**Mississippi Division of Medicaid**
**Drug Utilization Review (DUR) Board**
**Minutes of the September 25, 2008 Meeting**

**Members Attending:** Laura Gray, M.D.; LeeVoulters, M.D.; Edgar Donahoe, M.D.; Mark Reed, M.D.; Lee Merritt, R.Ph.; Vickie Veazey, R.Ph.; Jason Strong, Pharm D.;
**Members Absent:** Roy Arnold, R.Ph.; William Bastian, M.D.; Alvin Dixon, R.Ph.; Frank Wade, 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
**HID Staff:** Ashleigh Holeman, Pharm.D., Project Manager; Kathleen Burns, R.N. Call Center Manager

**Call to Order:**
Laura Gray, Chairperson of the Board, called the meeting to order at 2:05 p.m.

Dr. Gray asked that the Board introduce themselves explaining that the Board was by majority new appointees by the Governor.

Judith Clark continued with an overview of the Board's objectives and appreciation from The Division of Medicaid for the Board's acceptance to serve the State in this capacity.

**Old Business:**
The Board was asked prior to the meeting to familiarize themselves with the sets of minutes and criteria in the packet, as they had previously been reviewed clinically by the Board at prior meetings but were not approved due to the lack of a quorum. It was noted that the Board would be asked to accept all previously reviewed minutes and criteria in one vote rather than reading through all the items individually. At this point, Dr. Gray asked for a motion to accept all prior minutes and criteria as directed earlier. Motion by Dr. Voulters; seconded by Dr. Reed. All voted in favor of the motion.

**Cost Management Analysis:**
Dr. Holeman began by presenting reports reflecting several months of data. Antipsychotic agents continued to lead the top 15 therapeutic classes by the total cost of claims for March 2008 through June 2008. The top drugs based on number of claims were led by hydrocodone-acetaminophen and followed by Amoxicillin. Dr. Clayton pointed out the far right column as the National rank and how these drugs in our state compare to the top 200 rank. Dr. Holeman continued with the top 25 drugs based on total claims cost by pointing to the leader, Risperdal®, followed by Synagis®, Singulair®, Prevacid® and lastly Feiba VH®.

**Pharmacy Program Update:**
Dr. Clayton presented an overview of the Annual DUR Report to CMS. She continued with clarification of HID as the Retrospective DUR Vendor and ACS as the ProDUR Vendor. The ProDUR report reflects the number of claims and the cost savings, which indicated several million dollars of cost savings. The Retrospective DUR report did not allow as much cost savings but still indicated around $600,000. Dr. Clayton offered a copy of this report to the Board as a mail-out and presented a copy for onsite viewing. Ms. Clark then presented a report on how claims from pharmacists interacted with the Medicaid system, and she noted that the promptness of the transaction is less than 0.4 seconds. She continued with education about the electronic PA offered between ACS and HID systems, which allows for a relief of paper work for the physician and his/her staff. Ms. Clark noted that Medicaid population changes have moved the pharmacy to interact with children more than adults, with the majority of the Mississippi Medicaid population being children.

**FDA UPDATES:**

**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 immunosuppressive 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.

**DUR OVERVIEW:**

Dr. Holeman discussed the overview of the DUR intervention process with the Board members to enlighten the new members and as a review for the other members.

**OFF-LABEL USE OF ATYPICAL ANTIPSYCHOTICS FOR CHILDREN WITH ADHD AND/OR ODD:**

Dr. Holeman presented a report resulting from the increased PA requests HID receives daily for atypical antipsychotics being used in pediatric patients with the only diagnoses provided being ADHD or ODD,

neither of which are FDA-approved indications for medications in this class. This has raised concerns about the increased use of atypical antipsychotics in children and the future medical conditions that might arise from this off-label use. HID conducted an analysis of claims for children under 18 with medical claims indicating the diagnoses of ADHD and ODD only. It was found that the largest number of beneficiaries receiving atypical antipsychotics were between 13 and 16 years of age. There was also a substantial use of atypical antipsychotics in children as young as six with these diagnoses.
**Recommendation:** HID recommends a retrospective DUR criterion to identify these pediatric patients with ADHD and/or ODD who have received one or more atypical antipsychotics and do not have an FDA-approved diagnosis. Motion: Dr. Gray Seconded: Dr. Voulters; All voted in favor of motion.

**GENERALIZED ANXIETY DISORDER (GAD):**
Antidepressants are the preferred class for the treatment of GAD, with the selective SSRIs being the first-line agents. Lexapro® and paroxetine immediate-release are the only SSRIs with specific indications for GAD, although most treatment guidelines recommend treatment with any of the SSRIs. Benzodiazepines do have a role in the treatment of GAD, but treatment guidelines recommend that their use be short-term, not to exceed 2-4 weeks.
**Recommendations:** HID recommends distribution of a Medicaid Prescribing Update or "one-pager" that provides a description of this disorder and, more importantly, proper treatment recommendations for GAD based on treatment guidelines. This would be distributed by the Academic Detailers to the prescribers and as well as available by a link from the Division of Medicaid website. Motion: Dr. Reed; Seconded: Dr Voulters; all voted in favor of motion.

