. Genetic tests for HLA-B*5701 are available and all patients should be screened for the HLA-B*5701 allele before starting or restarting treatment with abacavir or abacavir-containing medications. Development of clinically suspected abacavir HSR requires immediate and permanent discontinuation of abacavir therapy in all patients, including patients negative for HLA-B*5701.

Sodium Polystyrene Sulfonate Suspension

7/16/2008: Roxane Laboratories, Inc. informed healthcare professionals of the recall of two lots of Sodium Polystyrene Sulfonate Suspension, USP, 15 g/60 mL Unit dose bottles (NDC 0054-0165-51; lot 856396A Exp April 2010, and lot 856693A Exp May 2010), a product used to treat hyperkalemia. A sample of one of the affected lots tested positive for a strain of yeast, which could potentially affect immunocompromised patients. Symptoms of a yeast infection range from thrush, skin rash, and blood infections. If patients develop an infection they should consult their physician. Pharmacists should determine if any of the referenced product has been dispensed and retrieve it. Additionally, pharmacists and wholesalers of the product should discontinue distribution and use of the referenced lots immediately and contact the manufacturer regarding returning the product.

Avastin (bevacizumab)

7/14/2008: Genentech, Inc. informed healthcare professionals of reports of several cases of microangiopathic hemolytic anemia (MAHA) in patients with solid tumors receiving Avastin in combination with sunitinib malate. Avastin is not approved for use in combination with sunitinib malate and this combination is not recommended. Twenty-five patients were enrolled in a Phase I dose-escalation study combining Avastin and sunitinib malate. The study consisted of 3 cohorts using a fixed dose of Avastin at 10mg/kg/IV every 2 weeks and escalating doses of sunitinib that included 25, 37.5, and 50 mg orally daily given in a 4 weeks on/ 2 weeks off schedule. Five of 12 patients at the highest sunitinib dose level exhibited laboratory findings consistent with MAHA. Two of these cases were considered severe with evidence of thrombocytopenia, anemia, reticulocytosis, reductions in serum haptoglobin, schistocytes on peripheral smear, modest increases in serum creatinine levels, and severe hypertension, reversible posterior leukoencephalopathy syndrome, and proteinuria. The findings in these two cases were reversible within three weeks upon discontinuation of both drugs without additional interventions. Healthcare

professionals should report cases of MAHA or any serious adverse events suspected to be associated with the use of Avastin.

Fluoroquinolone Antimicrobial Drugs

7/08/2008: FDA notified healthcare professionals that a BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.

Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in those over age 60, in kidney, heart, and lung transplant recipients, and with use of concomitant steroid therapy. Physicians should advise patients, at the first sign of tendon pain, swelling, or inflammation, to stop taking the fluoroquinolone, to avoid exercise and use of the affected area, and to promptly contact their doctor about changing to a non-fluoroquinolone antimicrobial drug. Selection of a fluoroquinolone for the treatment or prevention of an infection should be limited to those conditions that are proven or strongly suspected to be caused by bacteria.

Antipsychotics, Conventional and Atypical

6/16/2008: FDA notified healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis. In April 2005, FDA notified healthcare professionals that patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death. Since issuing that notification, FDA has reviewed additional information that indicates the risk is also associated with conventional antipsychotics. Antipsychotics are not indicated for the treatment of dementia-related psychosis. The prescribing information for all antipsychotic drugs will now include the same information about this risk in a BOXED WARNING and the WARNINGS section.

Tumor Necrosis Factor (TNF) Blockers (marketed as Remicade, Enbrel, Humira, and Cimzia)

6/03/2008: FDA issued an Early Communication About an Ongoing Safety Review to inform healthcare professionals that the Agency is investigating a possible association between the use of Tumor Necrosis Factor (TNF) blockers and the development of lymphoma and other cancers in children and young adults. FDA is investigating approximately 30 reports of cancer in children and young adults. These reports were submitted to FDA's Adverse Event Reporting System over a ten-year interval, beginning in 1998 through April 29, 2008. These reports describe cancer occurring in children and young adults who began taking TNF blockers (along with other immuno-suppressive medicines such as methotrexate, azathioprine or 6-mercaptopurine), when they were ages 18 or less, to treat juvenile idiopathic arthritis, Crohn's disease or other diseases. Approximately half of the cancers were lymphomas, including both Hodgkin's and non-Hodgkin's lymphoma. Long-term studies are necessary to provide

definitive answers about whether TNF blockers increase the occurrence of cancers in children because cancers may take a long time to develop and may not be detected in short-term studies. Until the evaluation is completed, healthcare providers, parents, and caregivers should be aware of the possible risk of lymphoma and other cancers in children and young adults when deciding how to best treat these patients.

Mycophenolate Mofetil [MMF] (marketed as CellCept)
Mycophenolic Acid [MPA] (marketed as Myfortic)
Inosine Monophosphate Dehydrogenase Inhibitors (IMPDH) Immunosuppressants

5/16/2008: FDA is aware of reports of infants born with serious congenital anomalies, including microtia and cleft lip and palate, following exposure to mycophenolate mofetil (MMF) during pregnancy. MMF, the active drug substance in CellCept, is an ester of the active metabolite mycophenolic acid (MPA), the active drug substance in Myfortic. In most cases, the mothers were taking MMF following an organ transplant to prevent organ rejection. However, some mothers taking MMF were being treated for immune-mediated conditions such as systemic lupus erythematosus (SLE) and erythema multiforme. Treatment began before their pregnancies and continued into the first trimester or until the pregnancy was detected. MMF and MPA increase the risk of spontaneous abortion in the first trimester and can cause congenital malformations in the offspring of women who are treated during pregnancy.

FDA is continuing to work with the manufacturers of these drug products to develop and implement means to mitigate the risks of fetal exposure. See the FDA Healthcare Professional Information Sheet containing considerations and recommendations for clinicians prior to prescribing MMF or MPA to women of childbearing potential.

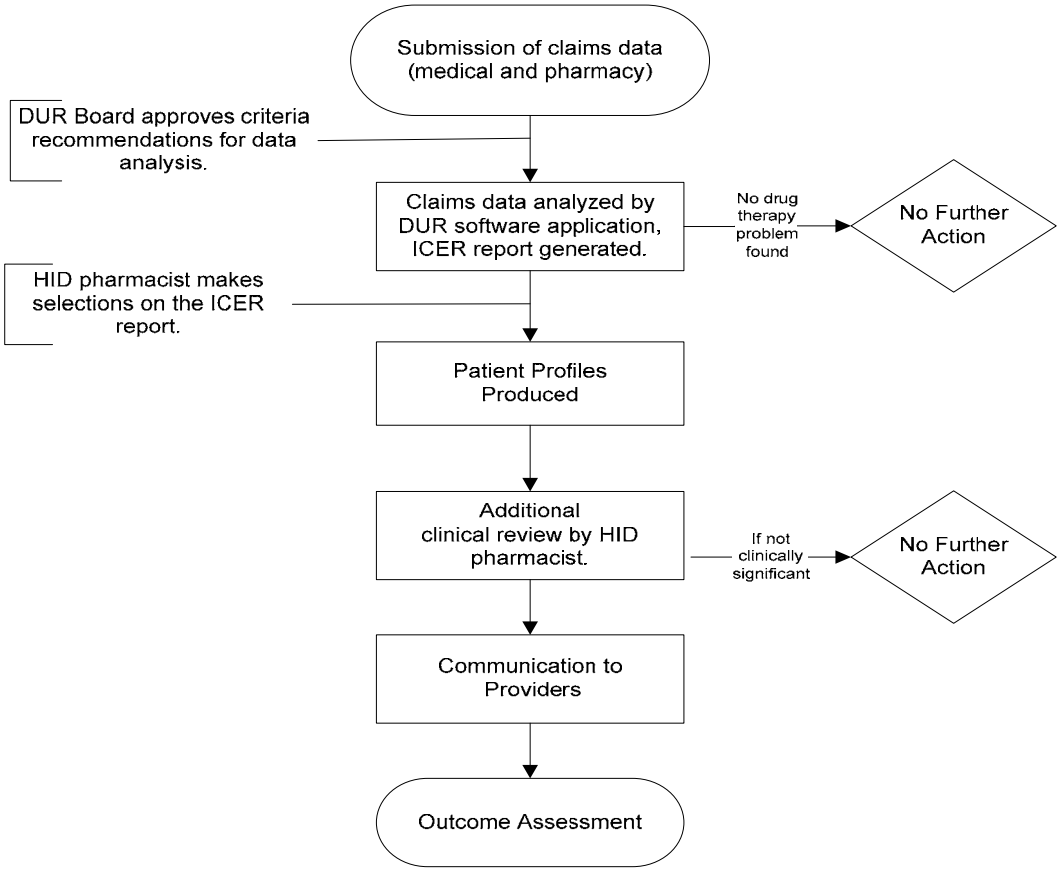
Enbrel (etanercept)

