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

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

Members Absent: Harold Blakely, R.Ph.; Troy Griffin; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., Director of the Medicaid Pharmacy Bureau; Terri Kirby, R.Ph.; Paige Clayton, Pharm.D.; Phyllis Williams, Interim Deputy Administrator of Health Services

HID Staff: Dennis Smith, R.Ph.; Samuel Warman, R.Ph.; Kathleen Burns, R.N.

Call to Order
Randy Calvert, R.Ph., acting chair, called the meeting to order at 2:07 p.m.

Ms. Clark introduced several new DUR Board members. New members include Roy Arnold, R.Ph.; Laura Gray, M.D.; Lee Voulters, M.D.; and John Wallace, M.D. Ms. Clark also introduced the new Interim Deputy Administrator of Health Services, Phyllis Williams.

Approval of Minutes
Dr. Montgomery made a motion to accept the minutes for the May 16, 2006 and November 16, 2006 meetings as submitted. Dr. Voulters seconded the motion. All voted in favor of approval.

Election of Officers
Ms. Clark asked the Board to nominate new officers before continuing the meeting. Mr. Strickland nominated Mr. Marascalco as Chair and Dr. Gray as Co-Chair. This was seconded by Dr. Montgomery. All voted in favor of this motion.

Updates
Cost Management Analysis
Mr. Smith presented a report on point of sale pharmacy costs for the months of October 2006 and December 2006. He began the report with an analysis of the top 15 therapeutic classes by total cost of claims. The top therapeutic class was antipsychotic agents, followed by anticonvulsants. Next, the top 25 drugs based on total number of claims were presented. Leading the list was azithromycin. Mr. Smith continued with the top 25 drugs based on total claims cost. The top drug in this analysis was Synagis.

DUR Activity Report
Mr. Smith explained to the new members the focus of retrospective DUR activities and defined the terminology used to describe these activities. This explanation summarized the process by

which pharmacy claims are filtered through the various DUR criteria to obtain the needed data and the role of the DUR Board in setting the criteria.

Pharmacy Program Update

Ms. Clark began her update with the statement that approximately 600,000 beneficiaries rely on pharmacy benefits thru Medicaid. The average cost per claim to Medicaid last month for generic medications was approximately 26 dollars, compared to over 156 dollars for brand name medications. Ms. Clark also stated that Medicaid processed approximately 420,000 claims in January 2007.

New Business

Mr. Smith presented several suggested RDUR intervention modules which were originally presented at the November 2006 meeting. These were presented again because of a lack of quorum at the November meeting.

Restasis®

Mr. Smith presented the results of a review conducted to identify concurrent use of Restasis® and medications with anticholinergic properties. Information was presented to reflect the incidence of this concurrent use at approximately 30 percent. Based on these findings, a criterion was recommended to identify patients who may benefit from a change in therapy allowing discontinuation of Restasis®. A motion was made by Dr. Phillips to accept the criterion, and the motion was seconded by Dr. Gray. All voted in favor of the motion.

Triptans and Antidepressants

The next intervention discussed was the concurrent use of triptans with SSRI or SNRI antidepressants. This review resulted from recent FDA action regarding the risk of serotonin syndrome in patients taking these medications concurrently. Approximately 14 percent of patients who were treated with a triptan also received one or more prescriptions for an SNRI or SSRI during the report period. A criterion was recommended to identify patients who may be at risk for serotonin syndrome due to the concurrent use of members of these drug classes. Mr. Strickland made a motion to approve this criterion, and Dr. Brown seconded the motion. All voted in favor of the motion.

Exubera®

The new inhaled insulin product, Exubera®, was then discussed. Mr. Smith summarized possible concerns around this agent, including potential waste associated with the recommended dosing regimen. After much discussion, the board was presented a motion by Dr. Voulters to table this vote and have HID report back to the board in three to six months on the activity on this medication. This was seconded by Dr. Phillips. All voted in favor.

Additional Criteria Recommendations

Mr. Smith presented the following additional retrospective DUR criteria recommendations:

- Combunox: Duration of Therapy – Combunox (oxycodone/ibuprofen) may be over-utilized. This medication is indicated for short-term (no more than seven days) management of acute moderate to severe pain.