**CARISOPRODOL UTILIZATION UPDATE:**
Based on directives from the DUR Board and the P & T Committee, the Division of Medicaid began requiring prior authorization on carisoprodol-containing products beginning on July 1, 2008. HID generated a report illustrating the periods leading up to and following the implementation of the PA for these products.
Based on the information submitted to the Board, the prior authorization process was a success in reducing overall utilization of carisoprodol as well as the number of beneficiaries receiving multiple prescriptions for these products. 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. 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®:**
Dr. Holeman presented an extensive report on Suboxone® and Subutex®, beginning by explaining that these are pharmacological agents designed to aid in the treatment of opioid dependence. Concern has been provoked among the HID Clinical Staff members based on prior authorization requests received for these two products. Many times these requests are for doses outside the recommended ranges set forth by the manufacturer, especially for first-time users of these agents. Considering that Suboxone® and Subutex® are used for the treatment of opioid dependence, concurrent use with opioid analgesics is a troubling issue. The Division of Medicaid spent roughly $13,000 in April 2008 alone on Suboxone® or Subutex® therapy that was not utilized in the appropriate manner by these beneficiaries. Of the 164 Mississippi Medicaid beneficiaries who received these medications 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 along with these products. It was noted that 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, data provided has proven, especially in the unsupervised residential setting, that there is potential for misuse of these products. The Division of Medicaid has placed quantity limits on opioid products of 62 tablets per every rolling 31 days. Currently, these quantity limits are not cumulative across all preparations of opioids. HID and The Division of Medicaid asked for a directive from the DUR Board in order to place cumulative limits of 62 tablets per every 31 days. Dr. Donahoe suggested that there be an exception made with this limit for the treatment of cancer and severe arthritis patients. It was noted that a physician may submit a Maximum Unit Override PA form to obtain additional medications for this critical group of patients. Motion: Dr. Gray; Seconded: Dr. Donahoe; All voted in favor of this motion.

**GROWTH SUPPRESSION AND ADHD TREATMENTS:**
A recent observation was made in the HID Call Center concerning some patients receiving growth hormones. It was noted that several children requiring prior authorization for growth hormones were also receiving ADHD agents as well. The question was raised whether the medications used to treat ADHD were the cause of the growth suppression in these patients, who were now requiring treatment with synthetic growth hormones. A Clinical study was done by the HID staff to determine if this might be a possibility. As a result, HID gathered utilization data for both therapeutic classes which indicated that the number of patients identified receiving both treatments was not overwhelming. Dr. Voulters provided information that many studies have been done and much data reviewed revealing that there is no correlation between ADHD medications and the growth suppression of patients requiring treatments with synthetic growth hormones. Therefore no criteria were recommended to further the study of this issue.

**ASTHMA:**
Based on a directive from DOM, HID developed a Medicaid Prescribing Update to highlight the updated treatment recommendations found within the new EPR3 Guidelines. This Update coordinated with the implementation of a new preferred drug lists that included changes to the respiratory agents beginning July 1, 2008. HID began the distribution of this document to prescribers by the Academic Detailing staff and made it available by a link from the Division of Medicaid website. Dr. Donahoe stated that by the end of 2008, generic albuterol inhalers will be obsolete and this will put a hardship on patients when considering the brand medication limits for adult Medicaid beneficiaries. He requested that DOM might make a carve-out for these medications as this was critical to the care of his severe asthma patients in the Delta. Ms. Clark was requested to take this to a higher authority for guidance on this sensitive issue. She agreed to do this immediately and would report back at possibly the next DUR Board meeting with the outcome of this request.

**SYNAGIS®:**
Dr. Holeman reviewed the implementation of the new 2008-2009 criteria and PA process for Synagis®. She noted a new statement added to the prior authorization form that the physician must sign stating that he acknowledges that he is responsible for the medication being given to the patient it is designated for and should that not be possible, then he would notify the specialty pharmacy immediately. The Division of Medicaid loses many thousands of dollars every year by medications being allowed to remain in the physician's refrigerators without Medicaid being credited back for this spent money. It is the intention of Medicaid to trim this waste in the upcoming season by asking the physicians to be responsible for the tracking of the spent dollars and reimbursement of dollars for unused Synagis®. It is also the intent that every beneficiary who qualifies for treatment with this medication will receive it without any delays. It is also encouraged that if Medicaid pays for a medication that it is given to the child it was intended for.

**OTHER CRITERIA RECOMMENDATIONS:**
Dr. Holeman reviewed the remaining 3 criteria that were left for approving. Motion: Dr. Voulters; Seconded: Ms Veazey; all voted in favor of the recommendations.

Dr. Gray reminded the Board of the next meeting on November 20, 2008 and asked for a motion that the meeting would be adjourned at 3:15 p.m. Motion: Dr. Voulters; Seconded: Dr. Reed

Respectfully Submitted:
Health Information Designs, Inc.