5/01/2008: Amgen and Wyeth Pharmaceuticals informed healthcare professionals of revisions to prescribing information for Enbrel. The revisions include a BOXED WARNING about infections, including serious infections leading to hospitalization or death that have been observed in patients treated with Enbrel. Infections have included bacterial sepsis and tuberculosis. The ADVERSE REACTIONS section of the label was updated to include information regarding global clinical studies and the rate of occurrence of tuberculosis in patients treated with Enbrel. Healthcare professionals should screen patients for latent tuberculosis infection before beginning Enbrel. Patients should be educated about the symptoms of infection and closely monitored for signs and symptoms of infection during and after treatment with the drug. Patients who develop an infection should be evaluated for appropriate antimicrobial treatment and, in patients who develop a serious infection, Enbrel should be discontinued.

Regranex (becaplermin) Gel

6/06/2008: FDA informed healthcare professionals that a Boxed Warning was added to prescribing information for Regranex that describes an increased risk of death from cancer in patients treated with three or more tubes of Regranex compared with those patients who did not use the product. FDA recommends that Regranex be used only when the benefits can be expected to outweigh the risks.

Overview of Retrospective Drug Utilization Review (RDUR) Intervention Process



Steps

- Paid Medicaid claims are submitted to HID by DOM's claims administrator.
- The therapeutic RDUR criteria, which are reviewed and approved by the DUR Board, are applied to each recipient record.
- An Initial Criteria Exception Report (ICER) is generated to aid in the selection of high risk profiles. An HID clinical pharmacist selects profiles for review.
- Selected patient profiles are generated.
- Each patient profile is reviewed by a clinical pharmacist to verify clinical significance. Profiles are coded for either action or no action.
- Each coded profile is again reviewed by a different pharmacist for quality control.
- Intervention letters and profiles are sent to appropriate providers. Providers are asked to provide feedback as to the action resulting from the letter.
- Activity and response are reported to DOM monthly and quarterly.

Off-label Use of Atypical Antipsychotics in Children for ADHD and ODD

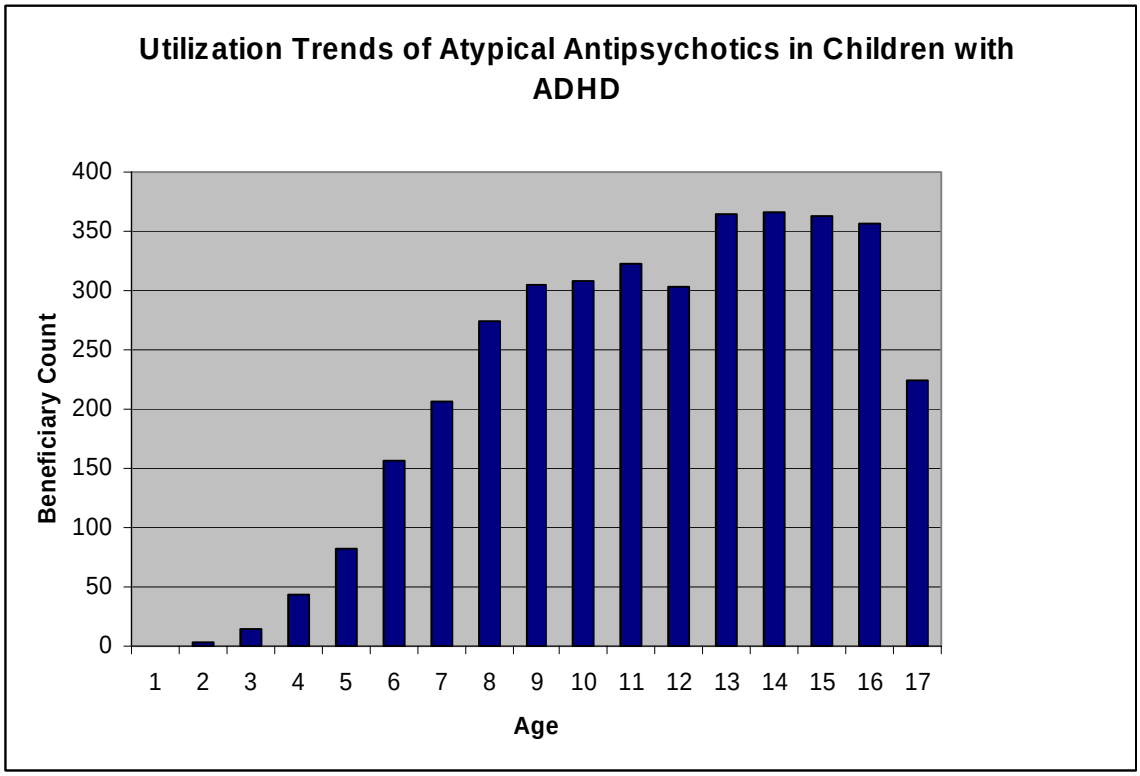
HID receives prior authorization requests every day for atypical antipsychotics for pediatric patients with the only diagnoses provided being ADHD (attention deficit hyperactivity disorder) or ODD (oppositional defiant disorder), neither of which are FDA-approved indications for medications in this class. The youngest age that any of the atypical antipsychotics is approved for is 5 years old, which is Risperdal® for use in children with irritability associated with autistic disorder. Abilify® is approved for adolescents from 13 years of age for schizophrenia. All of the other atypical antipsychotics (Geodon®, Invega®, Zyprexa®, and Seroquel®) are not approved for use in children or adolescents under the age of 18. This information, coupled with the large number of prior authorization requests seen for these medications in the pediatric population, raised concerns about the off-label use of atypical antipsychotics in children with ADHD and/or ODD.

In addition, utilization of atypical antipsychotics in the Mississippi Medicaid population continues to be one of the largest sources of drug expenditures for the program. For the month of February, five of the six atypical antipsychotics were in the Top 25 Drugs Based on Total Claims Cost report included in this packet, representing roughly $2.8 million in drug expenditures for the month.