- Combunox: High Dose – Combunox (oxycodone/ibuprofen) may be over-utilized. The

manufacturer's recommended maximum dosage is four tablets in a 24-hour period, with use not to exceed seven days

- Duloxetine: Hepatic Insufficiency – It is recommended that Cymbalta (duloxetine) not be administered to patients with any hepatic insufficiency. These patients experience decreased duloxetine metabolism and elimination. After a single 20mg dose of duloxetine, cirrhotic patients with moderate liver impairment had a mean plasma clearance about 15 percent that of age and gender matched healthy subjects, a five-fold increase in AUC, and a half-life approximately three times longer.

- Duloxetine: End Stage Renal Disease – Cymbalta (duloxetine) is not recommended in patients with end stage renal disease. A single 60mg dose of duloxetine resulted in Cmax and AUC values approximately 100 percent greater in patients with end stage renal disease receiving intermittent hemodialysis than in patients with normal renal function.

- Duloxetine: MAO Inhibitors – The concurrent use of Cymbalta (duloxetine) and monoamine oxidase inhibitors is contraindicated due to the risk for developing serotonin syndrome, which may include hyperthermia, tremor, myoclonus, and irritability. It is recommended that duloxetine not be used within 14 days of discontinuing treatment with an MAOI, and at least five days should be allowed after discontinuing duloxetine before starting an MAOI.

- Duloxetine: Thioridazine – Cymbalta (duloxetine) and thioridazine should not be co-administered. Duloxetine is a moderate inhibitor of CYP 2D6, and concurrent use with thioridazine, a CYP 2D6 substrate, may increase the risk of serious ventricular arrhythmias and sudden death associated with elevated plasma levels of thioridazine.

- Duloxetine: Narrow-Angle Glaucoma – Cymbalta (duloxetine) should be used with caution in patients with controlled narrow-angle glaucoma and is contraindicated in patients with uncontrolled narrow-angle glaucoma. In clinical trials, duloxetine has been shown to increase the risk of mydriasis.

- Duloxetine: Fluoxetine – Cymbalta (duloxetine) should be used with caution in patients receiving Luvox (fluvoxamine), a potent CYP 1A2 inhibitor. Elimination of duloxetine is mainly through hepatic metabolism involving P450 isozymes, CYP 2D6 and CYP 1A2. Concurrent use of these agents resulted in an approximate six-fold increase in the AUC and a 2.5-fold increase in the Cmax of duloxetine.

- Duloxetine: Potent 2D6 Inhibitors – Cymbalta (duloxetine) should be used with caution in patients receiving potent CYP 2D6 inhibitors (paroxetine, fluoxetine, and quinidine). The concurrent use of these agents may result in elevated concentrations of duloxetine.

- Duloxetine: Certain Tricyclic Antidepressants – Cymbalta (duloxetine) should be used with caution in patients receiving certain tricyclic antidepressants (desipramine, amitriptyline, nortriptyline, and imipramine). Duloxetine is a moderate inhibitor of CYP 2D6, and concurrent use with these agents may result in elevated TCA plasma concentrations. TCA plasma levels may need to be monitored, and TCA dose reduction may be necessary.

- Duloxetine: CYP 2D6 Metabolized Drugs – Cymbalta (duloxetine) should be used with caution in patients receiving drugs that are extensively metabolized by the CYP 2D6 isozyme and which have a narrow therapeutic index (Type 1C antiarrhythmics and phenothiazines). Duloxetine is a moderate inhibitor of CYP 2D6, and concurrent use with these agents may result in elevated plasma concentrations of the CYP 2D6 substrate.

- Duloxetine: High Dose – Cymbalta (duloxetine) may be over-utilized. The recommended dosing range is 40mg to 60mg per day. There is no evidence that doses greater than 60mg per day confer any additional benefit.

- Duloxetine: Underuse – After reviewing your patients' refill frequency for Cymbalta (duloxetine), we are concerned that they may be non-adherent to the prescribed dosing regimen, which may lead to sub-therapeutic effects.

- Proton Pump Inhibitors and Warfarin – There have been reports of increases in INR and prothrombin time in patients receiving proton pump inhibitors and warfarin concurrently. Monitor PT/INR when a proton pump inhibitor is added to, changed during, or discontinued from concomitant treatment with warfarin. Adjustment of the warfarin dose may be necessary in order to maintain the desired level of anticoagulation.

