DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
July 9, 2010

The Executive Formulary Committee convened on Friday, July 9, 2010 in Conference Room 240 - CO Building 2. The meeting was called to order by Dr. Matthews, Chair at 9:36 a.m.

Janet Adams, MSN, RN, CNS	Absent	Julie Graves Moy, M.D., M.Ph. (non-voting)	√
Emilie A. Becker, M.D.	√	Nina Muse, M.D. (non-voting)	Absent
Rosha Chadwick, R.Ph.	√	Peggy Perry (non-voting)	Absent
Jeanna Heidel, Pharm.D. (via phone)	√	Chris Adams (non-voting)	Absent
J. Brett Hood, M.D.	√	Mike Maples (non-voting)	Absent
Jeff Matthews, M.D.	√	Bob Burnett (non-voting)	Absent
Lisa Mican, Pharm.D. (for C. Hall, Pharm.D.)	√	Valerie Kipfer, MSN, RN (non-voting)	Absent
Connie Millhollon, RN	√	Jay Norwood, MSN, RN (non-voting)	Absent
Victoria Morgan, M.D. (via phone)	√	Vacant Center Position	
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Bill Race, M.D.	√	Vacant Center Position	
Robert L. Ward, D.O.	√		

Guest Present: Matt Vitek, Pharmacy Intern

Approval of Minutes of April 9, 2010

On a motion of Ms. Millhollon, seconded by Ms. Chadwick, the minutes of the April 9th meeting were approved as previously distributed.

Conflict of Interest Disclosure Forms

The attending Committee members indicated that there was no change in their conflict of interest disclosures.

Each individual completing a drug monograph completed their disclosure form. There was no significant conflict of interests.

Adverse Drug Reaction Reports

The Executive Formulary Committee received several adverse drug reaction reports. In the first case, a 54 year old Hispanic male was stable on multivitamin/mineral daily, quetiapine (Seroquel®) 300 mg twice a day, divalproex ER (Depakote ER®) 1,000 mg twice a day, levetiracetam (Keppra®) 750 mg twice a day, duloxetine (Cymbalta®) 60 mg daily, phenytoin (Dilantin®) 100 mg in the morning and 230 mg at bedtime, and vitamin D3 2,000 international units daily since 2009. In March 2010, the patient developed an infected furuncle for which sulfamethoxazole/trimethoprim (Bactrim DS®) one tablet twice a day was prescribed on March 8th. On March 16th, at 7:50 am, the patient had full body rash and the initial oxygen saturation was 79% on room air. The patient was started on oxygen and values fluctuated from 60% to 90%. The patient was given diphenhydramine (Benadryl®) 25 mg IM in the right deltoid and the patient was transferred to a medical hospital with urticaria and possible hypoxia. He was admitted with the diagnosis of allergic reaction and was administered IV steroids and diphenhydramine. The sulfamethoxazole/trimethoprim was discontinued. On March 19th, the patient returned to the hospital and was found to have developed erythema multiforme due to the sulfamethoxazole/trimethoprim and was continued on the oral prednisone taper for four days.