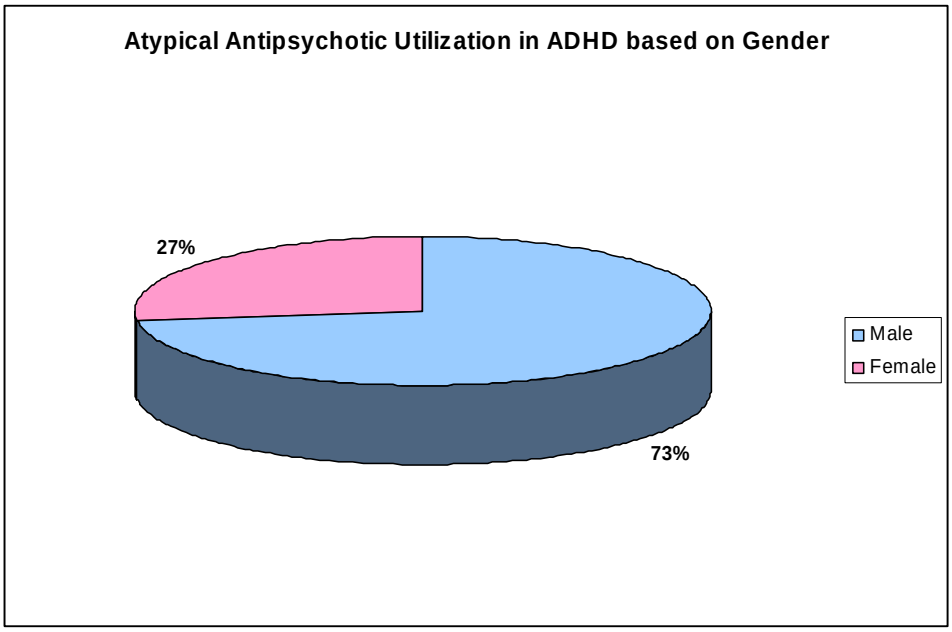
Method

Considering the high costs and potential off-label use of these products, HID conducted an analysis of claims for the entire therapeutic class in children under the age of 18 from 2/23/07 to 2/22/08. In order to be included in the analysis, the beneficiary must have had a diagnosis of ADHD and/or ODD. In addition, those patients with a diagnosis of schizophrenia, bipolar disorder or autism were excluded. Therefore, the data collected represents those patients under the age of 18 with one or more claims for an atypical antipsychotic, presumably for the treatment of ADHD or ODD.

Results



As the age increases, the number of pediatric beneficiaries receiving atypical antipsychotics for ADHD and/or ODD increases, with the largest number of beneficiaries being between 13 and 16 years old. However, there is substantial use of atypical antipsychotics in children as young as six with ADHD and/or ODD.



The majority of beneficiaries found in this analysis were male, approximately 73%. This is not startling, bearing in mind that ADHD and ODD are more common in male children and adolescents.

Summary

As seen above, it appears that atypical antipsychotics are possibly being used off-label for children with ADHD and/or ODD, with the largest group being male adolescents ages 13 to 16.

Recommendation

In an effort to discourage the off-label use of these powerful medications in a young population, a retrospective DUR criterion is recommended to identify those pediatric patients with ADHD and/or ODD who have received one or more atypical antipsychotics and do not have an FDA-approved diagnosis for these medications.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Accepted*	*Rejected*

1. Atypical Antipsychotics / Therapeutic Appropriateness _____ _____

Alert Message: The patient is under the age of 18 with a diagnosis of ADHD and/or ODD and is receiving an atypical antipsychotic with no evidence, in their diagnostic history, of a FDA approved indication for use. Atypicals antipsychotics have not been shown to be safe and effective for the treatment of ADHD or ODD. These agents have significant adverse effects which can be more prevalent and severe in pediatric patients.
Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases:

Util A	Util B	Util C(Negating)
Clozapine	ADHD	Schizophrenia
Risperidone	ODD	Autism
Quetiapine		Bipolar
Olanzapine		Major Depressive Disorder
Ziprasidone		
Aripiprazole		
Paliperidone		

Age Range: < 18 years of age
References:
Facts & Comparisons, 2008 Updates.
Olfson M, Blanco C, Liu L, Moreno C, Laje G: National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. Arch Gen Psychiatry 2006; 63:679–685.
Patel NC, Crismon ML, Hoagwood K, Johnsrud MT, Rascati KL, Wilson JP, Jensen PS: Trends in the use of typical and atypical antipsychotics in children and adolescents. J Am Acad Child Adolesc Psychiatry 2005; 44:548–556.
Correll CU, Carlson HE, Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents, J Am Acad Child Adolesc Psychiatry (2006)45:771-791.

Generalized Anxiety Disorder (GAD)

Introduction

Generalized anxiety disorder (GAD) is an anxiety disorder that is characterized by excessive, uncontrollable and often irrational worry about everyday events or issues that is disproportionate to the actual source of worry. These patients continually anticipate disaster and are overly concerned about health issues, money, family problems, or work difficulties. Patients with GAD cannot seem to get rid of their concerns, even though they usually realize that their anxiety is more intense than the situation warrants. They may also have trouble falling asleep or staying asleep. Physical symptoms that often accompany the anxiety include fatigue, headaches, muscle tension, muscle aches, difficulty swallowing, trembling, twitching, irritability, sweating, nausea, lightheadedness, having to go to the bathroom frequently, feeling out of breath, and hot flashes.

GAD affects about 6.8 million adult Americans and about twice as many women as men. This disorder comes on gradually and can begin across the life cycle, though the risk is highest between childhood and middle age. It is diagnosed when someone spends at least 6 months worrying excessively about a number of everyday problems.

Pharmacologic Management of GAD

Antidepressants are the preferred class for the treatment of GAD, with the selective serotonin reuptake inhibitors (SSRIs) being the first-line agents. Lexapro® and paroxetine immediate-release are the only SSRIs with specific indications for generalized anxiety disorder, although most treatment guidelines recommend treatment with any of the SSRIs. Once treatment at optimal dosing with one or more SSRIs has been tried and failed, second-line treatment should be considered with Effexor XR or Cymbalta, both of which are serotonin and norepinephrine reuptake inhibitors (SNRIs). Benzodiazepines do have a place in the treatment of GAD. However, treatment guidelines recommend that their use be short-term, not to exceed 2-4 weeks.

Recommendations

In recent DUR Board meetings, there has been extensive discussion about the improper use of benzodiazepines. In the February meeting, data was presented that showed only 14-25% of patients with an anxiety-related diagnosis who received one or more prescriptions for a benzodiazepine also received one or more prescriptions for maintenance therapy for anxiety, such as an SSRI or Effexor XR. As a result, a Medicaid Prescribing Update, or “one-pager”, has been created for GAD that provides a description of this disorder, and, more importantly, proper treatment recommendations for GAD based on treatment guidelines. 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.

Prescribing Information Update

Generalized Anxiety Disorder (GAD)

Mississippi Division of Medicaid

- *GAD is characterized by excessive anxiety or worry that has persisted for at least 6 months.*
- *GAD is a chronic illness that often requires prolonged treatment.*
- *The first-line pharmacological treatment option for GAD is a selective serotonin reuptake inhibitor (SSRI).*
- *Benzodiazepine therapy has a small role in the treatment of GAD and should not persist beyond 2-4 weeks.*

Generalized anxiety disorder (GAD) is one of several anxiety disorders classified by the DSM-IV. The characteristic feature associated with GAD is unrealistic or excessive anxiety and worry about a number of events or activities that has persisted for at least 6 months. Other diagnostic criteria include:

- Worry that is difficult to control
- Restlessness
- Easily fatigued
- Difficulty concentrating
- Irritability
- Muscle tension
- Sleep disturbances

Onset of GAD is usually in the early 20s, but it may be precipitated in later life by stressful life events. This illness is chronic in nature with multiple spontaneous exacerbations and remissions.