A motion was offered by Dr. Montgomery to approve all of the above criteria and seconded by Dr. Gray. All voted in favor of the motion.

Carisoprodol

Mr. Smith then presented a review of carisoprodol (Soma®). The Pharmacy and Therapeutics (P&T) Committee discussed this agent during the January 9, 2007 P&T Committee meeting. The issues of dependence, abuse, and drug-seeking behavior associated with carisoprodol were of major concern to the P&T committee. A one page Prescribing Information Update (One-pager) was presented by Mr. Smith and described to the Board. This document summarizes the basic prescribing recommendations for and risks associated with carisoprodol. The One-pager is intended for distribution to prescribers. After much discussion, the DUR Board recommended that the One-pager be distributed to prescribers by the academic detailing staff, along with a suggested tapering schedule for discontinuing carisoprodol. A motion was made by Dr. Phillips and seconded by Dr. Montgomery to also include the One-pager and tapering schedule in the April Bulletin. Dr. Phillips added that the DUR Board should revisit carisoprodol prescribing trends periodically and consider recommending action by the P&T Committee if favorable results are not seen.

Cough and Cold Products in Young Children

Mr. Smith presented a report on utilization of cough and cold medications in young children. In January, the Centers for Disease Control and Prevention (CDC) issued a Morbidity and Mortality Weekly Report (MMWR) article describing three deaths in infants less than 12 months of age that were associated with cough and cold medications. This report showed that during the fourth quarter of 2006, over 15,000 prescriptions were filled for these agents among beneficiaries under two years of age. A copy of the CDC report was provided to the Board members. Ms. Clark

offered that a pediatrician from University Medical Center would be invited to the next DUR Board meeting to discuss this issue further.

Boxed Warnings Update

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

Coumadin (warfarin sodium)

[Posted 10/06/2006] The FDA and Bristol-Myers Squibb notified pharmacists and physicians of revisions to the labeling for Coumadin to include a new patient Medication Guide, as well as a reorganization and highlighting of the current safety information to better inform providers and patients.

Isotretinoin - Accutane and generic isotretinoin

[Posted 10/06/2006] The FDA and the iPLEDGE program notified healthcare professionals and patients of an update to iPLEDGE, a risk management program to reduce the risk of fetal exposure to isotretinoin, which will eliminate one element of the program, the 23 day lock-out period for males and females of non-child bearing potential. This change does not affect female patients of child-bearing potential.

Lamictal (lamotrigine)

[Posted 09/29/2006] The FDA notified healthcare professionals and patients of new preliminary information from the North American Antiepileptic Drug Pregnancy Registry that suggests that babies exposed to Lamictal, indicated to treat seizures and bipolar disorder, during the first three months of pregnancy may have a higher chance of being born with a cleft lip or cleft palate. More research is needed to be sure about the possibility of the increased chance of cleft lip or cleft palate developing in babies of pregnant women who take Lamictal. Women who take Lamictal and are pregnant or are thinking of becoming pregnant should talk with their doctor. Patients should not start or stop using Lamictal without talking to their doctor.

Ortho Evra (norelgestromin/ethinyl estradiol)

[Posted 09/20/2006] Ortho-McNeil and the FDA notified healthcare professionals and patients about revisions to the prescribing information to inform them of the results of two separate epidemiology studies that evaluated the risk of developing a serious blood clot in women using Ortho Evra compared to women using a different oral contraceptive. The first study found that the risk of non-fatal venous thromboembolism (VTE) associated with the use of Ortho Evra contraceptive patch is similar to the risk associated with the use of oral contraceptive pills containing 35 micrograms of ethinyl estradiol and norgestimate. The second study found an approximate two-fold increase in the risk of medically verified VTE events in users of Ortho Evra compared to users of norgestimate-containing oral contraceptives containing 35 micrograms of estrogen. Although the results of the two studies differ, the results of the second study support FDA's concerns regarding the potential for Ortho Evra use to increase the risk of blood clots in some women. Prescribing information for Ortho Evra continues to recommend that women with concerns or risk factors for thromboemboli disease talk with their healthcare professionals about using Ortho Evra versus other contraceptive options.

