Minutes of the September 29, 2005
Drug Utilization Review (DUR) Board Meeting

Members Attending: Billy Brown, Pharm.D, Randy Calvert, RPh, John Mitchell, M.D., Andrea Phillips, M.D., Lee Anne Ross, Pharm.D, Rudy Runnels, M.D.

Members Absent: Montez Carter, RPh, Lee Montgomery, M.D.

Also Present: Judith Clark, RPh, Terri Kirby, RPh, Sharon Barnett-Myers - DOM
Dennis Smith, RPh, Sam Warman, RPh, Lew Anne Snow, R.N., Kathleen Burns, R.N. –HID

Dr. John Mitchell called the meeting to order at 2:03 p.m.

Approval of the minutes of the March 31, 2005 and June 23, 2005 DUR Board meetings.
Dr. Runnels made a motion to accept the minutes of both meetings as written. Dr. Ross seconded the motion. All voted in favor of the approval.

Updates:
Sickle Cell Therapy Update:
Dennis Smith, RPh presented data regarding the use of hydroxyurea in patients with sickle cell anemia. Data reviewed from 1/1/05 through 8/26/05 identified 1,902 Medicaid beneficiaries with a diagnosis of sickle cell anemia. Of the 1,902 beneficiaries identified:

- 9% received a prescription for hydroxyurea
- 91% did not receive a prescription for hydroxyurea
- 56% received one or more narcotic RX
- 44% did not receive a narcotic prescription

As requested by the Board, the prescribing physician's specialties, the age of the beneficiary and regional area of residence of the beneficiary were identified The majority of the prescriptions were written by general practitioners for beneficiaries 21 years of age and older with most of these beneficiaries residing in Hinds county.
Dennis Smith reviewed the retrospective DUR criteria which identified beneficiaries with a diagnosis of sickle cell anemia who appear to be receiving only narcotics for associated pain. The prescribing physicians for those beneficiaries identified would receive an intervention letter which stated the patient may benefit from the addition of hydroxyurea for pain prevention. Dr. Runnels asked that HID review data for these beneficiaries identified both 120 days after intervention and 12 months after intervention to identify the impact of the intervention letter.
Leigh Ann Ross made a motion to accept this criteria recommendation. Dr. Runnels seconded the motion. All voted in favor of the motion.

Cost Management Analysis:
Dennis Smith presented a brief cost management analysis report from July 1, 2005 through July 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.

Pharmacy Program Update:
Judith Clark, Director of Pharmacy Bureau, gave a brief report on recent pharmacy program expenditures. She stated that CNS would present, at the December meeting, a report on the over utilization of anti-psychotics. Ms. Clark distributed a copy of the products with quantity limits to the board members. She also provided the board members with the 90 day maintenance list.
Sharon Barnett-Myers, Deputy Director of Health Services, briefly thanked the Board members for their service. She continued that many MS Medicaid beneficiaries had been affected by Hurricane Katrina and DOM is working very hard to assist these beneficiaries. Judith Clark stated that to date MS DOM beneficiaries had been relocated to 27 different States and the pharmacy division has been dealing with different issues due to this relocation. Ms. Clark distributed to the Board a list of drugs to be considered for quantity limits.
After much discussion, a motion was made by Randy Calvert to impose a quantity limit on Triptans based on the recommended guidelines for the treatment of acute migraine headaches. The motion was seconded by Dr. Ross. All voted in favor of the motion.

New Business:

Dennis Smith, RPh presented an overview of the DUR intervention process to the Board.

Osteoporosis Targeted Disease Intervention Program
Osteoporosis Targeted Disease Intervention Program was presented by Dennis Smith, RPh. Mr. Smith explained that the purpose of the program was to increase the appropriate use of medications that treat bone diseases and prevent age-related and secondary causes of bone loss. The intent of this program is to alert prescribers of beneficiaries at increased risk for adverse outcomes and to provide them with information to aid in the review of current medication therapy. The board requested that HID compare the number of beneficiaries who meet the criteria as written versus the number of beneficiaries who simply have the diagnosis but according to claims data are not receiving any treatment.