Pharmacologic Management of GAD

Antidepressants are the preferred class for the treatment of GAD, with the selective serotonin reuptake inhibitors (SSRIs) being the first-line agents. Lexapro® and paroxetine immediate-release are the only SSRIs with specific indications for generalized anxiety disorder, although most treatment guidelines recommend treatment with any of the SSRIs. Once treatment at optimal dosing with one or more SSRIs has been tried and failed, second-line treatment should be considered with Effexor XR or Cymbalta, both of which are serotonin and norepinephrine reuptake inhibitors (SNRIs). Benzodiazepines do have a place in the treatment of GAD. However, treatment guidelines recommend that their use be short-term, not to exceed 2-4 weeks.

Preferred Drug List Status for GAD Medications

Preferred	Non-preferred
Paroxetine	Lexapro®
Citalopram	Cymbalta®
Sertraline	
Fluoxetine	
Effexor XR®	

References:

- Drug Facts and Comparisons 4.0. Copyright 2008 Wolters Kluwer Health, Inc.
- Management of Anxiety (Panic Disorder, with or without Agoraphobia, and Generalized Anxiety Disorder) in Adults in Primary, Secondary, and Community Care. NICE Clinical Guideline 22 (amended). UK, April 2007.
- Clinical Practice Guidelines: Management of Generalized Anxiety Disorder. Canadian Journal of Psychiatry, Vol 51, Suppl 2, July 2006.

Carisoprodol Utilization Update

Based on directives from the DUR Board and P & T Committee, the Division of Medicaid began requiring prior authorization for carisoprodol-containing products on July 1, 2008. Carisoprodol is a centrally-acting skeletal muscle relaxant that is indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults. It should only be used for short periods (up to 2 or 3 weeks) because adequate evidence of effectiveness for more prolonged use has not been established and because acute, painful musculoskeletal conditions are generally of short duration. Although carisoprodol is not a controlled substance, abuse associated with this drug is well-documented. Carisoprodol is used frequently by poly-drug abusers, especially those dependent on opioids. This troubling trend, coupled with the FDA-approved labeling for these products, generated the need for the prior authorization of these agents. The purpose of this report is to analyze the effectiveness of the prior authorization process concerning carisoprodol products.

Utilization

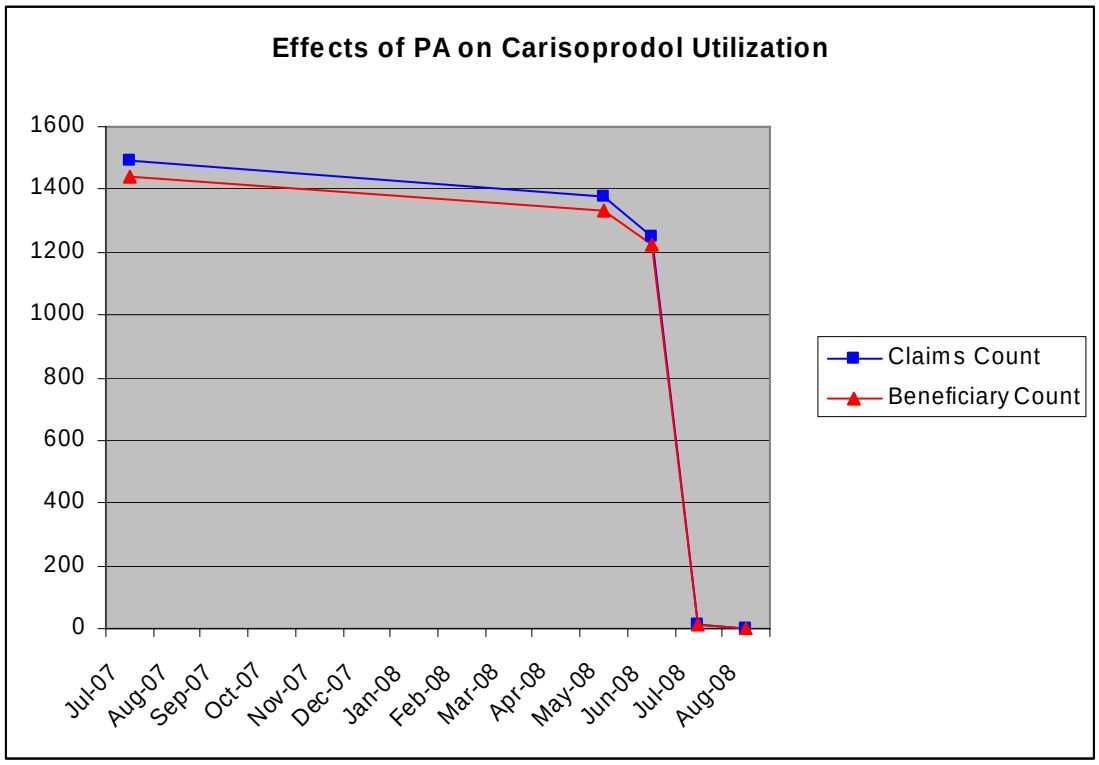
The table below illustrates the utilization of carisoprodol-containing products for certain time periods leading up to and following the implementation of the PA for such products.

Month/year	Claims Count	Beneficiary Count	Beneficiaries Receiving ≥ 2 RXs	Total DOM Cost
July 2007	1494	1443	51	$28,958.53
May 2008	1379	1335	44	$7,962.67
June 2008	1247	1223	24	$7,113.83
July 2008	14	14	0	$92.78
August 2008	3	3	0	$25.95

Based on the information above, the prior authorization process was a success in reducing overall utilization of carisoprodol as well as the number of beneficiaries receiving multiple prescriptions for carisoprodol products, which is outside their FDA-approved labeling. From April through June as academic detailers from HID began targeting providers who were high-prescribers of carisoprodol products, the number of beneficiaries receiving 2 or more prescriptions of carisoprodol products decreased steadily until the implementation of the PA. In addition, the total cost to the Division of Medicaid was significantly reduced. Compared to the months leading up to the PA implementation, the cost to DOM for carisoprodol-containing products decreased by nearly 98% in July 2008.

Dates of service	Total DOM Cost
7/1/07 – 6/30/08	$305,096.81
7/1/07 – 8/23/07	$53,821.74
7/1/08 – 8/23/08	$118.73

Based on the information presented in the table above, the Division is well on its way to reducing the total amount of dollars spent on carisoprodol utilization. From 7/1/08 – 8/23/08 (the most recent date that claims data was available), the amount of dollars spent on carisoprodol products decreased by ~99% from the same time period one year previous.



RDUR

As the carisoprodol issue became a heavily discussed topic among the DUR Board members, HID began targeting the issue through its RDUR program. The table below shows the results of this effort.

Month	Criteria Exceptions	Actions
Oct-07	317	Began reviewing carisoprodol medium- and high-alert profiles
Nov-07	350	
Dec-07	339	
Jan-08	354	Began reviewing all carisoprodol profiles
Feb-08	231	DUR Board recommended carisoprodol PA
Mar-08	130	
Apr-08	112	P&T Committee approved carisoprodol PA; Academic Detailers began seeing high prescribers of carisoprodol
May-08	116	May Provider Bulletin Article printed and distributed
Jun-08	76	June Provider Bulleting Article printed and distributed
Jul-08	113	Carisoprodol PA implemented
Aug-08	9	
Sep-08	0	

Once the criteria related to overutilization of carisoprodol-containing products were targeted for review, the positive effect in educating providers about the proper use of these products is clear. Beginning in January 2008, the number of exceptions generated for this criteria consistently declines until July 2008. It is speculated that, based on news of the impending PA of these products, many beneficiaries returned to their provider and/or pharmacy for carisoprodol products while they were still unrestricted. After this point in time, the number of exceptions generated was drastically reduced until reaching zero in September.