Ibuprofen and Aspirin Taken Together

[Posted 09/08/2006] The FDA notified consumers and healthcare professionals that taking Ibuprofen for pain relief and aspirin at the same time may interfere with the benefits of aspirin taken for the heart. Ibuprofen can interfere with the anti-platelet effect of low dose aspirin (81mg per day), that may render aspirin less effective when used for cardioprotection and stroke prevention. Although it is safe to use Ibuprofen and aspirin together, the FDA recommends that consumers contact their healthcare professional for more information on the timing of taking these two medicines together, so that both medicines can be optimally effective.

Dexedrine (dextroamphetamine sulfate)
[Posted 08/21/2006] The FDA and GlaxoSmithKline notified healthcare professionals of changes to the BOXED WARNING, WARNINGS, and PRECAUTIONS sections of the prescribing information for Dexedrine (dextroamphetamine sulfate), approved for the treatment of Attention-Deficit Hyperactivity Disorder and narcolepsy. The warnings describe reports of sudden death in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems.

Aptivus (tipranavir)
[Posted 06/30/2006] Boehringer Ingelheim and the FDA informed healthcare professionals of important new safety information for Aptivus (tipranavir) capsules co-administered with ritonavir (500mg/200mg) which includes an addition to the drug's Black Box Warning regarding reports of both fatal and non-fatal intracranial hemorrhage (ICH). Boehringer Ingelheim identified 14 reports of intracranial hemorrhage events, including eight fatalities, in 6,840 HIV-1 infected individuals receiving Aptivus capsules in combination antiretroviral therapy in clinical trials. Many of the patients experiencing ICH in the Aptivus clinical development program had other medical conditions (CNS lesions, head trauma, recent neurosurgery, coagulopathy, hypertension, or alcohol abuse) or were receiving concomitant medications, including anticoagulants and antiplatelet agents, that may have caused or contributed to these events. No pattern of abnormal coagulation parameters were observed in patients receiving Aptivus in general, or preceding the development of ICH. Routine measurement of coagulation parameters is not currently indicated in the management of patients on Aptivus. An increased risk of ICH was previously observed in patients with advanced HIV-1 disease/AIDS. Further investigations are ongoing to assess the role of Aptivus in ICH.

Ketek (telithromycin)
[Posted 06/29/2006] The FDA notified healthcare professionals and patients that it completed its safety assessment of Ketek (telithromycin), indicated for the treatment of acute exacerbation of chronic bronchitis, acute bacterial sinusitis, and community acquired pneumonia of mild to moderate severity, including pneumonia caused by resistant strep infections. The drug has been associated with rare cases of serious liver injury and liver failure, with four reported deaths and one liver transplant after the administration of the drug. The FDA determined that additional warnings are required and the manufacturer is revising the drug labeling to address this safety concern. The FDA is advising patients taking Ketek and their doctors to be on the alert for signs and symptoms of liver problems. Patients experiencing such signs or symptoms should discontinue Ketek and seek medical evaluation, which may include tests for liver function.

Paxil (paroxetine hydrochloride) Tablets and Oral Suspension
Paxil CR (paroxetine hydrochloride) Controlled-Release Tablets
[Posted 05/12/2006] GlaxoSmithKline (GSK) and the FDA notified healthcare professionals of changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the prescribing Information for Paxil and Paxil CR. These labeling changes relate to adult patients, particularly those who are younger adults. A recent meta-analysis conducted of suicidal behavior and ideation in placebo-controlled clinical trials of paroxetine in adult patients with psychiatric disorders including Major Depressive Disorder (MDD), other depression, and non-depression disorders. Results of this analysis showed a higher frequency of suicidal behavior in young adults treated with paroxetine compared with placebo. Further, in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo. This difference was statistically significant. As the absolute number and incidence of events are small, however, these data should be interpreted with caution. All of the reported events of suicidal behavior in the adult patients with MDD were non-fatal suicide attempts, and the majority of these attempts (eight of 11) were in younger adults aged 18-30. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24. It is important that all patients, especially young adults and those who are improving, receive careful monitoring during paroxetine therapy regardless of the condition being treated.

Next Meeting Information:
Ms. Clark reminded the Board of the next scheduled meeting on May 17, 2007.
Randy Calvert adjourned the meeting at 3:40 p.m.

Respectfully Submitted:
Health Information Designs