Prevention of Cardiovascular Disease
Leigh Ann Ross presented information on the prevention of cardiovascular events. Dr. Ross stated that mortality and morbidity associated with cardiovascular disease continues to be a challenge in the Medicaid population of Mississippi. She presented the following interventions associated with the prevention of cardiovascular events.

1. Diabetes/Hypertension/Cardiovascular Drugs
   This patient has a history of diabetes and hypertension and may benefit from the addition of an anti-hypertensive agent to reduce cardiovascular morbidity and mortality. The coexistence of these conditions imposes a need for a significantly lower goal blood pressure (130/80 mm Hg) than the goal recommended for a non-diabetic patient with hypertension (140/90 mm Hg). If lifestyle modifications alone are no longer effective consider JNC-7 pharmacologic treatment recommendations for the selection of the optimal anti-hypertensive therapy.

2. Certain Antihypertensive Agents/Post MI/Beta-blockers, ACEI & Aldosterone Antagonists
   This patient has a diagnosis of myocardial infarction and is on an anti-hypertensive medication. The current JNC-7 report recommends a beta-blocker, ACE inhibitor or an aldosterone antagonist as optimal antihypertensive therapy for hypertensive post myocardial infarction patients, if no contraindications are present.

3. Certain Antihypertensive Agents/Stroke/Thiazide diuretics & ACEI
   This patient has a history of stroke and is on an anti-hypertensive medication. The current JNC-7 report suggests that recurrent stroke rates are lowered by the combination of an ACE inhibitor and a thiazide-type diuretic, if no contraindications are present.

4. Certain Antihypertensive Agents/Chronic Kidney Disease/ACEI & ARB
   This patient has a diagnosis of chronic kidney disease and is on an anti-hypertensive medication. The current JNC-7 report recommends an ACE inhibitor or angiotensin II receptor antagonist as optimal antihypertensive therapy in these patients, if no contraindications are present.

5. Diabetes/Proteinuria/Negating ACEI & ARB
   Diabetics (hypertensive and normotensive) with microalbuminuria may benefit from the addition of an ACE inhibitor or an ARB to their therapy to reduce the rate of progression of renal disease.

6. Diabetes/Hypertension/Negating ACEI & ARB
   Diabetics with hypertension and nephropathy may benefit from the addition of an ACE inhibitor or angiotensin receptor antagonist to their therapy to reduce the rate of progression to renal disease.

7. Diabetes/Hypertension or Diabetic Nephropathy/Negating ACEI & ARB
   According to the JNC 7 report, the hypertension treatment goal for patients with diabetes is a blood pressure of < 130/80-mm Hg. In order to achieve this goal, multiple antihypertensive agents may be required. Adding an ACEI or an ARB should be considered if no contraindications are present. These agents also have been shown to delay the progression of nephropathy in diabetic patients with microalbuminuria.

Dr. Andrea Phillips made a motion to accept interventions # 1, #2, #4, # 5 and # 7. The motion was seconded by Randy Calvert. All voted in favor of the motion.

Retrospective DUR Criteria Recommendations:
Dennis Smith presented the following retrospective DUR criteria recommendations:

- Tizanidine / CYP1A2 Inhibitors- Caution is recommended when considering concomitant use of tizanidine with other inhibitors of CYP1A2, such as antiarrhythmics (amiodarone, mexiletine, propafenone), cimetidine, fluoroquinolones (ciprofloxacin, norfloxacin) and ticlopidine. The concurrent use of these agents may increase the risk of profound hypotension, somnolence and dizziness.
- Overactive Bladder Medications / Therapeutic Duplication- Therapeutic duplication of medications to treat overactive bladder may be occurring. Concomitant use of these drugs may cause additive adverse effects.
- Darifenacin / High Dose- Enablex (darifenacin) may be over-utilized. The recommended maximum dose is 15 mg per day.
- Darifenacin / Potent 3A4 Inhibitors- The daily dose of Enablex (darifenacin), a CYP 3A4 substrate, should not exceed 7.5 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, ritonavir, nelfinavir, clarithromycin, and nefazodone). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects of darifenacin.
- Darifenacin / Hepatic Impairment- The daily dose of Enablex (darifenacin) should not exceed 7.5 mg once daily for patients with moderate hepatic impairment. Darifenacin is not recommended for use in patients with severe hepatic impairment.
- Darifenacin / CYP2D6 Substrates- Caution should be exercised when Enablex (darifenacin), a moderate 2D6 inhibitor, is used concomitantly with medications that are predominantly metabolized by CYP2D6 and which have a narrow therapeutic window (e.g. flecainide and thioridazine). Concurrent use with darifenacin may result in elevated plasma concentrations of the substrates and increase risk of adverse effects.
- Darifenacin / Digoxin- Caution should be exercised when Enablex (darifenacin) is used concomitantly with digoxin. Concurrent use of darifenacin (30mg daily) with digoxin (0.25mg) at steady state resulted in a 16% increase in digoxin exposure. Routine monitoring of digoxin should continue.
- Darifenacin / Narrow Angle Glaucoma-Enablex (darifenacin), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Darifenacin is contraindicated in patients with uncontrolled narrow-angle glaucoma.
- Darifenacin / Urinary Retention- Enablex (darifenacin), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and in patients who are at risk for these conditions.
- Darifenacin / GI Obstruction-Decreased GI Motility - Enablex (darifenacin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Darifenacin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with severe constipation, ulcerative colitis, and myasthenia gravis.
- Anticholinergic Agents / Therapeutic Duplication- The concomitant use of anticholinergic agents may increase the frequency and/or severity of dry mouth, constipation, blurred vision and other anticholinergic adverse effects.
- Solifenacin / High Dose -Vesicare (solifenacin) may be over-utilized. The recommended maximum dose is 10 mg per day. Higher doses have resulted in a higher incidence of adverse reactions.

- Solifenacin / Hepatic Impairment- The daily dose of Vesicare (solifenacin) should not exceed 5.0 mg for patients with moderate hepatic impairment. Solifenacin is not recommended for use in patients with severe hepatic impairment.
- Solifenacin / Renal Impairment- The daily dose of Vesicare (solifenacin) should not exceed 5.0 mg for patients with severe renal impairment (Ccr less than 30 ml/min). Significant increases in the AUC and elimination half-life have been noted with single oral doses of solifenacin 10 mg and have been correlated to the degree of renal impairment.
- Solifenacin / Potent 3A4 Inhibitors- The daily dose of Vesicare (solifenacin), a CYP 3A4 substrate, should not exceed 5.0 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, ritonavir, nelfinavir, clarithromycin, and nefazodone). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects.
- Solifenacin / Narrow Angle Glaucoma- Vesicare (solifenacin), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Solifenacin is contraindicated in patients with uncontrolled narrow-angle glaucoma.
- Solifenacin / Urinary Retention & Gastric Retention - Vesicare (solifenacin), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and in patients who are at risk for these conditions.
- Solifenacin / GI Obstruction-Decreased GI Motility -Vesicare (solifenacin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Solifenacin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with constipation, ulcerative colitis, and myasthenia gravis.
- Solifenacin / QT Prolongation & QT Prolongation Drugs -Vesicare (solifenacin) should be administered with caution to patients with a history of QT prolongation or on medications known to prolong the QT interval. A significant effect on QTc has been observed following the administration of solifenacin (10 or 30 mg) in healthy female volunteers. The QT prolonging effect was greater with the 30 mg dose as compared with the 10 mg dose and did not appear to be as great as that of the positive control moxifloxacin at its therapeutic dose.
- Tolterodine IR & XL/High Dose- Detrol/Detrol XL (tolterodine) may be over-utilized. The manufacturer's recommended dose is 4.0 mg daily.
- Tolterodine IR/Hepatic Impairment- The daily dose of Detrol or Detrol XL (tolterodine) should not exceed 2.0 mg for patients with significantly reduced hepatic or renal function.
- Tolterodine//Potent 3A4 Inhibitors -The daily dose of Detrol/ Detrol XL (tolterodine), a CYP 3A4 substrate, should not exceed 2.0 mg when coadministered with a potent CYP3A4 inhibitor (e.g., ketoconazole itraconazole, erythromycin, clarithromycin, cyclosporine and vinblastine). Exceeding the recommended dose during concurrent therapy may increase the risk of adverse effects of tolterodine.
- Oxybutynin/High Dose (Adults) - Ditropan (oxybutynin immediate-release) may be over-utilized. The manufacturer's recommended maximum dose is 5 mg 4 times per day.