Conclusions

Clearly, the prior authorization of carisoprodol-containing products has been a success in limiting their use to what is outlined in the FDA-approved labeling. The number of beneficiaries receiving numerous prescriptions on a monthly basis was reduced to zero, as well as profiles being sent to providers regarding overutilization of these products. It is evident that the Division of Medicaid took the proper steps in reigning in potential misuse of carisoprodol products at the expense of the State.

Important Issues Surrounding Suboxone®/Subutex® Use

Suboxone® and Subutex® are pharmacological agents designed to aid in the treatment of opioid dependence in both the inpatient and outpatient setting. Buprenorphine is the primary active ingredient in Suboxone®, and it is a partial opioid agonist. It has a high affinity for the mu opioid receptor and a lower intrinsic activity than full opioid agonists. Suboxone® also contains naloxone to discourage diversion and abuse. When taken orally, naloxone has no clinically significant effect. However, when Suboxone® is crushed and injected, the naloxone component attenuates the effects of buprenorphine and precipitates withdrawal symptoms in an opioid-dependent person. Subutex® contains only the buprenorphine; as a result, it should only be administered in a residential setting or physician's office under direct supervision. Subutex® should only be administered outside of these settings if the patient is pregnant, as it is the preferred medication for treatment of opioid dependence in pregnant women.

Appropriate Dosing

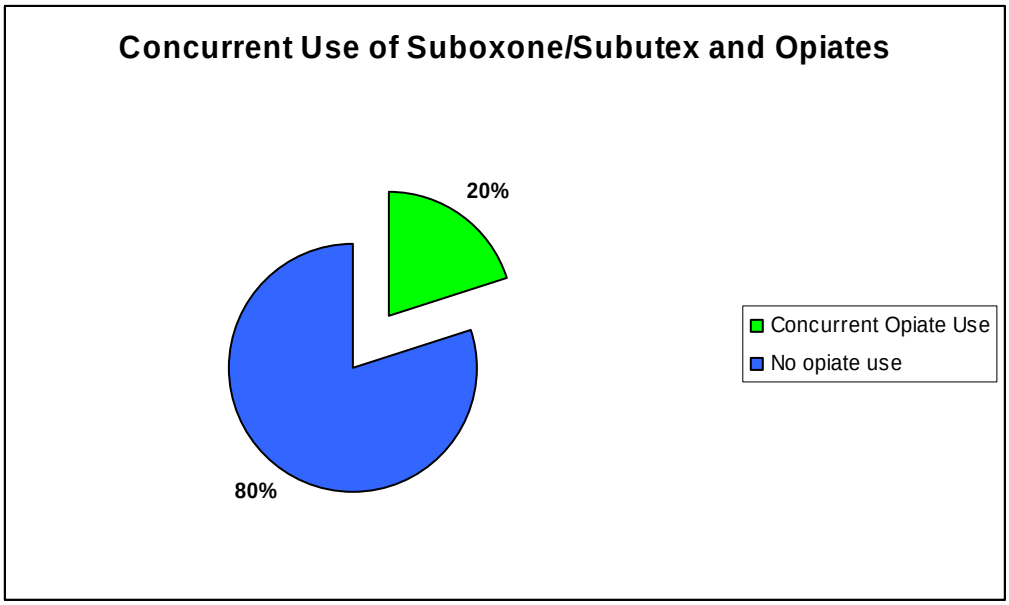
Suboxone®/Subutex® are non-preferred agents and are subject to the prior authorization process. Concern has been provoked among the HID Clinical Staff members based on prior authorization requests received for Suboxone®/Subutex®. Many times these requests are for doses outside the recommended ranges set forth by the manufacturer, especially for first-time users of these agents. The chart below illustrates the maximum recommended daily doses for these agents, based on buprenorphine strength, as recommended by the manufacturer.

Maximum Recommended Daily Dose		
Day	*Short-acting opioid*	*Long acting opioid*
1	8	8
2	12	10
3	16	16
Maintenance	32*	32*

**Clinical evidence suggests optimal doses will be between 12 and 16mg for most patients on maintenance therapy. Higher doses have been utilized as needed, but doses greater than 32mg are not generally needed.*

Concurrent Opioid Use

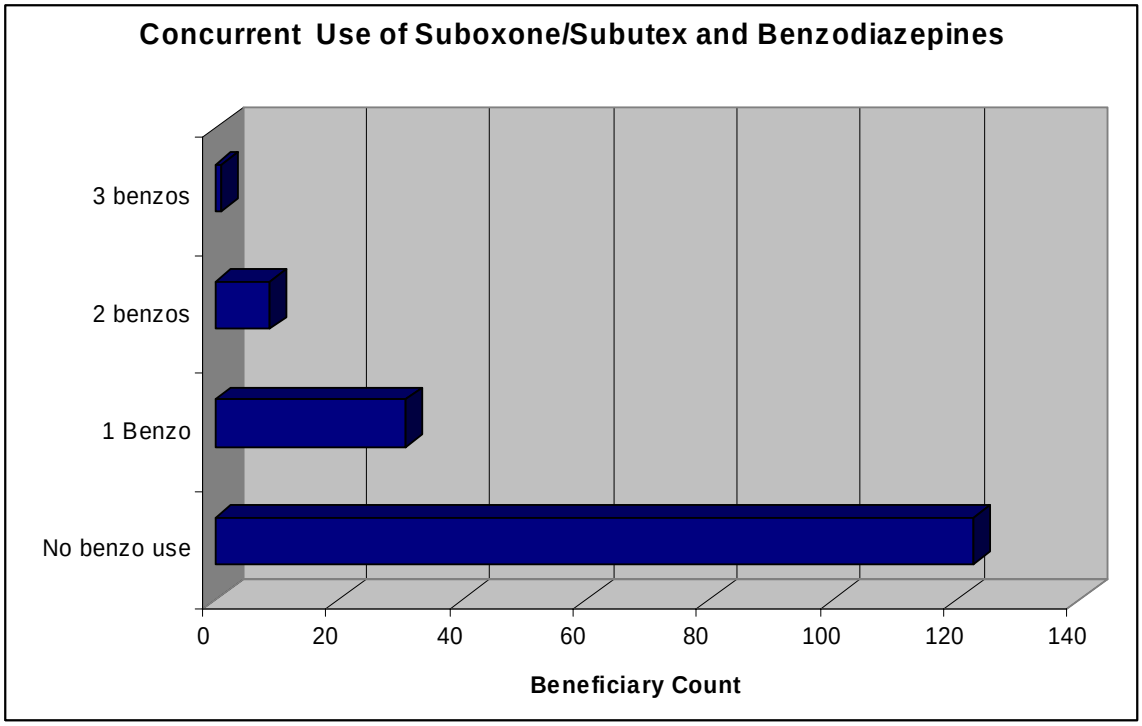
Considering that Suboxone®/Subutex® are used for the treatment of opioid dependence, concurrent use with opioid analgesics is a troubling issue. In April 2008, 164 Mississippi Medicaid beneficiaries received a prescription for Suboxone® or Subutex®. Of these beneficiaries, 33 also received at least one prescription for an opiate after receiving their Suboxone®/Subutex® prescription. The Division of Medicaid spent roughly $13,000 in April 2008 on Suboxone® or Subutex® therapy that was not utilized in the appropriate manner by these beneficiaries.



