Minutes of the March 31, 2005
Drug Utilization Review (DUR) Board Meeting

Members Attending: Billy Brown , PharmD, Randy Calvert, RPh., Montez Carter, RPh., John Mitchell, M.D., Lee Montgomery, M.D., Joe McGuffee, RPh., Lee Anne Ross, PharmD., Rudy Runnels, M.D., Cynthia Undesser, M.D.,

Members Absent: Tim Alford, M.D., Clarence Dubose, RPh., Andrea Phillips, M.D.

Also Present: Judith Clark, RPh., Gay Gibson, R.N., Phillip Meredith, M.D., Sharon Barnett-Myers, Richard Roberson – DOM
Lew Anne Snow, R.N., Kathleen Burns, R.N., Sam Warman, RPh., HID

Dr John Mitchell called the meeting to order at 2:05p.m.

Approval of the minutes of last meeting (November 18, 2004): Dr. Undesser made a motion to accept the minutes as written. Montez Carter seconded the motion. All voted in favor of the approval.

Reports:
Update on Inappropriate Therapy for the Elderly
Sam Warman presented information about the following interventions regarding inappropriate therapy for the elderly:

- Inappropriate Therapy for the elderly: Ambien and Sonata
- Inappropriate Therapy for the elderly: long half-life Benzodiazepine Anxiolytics and Sedatives
- Inappropriate Therapy for elderly: Barbiturate Sedative/Hypnotics
- Inappropriate Therapy for elderly: certain Tertiary Tricyclic Amines

There were 697 educational intervention letters with attached response forms mailed to prescribers for the identified recipients. There were 919 fewer prescriptions written for the identified beneficiaries after intervention letters were mailed to physicians. This reduction in prescriptions resulted in a cost savings of about $98.32 per beneficiary. No vote was taken on the recommendations at this time due to the implementation of a CNS program approved by DOM.

Effect of Recent News on Cox-2 Inhibitor Utilization:
Sam Warman presented a review on the utilization of COX-2 Inhibitors following the voluntary removal of Vioxx from the market in September 2004. The information presented showed that prescriptions for Celebrex and Bextra remained almost equal in number as prior to September 2004. There was a significant increase in the NSAID therapeutic class as well as narcotic analgesics. Judith Clark explained that the P&T Committee voted to leave the COX-2 inhibitors on prior authorization pending the FDA review of COX-2 inhibitors.

Antibiotic Utilization in Children:
Sam Warman presented a report regarding antibiotic and antihistamine utilization in children. Data from December 2003 through November 2004 for children 0-20 years of age was reviewed for total prescriptions per month for both antibiotic and antihistamine therapy. Using data from December 1, 2003 through December 31, 2003 as an example, there were 2,617 beneficiaries who received Zithromax and another antibiotic during this time period. After much general discussion the board asked that further review be done regarding duplicate antibiotic therapy in children. The DUR Board asked that the following information be included in the review:

- Specific geographical areas
- Review areas of care – i.e. ER visits vs. clinic or physician office visits
- ICD-9 codes assigned to visit
- Specific time frame of 72 hours to 5 days after initial antibiotic RX

Montez Carter made a motion that these interventions be revisited following an enhanced review. Dr. Undesser seconded the motion. All voted in favor of the motion.

Retrospective DUR Criteria Recommendations:
Sam Warman presented the following retrospective DUR criteria recommendations for the first quarter 2005:

- Narcotic/Sickle Cell/Hydroxyurea- The patient has sickle cell anemia and appears to be receiving only narcotics for associated pain. The patient may benefit from the addition of hydroxyurea for pain prevention.
  - Cynthia Undesser made a motion to accept this criteria recommendation. Leigh Ann Ross seconded the motion. All voted in favor of the motion.
- Estazolam/Azole Antifungals-Concomitant use of estazolam with CYP3A4 enzymes inhibitors, ketoconazole or itraconazole may result in estazolam toxicity.
  Estazolam/ 3A4 inhibitors-Concomitant use of estazolam with drugs that exhibit significant inhibition of 3A4 metabolism may result in elevated estazolam concentrations.
  Estazolam/certain CYP3A4 inducers-Concomitant use of estazolam with potent CYP3A4 enzyme inducers would decrease estazolam concentrations.
  - Dr. Montgomery motioned that the DUR Board recommend to the P&T Committee that estazolam be removed from the preferred drug list due to the extensive list of interactions/dangers associated with the medication. Dr. Montgomery also recommended that a list of the prescribers using this group of medications in the last 60 days be sent an appropriate letter. Joe McGuffee seconded the motion. All voted in favor of the motion.
- Valdecoxib/therapeutic appropriateness-serious skin reactions have been reported in patients receiving Bextra. Valdecoxib should be discontinued at the first appearance of a skin rash, mucosal lesions, or any sign of hypersensitivity. Valdecoxib contains sulfa, and patients with a history of allergic reactions to sulfa may be at a greater risk of skin reactions.
  Valdecoxib/therapeutic appropriateness –Bextra is contraindicated for treatment of postoperative pain immediately coronary artery bypass surgery (CABG). Patients treated with valdecoxib for pain following CABG have a higher risk for cardiovascular/thromboembolic events, deep surgical infections or sternal wound complications.

- Dr Montgomery motioned that the recommendations be approved. Dr. Montgomery also asked that DOM consider adding the following questions to the PA process for Bextra:
    - Does patient have an allergy to Sulfa?
    - Has patient had a CABG procedure within the last 6 months?

  Dr. Ross seconded the motion. All voted in favor of the motion.

- Celecoxib/ Overutilization- Recent clinical trials involving the use of this category to prevent colon polyps were halted due to an increased risk of CV events. Patients taking 400 mg of celecoxib twice a day have a 3.4 times greater risk of CV events compared to placebo and 2.5 times greater for 200 mg twice a day. The FDA is advising that all physicians prescribing celecoxib consider the evolving information in evaluating the risks and benefits for the individual patient. Ms. Clark stated the P&T Committee asked that the DUR Board consider placing a maximum dose allowed on all COX-2 inhibitors.
    - Dr. Montgomery made a motion to change the maximum quantity currently allowed by DOM from 150% of the recommended dose to 100% of the recommended dose. Joe McGuffee seconded the motion. Dr. Mitchell asked for a review of all NSAIDS and COX2 inhibitor prescriptions where the quantity dispensed was over the recommended maximum dose. Dr. Mitchell requested that the report include diagnosis information as well as physician specialty information.

Black Box Warnings and Updates:

Sam Warman presented black box warnings issued by the FDA concerning the following:

- Crestor- FDA issued a public health advisory describing revisions to the WARNINGS, DOSAGE AND ADMINISTRATION, CLINICAL PHARMACOLOGY, and PRECAUTIONS sections of the labeling. The revisions include results from a Phase 4 pharmacokinetic study in Asian-Americans and highlight important information on the safe use of Crestor to reduce the risk for serious muscle toxicity (myopathy/rhabdomyolysis), especially at the highest approved dose of 40 mg. At this time, the FDA is also making statements about the muscle and kidney safety of Crestor based on extensive review of available information.

- Agrylin- Shire and FDA notified healthcare professionals about changes to the CONTRAINDICATIONS and WARNINGS sections of the prescribing information for Agrylin (anagrelide hydrochloride), a medication approved for the treatment of thrombocythemia secondary to myeloproliferative disorders to reduce platelet count and the risk of thrombosis and to ameliorate associated symptoms including thrombohemorrhagic events. Pharmacokinetic studies have revealed an 8-fold increase in total exposure (AUC) to anagrelide hydrochloride in patients with moderate hepatic impairment. Use of anagrelide hydrochloride has not been studied in patients with severe hepatic impairment. Labeling changes include the contraindication to the use of Agrylin in patients with severe hepatic impairment. The WARNINGS section describes the need for dosage reduction in patients with moderate hepatic impairment and the necessity of monitoring these patients carefully for cardiovascular effects.

- Gabitril- FDA and Cephalon, Inc. notified healthcare professionals and the public that a Bolded Warning has been added to the labeling for Gabitril (tiagabine) to warn

prescribers of the risk of seizures in patients without epilepsy being treated with Gabitril. FDA has received reports of the occurrence of seizures in more than 30 patients prescribed Gabitril for conditions other than epilepsy. Most of these uses were in patients with psychiatric illnesses. Such off label prescribing is a common practice among physicians. Because of the risk of seizures, however, in addition to adding the Bolded Warning to product labeling, the sponsor has agreed to undertake an educational campaign, targeted to healthcare professionals and patients, in which such off-label use will be discouraged.