- Oxybutynin/High Dose-Pediatric-Ditropan (oxybutynin immediate-release) may be over-utilized. The manufacturer's recommended maximum dose is 5 mg 3 times per day.
- Oxybutynin Extended Release/High Dose-Ditropan XL (oxybutynin extended-release) may be over-utilized. The manufacturer's recommended maximum dose is 30 mg per day.
- Oxybutynin Extended Release/Hepatic & Renal Impairment- Ditropan/Ditropan XL (oxybutynin) should be used with caution in patients with renal or hepatic impairment.
- Oxybutynin Transdermal / High Dose- Oxytrol (oxybutynin transdermal) may be over-utilized. The manufacturer's recommended dose is one 3.9 mg/day system applied twice weekly (every 3 to 4 days).
- Oxybutynin/Contraindications- Ditropan (oxybutynin), an anticholinergic agent, is contraindicated in patients with urinary retention, gastric retention and other severe conditions of decreased gastrointestinal motility, uncontrolled narrow-angle glaucoma, paralytic ileus and in patients who are at risk for these conditions.
- Oxybutynin / Disease State Precautions- Ditropan (oxybutynin), an anticholinergic agent, should be used with caution in patients with hyperthyroidism, cardiac arrhythmias, congestive heart failure, coronary heart disease, hiatal hernias, hypertension, autonomic neuropathy, ulcerative colitis and prostatic hypertrophy. Oxybutynin may aggravate the symptoms of these conditions.
- Oxybutynin / GI Obstruction-Decreased GI Motility- Ditropan/Ditropan XL (oxybutynin), an anticholinergic agent, should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Oxybutynin, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with severe constipation, ulcerative colitis, and myasthenia gravis.
- Oxybutynin/GERD- Ditropan/Ditropan XL/Oxytrol (oxybutynin) should be used with caution in patients who have gastrointestinal reflux or who are concurrently taking drugs (such as bisphosphonates) that can cause or exacerbate esophagitis.
- Flavoxate/High Dose - Flavoxate may be over utilized. The manufacturer's recommended maximum dose is 800 mg (200 mg 4 times a day).
- Flavoxate/Contraindications- Flavoxate, an anticholinergic agent, is contraindicated in patients who have pyloric or duodenal obstruction, obstructive intestinal lesions or ileus, achalasia, GI hemorrhage, or obstructive uropathies of the lower urinary tract.
- Flavoxate/Glaucoma -Flavoxate should be used with caution in patients who have glaucoma. Flavoxate is an anticholinergic agent and use in these patients may aggravate the condition.
- Trospium / High Dose - Sanctura (trospium) may be over-utilized. The manufacturer's recommended daily dose is 20 mg twice daily.
- Trospium /Renal Impairment- The daily dose of Sanctura (trospium) should not exceed 20 mg once daily at bedtime for patients with severe renal impairment (Ccr less than 30 ml/min).
- A 4.5-fold and 2-fold increase in mean AUC and Cmax respectively and the appearance of an additional elimination phase with a long half-life (33hr) was detected in patients with severe renal sufficiency.