Concurrent Benzodiazepine Use

According to the prescribing information, patients taking Suboxone® or Subutex® should be warned about the dangers of misusing benzodiazepines when taking these products. Overdose deaths due to respiratory depression have occurred when buprenorphine products and benzodiazepines were concomitantly abused via the parenteral route. Also, on at least one occasion, a buprenorphine overdose has been associated with oral benzodiazepine ingestion.

Of the 164 Mississippi Medicaid beneficiaries who received a prescription for Suboxone® or Subutex® in April 2008, 41 of these beneficiaries also received at least one prescription for a benzodiazepine. 10 of these same beneficiaries received 2 or more prescriptions for a benzodiazepine concurrently with Suboxone® or Subutex®.



While this concurrent use only constitutes 25% of the Suboxone®/Subutex® users, it still represents a potentially fatal threat to these patients.

Opioid Quantity Limits

The Division of Medicaid has placed quantity limits on opioid products of 62 tablets per every 31 rolling days. Currently, these quantity limits are *not* cumulative across all preparations of opioids. For example, a patient could receive 62 tablets of hydrocodone/acetaminophen 7.5mg/650mg on August 1, and then return to the pharmacy and receive another 62 tablets of hydrocodone/acetaminophen 5mg/500mg on August 10. While this policy is not consistent with the initial intent of placing quantity limits on these products, the Division of Medicaid will need a directive from the DUR Board in order to place cumulative limits of 62 tablets per every 31 days on these products.

Conclusion

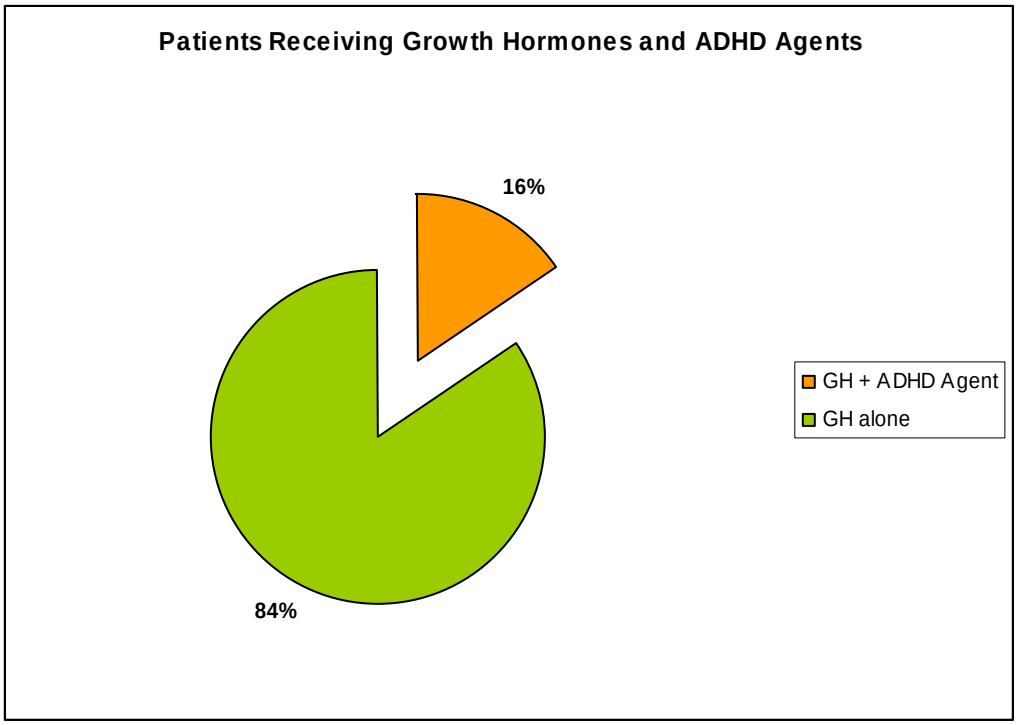
The introduction of Suboxone®/Subutex® to the market has provided physicians and other health care professionals another tool to help provide treatment to patients who are addicted to opiates. These agents allow for office-based treatment of drug addiction, thereby increasing treatment retention rates and patient freedom to continue the normal activities of daily living. However, as seen in the data provided above, there is potential for misuse of Suboxone®/Subutex®, especially in the unsupervised residential setting. These issues should be considered when treating patients with Suboxone®/Subutex®.

Growth Suppression and ADHD Treatments

Synthetic growth hormones are utilized for a variety of conditions that are characterized by a deficiency of endogenous growth hormone (GH). These conditions include, but are not limited to, Prader-Willi Syndrome, intrauterine growth retardation, Turner Syndrome, and SHOX deficiency. The various products in this class are differentiated primarily in terms of approved indications, dosing frequency, and delivery mechanisms. However, one common characteristic that all of these products share is cost. This therapeutic class is an expensive one. From 6/29/07 to 6/28/08, the average cost per claim for this class was approximately $2800.

A recent observation was made in the HID Call Center concerning some patients receiving growth hormones. It was noted that several children requiring prior authorizations for growth hormone were also receiving one of the ADHD agents as well. The question was raised whether the medications used to treat ADHD were the cause of growth suppression in these patients, who were now requiring treatment with synthetic growth hormones. According to the fourth edition of *Pharmacotherapy: A Pathophysiologic Approach*, growth delay is possible with stimulant use. The proposed mechanisms behind this delay include alterations in growth hormone secretion and suppression of appetite leading to reduced caloric intake. Studies in children have indicated that this growth delay may be temporary, with normalization of height and weight occurring in midadolescence. Additional evidence exists to suggest that these growth delays are a result of ADHD itself and not the treatment agents for the condition. However, there are other studies that directly correlate the use of stimulants for ADHD with growth suppression seen in these children.

As a result, HID gathered utilization data for both therapeutic classes (Growth Hormones and ADHD Agents) for one year, from 6/29/07 to 6/28/08. These searches were then intersected to identify those patients receiving both treatment modalities. The results are shown below.



Of the 122 patients found during the mentioned time frame who received growth hormone, 19 also received one of the agents used to treat ADHD. These patients ranged in age from 7 to 19 years old. The cost of growth hormone treatment for these 19 patients was $272,274.48. This represents a cost of roughly $14,000.00 per patient, and ~15% of the cost of growth hormone treatment for all patients during this time period. None of the 19 patients found were receiving both therapies from the same physician, which may indicate that the individual providers are unaware of what the other is prescribing for a given patient. However, only 7 of the 19 patients found in the intersection were on the highest dose of the growth hormone product they were using, which doesn't suggest a trend that those patients on ADHD medications require higher doses of growth hormones.

While the number of patients identified that are receiving both treatments is not overwhelming, the cost associated with the treatment for growth suppression for these patients is. ***If*** these patients experienced growth delay as a result of treatment with an ADHD medication, interventions to educate providers about this potential phenomenon in hopes of preventing significant growth delay in these patients could result in potentially significant cost-savings for Mississippi Medicaid. A retrospective DUR criterion is recommended to identify those patients receiving treatment with an ADHD agent in an effort to educate providers about the potential risk of growth suppression associated with their use.

Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma

In September 2007 a panel commissioned by the National Asthma Education and Prevention Program and coordinated by the National Heart, Lung and Blood Institute of the National Institutes of Health released the *Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma.* These guidelines were framed by the 1997 EPR2 Guidelines and the 2002 update, with revised recommendations made based on literature reviews.