- Phenergan- FDA and Wyeth notified healthcare professionals of revisions to the CONTRAINDICATIONS, WARNINGS/Use in Pediatric Patients, and DOSAGE AND ADMINISTRATION sections of the prescribing information for Phenergan. Phenergan is contraindicated for use in pediatric patients less than two years of age because of the potential for fatal respiratory depression. Post marketing cases of respiratory depression including fatalities, have been reported with use of Phenergan in pediatric patients less than two years of age. Caution should also be exercised when administering Phenergan to pediatric patients two years of age and older. Dr. Mitchell asked if DOM was covering Phenergan prescriptions for children after this warning was issued by the FDA. Ms. Clark explained that DOM does not deny for Black Box Warnings.
  - Dr. Montgomery made a motion to send intervention letters containing the FDA black box warning to physicians who continue to prescribe Phenergan for children less than 24 months of age. Joe McGuffee requested that this information also be included in the DOM Bulletin as an educational alert. A motion was made by Dr. Undesser to accept both Dr. Montgomery's motion and to also include the request made by Joe McGuffee. Dr. Ross seconded the motion. All voted in favor of the motion.

- Estraderm-The Women's Health Initiative (WHI) study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50-79 years of age) during 5 years of treatment with oral conjugated equine estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) relative to placebo. The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with oral conjugated equine estrogens plus medroxyprogesterone acetate relative to placebo. It is unknown whether this finding applies to younger postmenopausal women or to women taking estrogen alone. Other doses of oral conjugated estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar.

Suggested Interventions:
Sam Warman presented several intervention recommendations. Each suggested intervention included the number of recipients identified during profile review as being at risk for the specific intervention. These suggested intervention included.

- Inappropriate Therapy for Elderly-long half-life benzodiazepine anxiolytics
- Inappropriate Therapy for Elderly-barbiturate sedative/hypnotic
- Inappropriate Therapy for Elderly- certain tertiary TCA's
- Inappropriate Therapy for Elderly- famotidine
- Inappropriate Therapy for Elderly- Sonata and Ambien
- Drug (actual) disease precaution – adverse cardiovascular effects COX-2 inhibitors
- Celecoxib/overutilization
- Valdecoxib/therapeutic appropriateness

After much discussion, the DUR Board decided to postpone approval of the suggested interventions until after implementation of the CNS/DOM program.

Cost Analysis:
Sam Warman presented a brief cost management analysis report from January 1, 2005 through January 31, 2005. This report included the top 15 therapeutic classes by total cost of claims, the top 25 drugs based on number of claims and the top 25 drugs based on total claims cost for this time period. Dr Montgomery asked that the board be given a list of specific medications included under miscellaneous therapeutic agents and miscellaneous anticonvulsants for the next DUR Board meeting.

Academic Detailing:
Lew Anne Snow gave an overview of the new Academic Detailing program. Three new Medicaid Pharmacy Specialists, representing all areas of the state, were introduced to the DUR Board. Under the direction of the Division of Medicaid, the Medicaid Pharmacy Specialists will provide education regarding all aspects of the Mississippi Division of Medicaid pharmacy program to prescribing providers throughout the state

Pharmacy Updates:
Judith Clark, Director of Pharmacy Bureau, gave a brief report on recent pharmacy program expenditures. Mrs. Clark distributed a copy of the preferred drug list to the board members. She also provided the board members with a list of preferred vs. non-preferred antihistamines and antihistamine/decongestant combination products. A copy of the DUR Board by-laws was given to every Board member. Mrs. Clark reminded the board members of the attendance requirement addressed in the by-laws.

CNS presentation:
Judith Clark introduced Billy E. Jones, M.D., Medical Director and Frankie Rutledge, account manager for Comprehensive NeuroScience, Inc. Dr. Billy Jones gave the board an overview of the behavioral pharmacy management system. Supported by a grant from Eli Lilly, CNS will partner with the MS Division of Medicaid to encourage appropriate utilization of behavioral drugs.

There being no other business, Dr. Mitchell asked for a motion to adjourn the meeting. Joe McGuffee made a motion to adjourn. Leigh Ann Ross seconded the motion. All voted in favor of the motion. The meeting was adjourned at 4:15 p.m.

Respectfully submitted:
Health Information Designs