- Trospium / Urinary & Gastric Retention- Sanctura (trospium), an anticholinergic agent, is contraindicated in patients with urinary retention or gastric retention and patients at risk for these conditions.
- Trospium / Narrow Angle Glaucoma- Sanctura (trospium), an anticholinergic agent, should be used with caution in patients being treated for narrow-angle glaucoma and only when the potential benefits outweigh the risks. Trospium is contraindicated in patients with uncontrolled narrow-angle glaucoma.
- Trospium / GI Obstruction-Decreased GI Motility- Sanctura (trospium) should be administered with caution to patients with GI obstructive disorders because of the risk of gastric retention. Trospium, like other anticholinergic drugs, may decrease GI motility and should be used with caution in patients with ulcerative colitis, intestinal atony and myasthenia gravis.
- Trospium/Drugs Eliminated by ATS- Sanctura (trospium) is eliminated via active tubular secretion and possesses the potential for pharmacokinetic interactions with other drugs that are eliminated by the same route (e.g., digoxin, procainamide, morphine, vancomycin, metformin, and tenofovir). Coadministration of trospium with drugs that are eliminated by active tubular secretion may increase the serum concentration of trospium and/or the coadministered drug because of competition for this elimination pathway. Careful patient monitoring is recommended
- Telithromycin / Pimozide- The concurrent use of Ketek (telithromycin) and pimozide is contraindicated due to increased risk of cardiotoxicity (e.g., QT prolongation, torsades de pointes, cardiac arrest). Although no formal drug interaction studies have been conducted, telithromycin may inhibit pimozide CYP 3A4-mediated metabolism causing elevated plasma levels. Both agents are known to cause QTc prolongation.

Dr. Rudy Runnels made a motion to accept these criteria recommendations. The motion was seconded by Dr. Ross. All voted in favor of the motion,

Utilization Analysis:

Zelnorm

Data regarding the utilization of Zelnorm in Medicaid beneficiaries was presented by Sam Warman. Utilization date using paid claims data from 8/27/04 through 8/26/05 suggested that beneficiaries received an average of three prescriptions yearly and that 57% of these recipients received this agent in the absence of an approved indication.

Based on manufacturers labeling, HID recommended that beneficiaries be able to receive Zelnorm appropriately and without restriction up to 3 months in a calendar year. However, any prescription exceeding the 90^{th} day would require a clinical review through the prior authorization process.

A motion was made by Dr. Andrea Phillips to send this recommendation to the P& T Committee for further review. Dr. Runnels seconded the motion.

Zofran

Dennis Smith presented utilization data from 1/1/05 through 8/26/05 regarding the use of Zofran in Medicaid beneficiaries. Mr. Smith stated that the goal of this analysis was evaluate utilization trends among Mississippi Medicaid recipients and explore possible interventions to encourage treatment consistent with the product labeling. Although this medication is an

important agent in the treatment of cancer chemotherapy-related and post operative nausea and vomiting, the proper utilization offers DOM a significant opportunity for cost savings. HID recommended monthly quantity limits to discourage the use of this agent for non-approved conditions and to manage the dosage and length of therapy consistent with the diagnosis. After discussion by the board the following quantity limits were recommended:
Zofran 4 mg – 12 tablets per month
Zofran 8 mg – 12 tablets per month
Zofran 24 mg – 5 tablets per month
Zofran 4mg/ 5 ml oral solution – 100 ml

A motion was made by Dr. Runnels to accept the recommendations presented. The motion was seconded by Dr. Phillips. All voted in favor of the motions.

Childrens Medical Necessity Prior Authorization
Dennis Smith gave a brief overview of the Childrens Medical Necessity prior authorization process.

Black Box Warnings:
Dennis Smith presented black box warnings issued by the FDA concerning the following:
Duragesic transdermal system:
Janssen and FDA notified healthcare professionals of changes to the Boxed warning/warnings, contraindications, precautions and Dosage and administrations sections of the prescribing information for Duragesic. These changes include important safety information in the areas of the labeling: Use only in Opioid-tolerant patients, misuse, abuse and diversion, hypoventilations, interactions with CYP3A4 inhibitors, damage or cut patches, accidental exposure with Fentanyl, Chronic pulmonary disease, head injuries and intracranial pressure. Interactions with other CNS depressants and interactions with alcohol and drugs of abuse.

There being no other business, Dr. Mitchell asked for a motion to adjourn the meeting. Dr. Rudy Runnels made a motion to adjourn. Dr. Phillips seconding the motion. All voted in favor of the motion. The meeting was adjourned at 4:07 p.m.

Respectfully submitted:
Health Information Designs