One of the key differences from previous versions of these guidelines is the separation of recommendations based on age. The 2007 report includes recommendations for the management of children 0-4 and 5-11 years of age separately from the recommendations for managing asthma in youth ≥12 years of age and adults. Also, the stepwise approach to managing asthma has been expanded to include six steps of care in order to simplify the actions within each step. For example, previous reports had several progressive actions within a single step, while the current guidelines separate the actions into different steps for more clarity and ease of use.

Based on a directive from DOM, HID developed the following Medicaid Prescribing Update to highlight the updated treatment recommendations found within the new EPR3 Guidelines. Coordinated with the implementation of a new Preferred Drug List that included changes to the respiratory agents, HID began distribution of this document to prescribers by the Academic Detailing staff in July 2008. This Medicaid Prescribing Update, along with others on additional topics, is also available by a link from the Division of Medicaid website.

Prescribing Information Update

Asthma

Mississippi Division of Medicaid

An updated version of the NIH Asthma Guidelines was released in September 2007. One of the main differences from the 1997 report is that recommendations for the management of children ages 0-4 and 5-11 are presented separately from those patients ages 12 and above. In addition, the stepwise approach has been expanded to include more steps of care in order to simplify the actions within each step. The chart below summarizes the recommendations in the 2007 report.

Step	Age 0-4	Age 5-11	Age ≥ 12
1	***Preferred*** – SABA prn	***Preferred*** – SABA prn	***Preferred*** – SABA prn
2	***Preferred*** – Low-dose ICS ***Alternative*** – Cromolyn or montelukast	***Preferred*** – Low-dose ICS ***Alternative*** – Cromolyn, LTRA, nedocromil, or theophylline	***Preferred*** – Low-dose ICS ***Alternative*** – Cromolyn, LTRA, nedocromil, or theophylline
3	***Preferred*** – Medium- dose ICS	***Preferred*** – EITHER Low-dose ICS + either LABA, LTRA or theophylline OR Medium dose ICS	***Preferred*** – Low-dose ICS + LABA OR Medium-dose ICS ***Alternative*** – Low-dose ICS + either LTRA, theophylline or zileuton
4	***Preferred*** - Medium-dose ICS + either LABA or montelukast	***Preferred*** – Medium-dose ICS + LABA ***Alternative*** – Medium-dose ICS + either LTRA or theophylline	***Preferred*** – Medium-dose ICS + LABA ***Alternative*** – Medium-dose ICS + either LTRA, theophylline, or zileuton
5	***Preferred*** – High-dose ICS + either LABA or montelukast	***Preferred*** – High-dose ICS + LABA ***Alternative*** – High-dose ICS + either LTRA or theophylline	***Preferred*** – High-dose ICS + LABA AND Consider omalizumab for patients who have allergies
6	***Preferred*** – High-dose ICS + either LABA or montelukast Oral systemic corticosteroids	***Preferred*** – High-dose ICS + LABA + oral systemic corticosteroid ***Alternative*** – High-dose ICS + either LTRA or theophylline + oral systemic corticosteroid	***Preferred*** – High-dose ICS + LABA + oral corticosteroid AND Consider omalizumab for patients who have allergies

- SABA as needed for symptoms; frequency depends on severity of symptoms
- With viral URI, SABA every 4 to 6 hours up to 24 hours; short course of oral corticosteroids may be warranted depending on severity of episode.
- Frequent use of SABA may indicate the need to step up treatment. See full 2007 report for further recommendations
- By 12/31/2008, production of CFC inhalers should be phased out and replaced by HFA inhalers, per the Montreal Protocol. Proper education of patients regarding the differences between these devices is important. More information can be found on the American Lung Association website at www.lungusa.org/cfcfree.

SABA—Short acting beta agonist; ICS—inhaled corticosteroids; LABA—long-acting beta agonist; LTRA—leukotriene receptor antagonist

References:

Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007, National Heart, Lung and Blood Institute. http://www.nhlbi.nih.gov/guidelines/asthma/index.htm.

MISSISSIPPI DIVISION OF MEDICAID
PREFERRED DRUG LIST - PULMONOLOGY

Effective July 1, 2008
(Changes to previous PDL highlighted)

THERAPEUTIC DRUG CLASS	PREFERRED AGENTS	NON-PREFERRED AGENTS (Require PA unless otherwise indicated)
BRONCHODILATORS, ANTICHOLINERGIC	**ANTICHOLINERGICS**	
	ATROVENT HFA (ipratropium) ipratropium SPIRIVA (tiotropium)	
	ANTICHOLINERGIC-BETA AGONIST COMBINATIONS	
	albuterol/ipratropium COMBIVENT (albuterol/ipratropium)	
BRONCHODILATORS, BETA AGONIST	**INHALERS, SHORT-ACTING**	
	albuterol MAXAIR (pirbuterol) PROAIR HFA (albuterol) PROVENTIL HFA (albuterol) VENTOLIN HFA (albuterol)	ALUPENT (metaproterenol) XOPENEX HFA (levalbuterol)
	INHALERS, LONG-ACTING	
		FORADIL (formoterol) SEREVENT (salmeterol)
	INHALATION SOLUTION	
	albuterol metaproterenol	ACCUNEB (albuterol) BROVANA (arformoterol) XOPENEX (levalbuterol)
	ORAL	
	albuterol metaproterenol terbutaline	
GLUCOCORTICOIDS, INHALED	**GLUCOCORTICOIDS**	
	AEROBID (flunisolide) AEROBID-M (flunisolide) ASMANEX (mometasone) AZMACORT (triamcinolone) FLOVENT DISKUS (fluticasone) FLOVENT HFA (fluticasone) PULMICORT (budesonide) Respules QVAR (beclomethasone)	PULMICORT (budesonide) Flexhaler
	GLUCOCORTICOID/BRONCHODILATOR COMBINATIONS	
	ADVAIR (fluticasone/salmeterol) SYMBICORT (budesonide/formoterol)	
LEUKOTRIENE MODIFIERS	ACCOLATE (zafirlukast) SINGULAIR (montelukast)	ZYFLO CR (zafirlukast)
XANTHINE DERIVATIVES	aminophylline dyphylline oxtriphylline theophylline	

Unless otherwise specified, the listing of a particular brand or generic name includes all dosage forms of that drug.
In some cases, Medicaid may opt to prefer a brand name drug over its generic equivalent. This occurs when the net price of the brand product is lower than the generic equivalent.

Synagis®: Updates for 2008-2009 Season

Per Mississippi Division of Medicaid (DOM) policy, Synagis® (palvizumab) coverage requires prior authorization for all beneficiaries. The approval criteria are based on manufacturer labeling and closely parallel the American Academy of Pediatrics recommendations. All requests for prior authorization of Synagis® are reviewed by the clinical staff of Health Information Designs (HID).

Although the criteria and prior authorization forms for the upcoming season are very similar to those from the previous season, there are some important changes that have been made to further ensure that the beneficiaries who would benefit the most from this medication receive proper treatment and that this delivery is carried out in the most cost-effective manner possible.

Criteria Updates

- Second season requests for those beneficiaries in Category 3 will require documentation of ***continued*** medical therapy for either severe chronic lung disease (CLD) or hemodynamically significant congenital heart disease (HSCHD) on the prior authorization request and in the patient record. In addition, evidence of such therapy must be present in paid pharmacy claims.
- Risk factors that have been removed for consideration of approval include: HIV/AIDS, multiple births, and congenital airway abnormalities.

