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:
Board Chairman Frank Marascalco 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, noting that the same classes generally continue to lead the report of the top15 therapeutic classes by total cost of claims from month to month. Dr. Brown noted that antibiotics continue to remain as one of the top classes and the Board still questions whether this reflects over-utilization of antibiotics for unnecessary indications. Ms. Clark suggested that HID run reports of beneficiaries from birth 12 years to determine misuse. She continued by recommending a study of the six month period starting in October 2007 to identify individuals receiving more than one antibiotic with multiple prescribers. Dr. Montgomery suggested the possibility that the recommendations against the use of cold and cough preparations in young children may be driving an increase in the 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. Suggestions were made that DOM consider using HID's Newsletter to encourage prescribers to avoid antibiotic overuse and that DOM post educational information aimed at parents in regional Medicaid offices.

Pharmacy Program Update:
Ms. Clark reminded the Board that the tamper-resistant prescription requirements will go into effect on April 1, 2008. DOM will communicate with providers prior to this implementation date by blast faxes and other appropriate notices. She stated that the March provider bulletin will also include articles addressing this implementation.

Dr. Clayton introduced Eric Cornell, a pharmacy student serving a rotation in the DOM Pharmacy Bureau. Eric was asked to present information regarding new abuse trends of promethazine with codeine syrup. He informed the Board that illicit use of this preparation probably began in Houston, Texas under many street names. A small quantity, approximately one ounce, of the product is combined with Sprite and a piece of hard candy. He noted that one ounce is approximately a full daily adult dose of codeine. The Bureau of Narcotics confirmed that abuse and diversion of this preparation is a growing concern in metropolitan Jackson. DOM elected to remove promethazine with codeine syrup from coverage effective November 1, 2007.

Mr. Smith continued by presenting an updated report from the CDC on the prevalence of RSV in Mississippi. This graphic report indicated consistent downward trends in both the number of tests for RSV and the percentage of positive test results within Mississippi. These finding were consistent with national RSV trends. The Synagis® Season for MS Medicaid patients will end on March 31st, 2008.

New Business:

Overview of RDur Process:

This overview 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 this group of drugs with abuse potential. These medications have continued to concern the Board, perpetually remaining on reports of top 25 drugs by number of 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 dually-eligible beneficiaries. Regarding Ambien® (zolpidem) overuse, Dr. Montgomery suggested contacting prescribers through an education letter in an effort to alter prescribing habits. Dr. Brown suggested that HID try to identify prescribers with a pattern of prescribing all three of these medications per patient. Dr. Montgomery suggested that HID run these numbers on a per capita basis by age to control for other factors. A lengthy discussion was held about how to further curtail the over-utilization of carisoprodol. The board recommended that the P&T Committee consider prior authorization of carisoprodol. HID will assist DOM in preparing this recommendation.

Labeling Update for Desmopressin Acetate Nasal Spray

Dr. Holeman reported on labeling updates for 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. These criteria will be presented to the board for approval during the next meeting.

Pharmacy Coverage of Tobacco Cessation Products
Dr. Holeman presented a review of the use of smoking cessation products, in light of the recent addition of Chantix® as a MS Medicaid covered product. This product has had utilization of approximately five times that of the covered nicotine-replacement products. Mississippi Medicaid has made a 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 briefly reviewed several new recommendations with the Board, but no vote was taken due to a lack of a quorum.

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