Prior Authorization Form Updates

- Space provided to indicate current weight and date of provided weight, to ensure that the proper dose is administered to the patient
- Space provided for additional information to consider for second season requests
- A statement to make providers aware that it is their responsibility to ensure that: 1) each vial of Synagis® provided to their clinic will be administered to the patient it was assigned, or 2) clinic staff will notify the dispensing pharmacy immediately when the medication provided to their clinic cannot be administered to the intended patient. The statement reads:

  Mississippi Medicaid is a federally-subsidized health care program funded with public dollars. As such, I confirm that this medication will be administered to the patient for whom it is dispensed. If I or my staff are unable to administer this medication to the designated patient, I acknowledge that I am responsible for notifying the dispensing pharmacy immediately.

SYNAGIS (PALVIZUMAB)

MS Medicaid will approve the administration of Synagis® for children meeting the American Academy of Pediatrics (AAP) Redbook recommendations for RSV immunoprophylaxis. The criteria detailed below are based on the AAP recommendations.

Beneficiaries must meet criteria in one of four categories:

Category 1 Prematurity of ≤ 28 weeks gestation Age: ≤ 1 year	Category 2 Prematurity of 29-32 weeks gestation Age: ≤ 6 months at the start of Respiratory Syncytial Virus season.
Category 3 Prematurity of ≤ 35 weeks gestation Age: 0 – 24 months old Risk factor(s) as noted below are present, documented and indicated on PA form.	Category 4 33 - 35 weeks gestation Age: 0-6 months old during RSV season Risk factor(s) as noted below are present, documented an indicated on PA form. No diagnosis of CLD is required.

Coverage limitations:

- Authorization will end at age 24 months (last day of child's birthday month). Extension beyond age 24 months will be considered on an individual basis when supported by clinical documentation of extreme necessity.
- Authorization will be granted for administration between October 27 and March 31.
- Second season authorizations will be limited to severe CLD and HSCHD who continue to require medical therapy.
- Coverage will be limited to five doses. Doses administered during hospitalization will be included as part of these five covered doses.

RSV Risk Factors
For categories 3 and 4 (First season requests only):
One of the following are considered sufficient:

- Chronic lung disease requiring medical treatment within the past six months (e.g. diuretics, systemic steroids, oxygen on a continuous basis, bronchodilators or ventilation-dependent; or
- Hemodynamically significant Congenital Heart Disease [simple, small Atrial Septal Defects (ASD), Ventricular Septal Defects (VSD), and Patent Ductus Arteriosus (PDA) are not eligible]

OR

For category 3 (Second season requests only):
One of the following must be present (with documentation of continued medical therapy):

- Severe chronic lung disease (CLD); or
- Hemodynamically significant congenital heart disease (HSCHD)

OR

For category 4 (First season requests only):
Two of the following are considered sufficient:

- Exposure to tobacco smoke in the home; and/or
- School age Siblings; and/or
- Day Care; and/or
- Severe neuromuscular disease

FAX TO: 1-800-459-2135

HEALTH INFORMATION DESIGNS, INC.
P.O. BOX 320506
Flowood, MS 39232
Phone: (800) 355-0486

2008-2009 SYNAGIS

PRIOR AUTHORIZATION REQUEST FORM
October 27 - March 31 for a total of 5 injections

BENEFICIARY INFORMATION

Beneficiary's Name: _____ Beneficiary's Medicaid #: _____

DOB:_____ City: _____
Month Day 4 Digit Year

PRESCRIBER INFORMATION

NPI #: _____

Prescribing Physician: _____

Medicaid ID #: _____

Phone #:_____

City: _____ State:_____

Fax #:_____

Mississippi Medicaid is a federally-subsidized health care program funded with public dollars. As such, I confirm that this medication will be administered to the patient for whom it is dispensed. If I or my staff are unable to administer this medication to the designated patient, I acknowledge that I am responsible for notifying the dispensing pharmacy immediately.

I hereby certify that I am the ordering physician/nurse practitioner/physician assistant identified in this form and I deem the prescribed medication to be necessary for the patient listed. I understand that any falsification, omission or concealment of material fact may subject me to civil penalties, fines or criminal prosecution.

_____
Physician's Signature and date

PHARMACY INFORMATION

Provider ID#_____

Dispensing Pharmacy:_____

Phone #:_____

City: _____ State:_____

Fax #:_____

DRUG/CLINICAL INFORMATION

NDC#:_____ Gestational Age:____wks Birth Weight: _____lbs ____oz

Current Weight: _____lbs ____oz Date last weighed: _____

First Season Requests:

Did the patient receive Synagis in the hospital? Yes___ No___ If Yes, list date(s) of administration:_____

Risk Factors: Check all that apply to *first season* requests only.

___ Chronic Lung Disease requiring medical treatment within the past six months (e.g. diuretics, systemic steroids, oxygen on continuous basis, bronchodilators or ventilator-dependent).
___ Hemodynamically Significant Congenital Heart Disease
___ Exposure to tobacco smoke in the home
___ School Age Siblings living in the home
___ Day Care
___ Severe neuromuscular disease

Second Season Requests:

Risk Factors: Check all that apply to *second season* requests only.

___ Severe CLD requiring continued medical therapy
___ HSCHD (hemodynamically significant congenital heart disease)

Additional Rationale for Second Season: _____

_____

_____

***Supporting documentation must be available in the patient record.

RSV prophylaxis approval will terminate at the end of RSV season. Authorization will end at age two (2) on the last day of the child's birthday month.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2008

Recommendations	*Approved*	*Rejected*

1. Fluoroquinolones / Black Box Warning _____ _____

Alert Message: Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in those over 60, in kidney, heart, and lung transplant recipients, and with use of concomitant steroid therapy. Patients should be advised to stop the fluoroquinolone at the first sign of tendon pain, swelling, or inflammation, to avoid exercise and use of the affected area, and to promptly contact the prescriber about changing to a non-fluoroquinolone antimicrobial drug.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

Util A	Util B	Util C
Ciprofloxacin		
Gemifloxacin		
Levofloxacin		
Moxifloxacin		
Norfloxacin		
Ofloxacin		

References:
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

2. Conventional Antipsychotics / Black Box Warning _____ _____

Alert Message: Conventional antipsychotics are not approved for the treatment of dementia-related psychosis. The FDA has determined through epidemiological studies that elderly patients with dementia-related psychosis treated with conventional antipsychotics are at an increased risk of death compared to placebo.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

Util A	Util B	Util C (Negating)
Prochlorperazine		Schizophrenia
Haloperidol		Bipolar Disorder
Loxapine		
Thioridazine		
Molindone		
Thiothixene		
Pimozide		
Fluphenazine		
Trifluoperazine		
Chlorpromazine		
Perphenazine		

Age Range: 65 year of age or older
References:
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

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

3. Erythropoiesis Stimulating Agents / Black Box Warning _____ _____

Alert Message: Erythropoieses stimulating agents (ESAs) are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure. ESAs have been shown to shorten the overall survival and/or time to tumor progression in patients with breast, non-small cell lung, head and neck, lymphoid and cervical cancers. To minimize this risk, use ESAs only for the treatment of anemia due to concomitant myelosuppressive chemotherapy, use the lowest dose needed to avoid red blood cell transfusions, and discontinue use after completion of the chemo course.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Diseases:

Util A	Util B	Util C
Aranesp	Breast Cancer	
Epogen/Procrit	Non-small Cell Lung Cancer	
	Head and Neck Cancer	
	Lymphoid Cancers	
	Cervical Cancer	

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Procrit Prescribing Information, August 2008. Ortho Biotech Products, L.P.
Epogen Prescribing Information, August 2008, Amgen.
Aranesp Prescribing Information, August 2008, Amgen.