In the second case, a 49 year old female was admitted to an inpatient psychiatric hospital for the treatment of schizoaffective disorder, bipolar type and polysubstance dependence in institutional remission. Her medical conditions include hypothyroidism, type 2 diabetes, hepatitis C, hypertension, anemia, back pain, positive PPD with history of treatment with isoniazid, constipation, leukopenia, neutropenia, thrombocytopenia, obesity per BMI, insomnia, congestive heart failure by history and cataracts. On February 21st, the patient was transferred to a local medical hospital due to hypothermia (oral temperature of 90.1 and 93.7 degrees). She was also complaining of bilateral lower extremity weakness. The patient was receiving the following medications: fluphenazine (Prolixin®) 25 mg/day; olanzapine (Zyprexa®) 40 mg/day; furosemide (Lasix®) 40 mg/day, levothyroxine (Synthroid®) 100 mcg/day; lisinopril (Zestril®) 20 mg/day, ciprofloxacin (Cipro®) 500 mg twice a day, benztropine (Cogentin®) 1 mg/day, clonazepam (Klonopin®) 1.5 mg/day, docusate calcium (Surfak®) 240 mg/day, multivitamin daily, oxcarbazepine (Trileptal®) 1,800 mg/day, pioglitazone (Actos®) 15 mg/day, trazodone (Desyrel®) 50 mg/day and zolpidem (Ambien®) 10 mg/day. The hypothermia was treated with antibiotics and warming blankets. While at the medical hospital, she was also found to have pancytopenia (thought to be due to hepatitis C) and urinary retention (possibly due to dehydration/decreased oral intake). The medical hospital discontinued the following medications: oxcarbazepine, benztropine, ciprofloxacin, fluphenazine, furosemide, lisinopril, and trazodone. Olanzapine was decreased from 40 mg/day to 20 mg/day. The hypothermia and urinary retention resolved prior to discharge from the medical hospital. Upon return to the psychiatric hospital, the patient was continued on olanzapine 10 mg twice a day. The following medications were started after her return to the psychiatric hospital: lisinopril 20 mg/day, pioglitazone 15 mg/day, clonazepam 2 mg TID, perphenazine (Trilafon®) 4 mg/day, omeprazole (Prilosec®) 20 mg/day, levothyroxine 100 mcg/day, multivitamin daily, cefuroxime (Ceftin®) 500 mg BID, oxcarbazepine 600 mg/day and doxycycline (Vibramycin®) 100 mg BID. On March 31st, the patient was found to have hypothermia a second time, with an axillary temperature of 93.5 degrees. She did not have any weakness, complaints, or other vital sign instability during this episode of hypothermia. She was treated at the psychiatric hospital with a warm coat and blankets. Two hours later, her rectal temperature was 94.3 degrees. She was then transferred to the medical hospital, where her temperature stabilized. A CT of the head and chest x-ray were within normal limits. Olanzapine, perphenazine and oxcarbazepine were discontinued. The lisinopril was discontinued due to borderline low blood pressure. It was thought that the hypothermia was due to the antipsychotic/psychotropic medications. Olanzapine was restarted due to her psychiatric symptoms. However oxcarbazepine and perphenazine were not restarted. No further incidences of hypothermia have occurred at the time of the report.

The last case involved a 33 year old African American male with schizophrenia with a long standing delusion of having snakes and worms in his eyes, brain and sometimes in his "belly." On February 8th, he began to refuse psychiatric medication and meals and complained of snakes in his belly. He also complained of some nausea but no vomiting. On February 9th at 4 pm, he stated that his stomach hurt all around and it was noted that he had not eaten since breakfast on February 8th. At that time he had a temperature of 101 degrees and a pulse of 107, with abdominal guarding primarily in the right lower quadrant, no rebound and his abdomen looked more protuberant

than usual. The patient was sent to the emergency room for evaluation. At the emergency room he was diagnosed with pancreatitis with markedly elevated amylase (1,484 U/L) and lipase (427 U/L). He has no history of pancreatitis and does not use alcohol. Gallstones were ruled out. Medications at the time of hospitalization for pancreatitis included: risperidone (Risperdal®) 2 mg TID, trihexyphenidyl (Artane®) 5 mg at bedtime, divalproex (Depakote®) 1,000 mg BID, niacin, venlafaxine (Effexor®) XR and aspirin. His divalproex was discontinued and he was orally restricted except for water and was given IV rehydration. On February 11th the lipase decreased to 392 U/L and the amylase to 104 U/L and the patient reported less abdominal pain. Vital signs were within normal limits and the patient was afebrile. On February 13th the lipase and amylase increased and his diet was changed to water only. The amylase and lipase decreased on February 14th and the patient's diet was changed back to full liquid. The patient returned to the psychiatric hospital on February 20th with improvement in the pancreatitis. On March 1st, a follow up CT of abdomen/pelvis indicated that the pancreatitis was fully resolved.

New Drug Applications

(Please refer to <u>Attachment A</u> for the monographs and applications that were considered when determining action by the committee.)

benzonatate (Tessalon® Perles) - presented by Dr. Mican (developed by Saadia Ali, Pharmacy Intern)

Benzonatate acts peripherally by anesthetizing the stretch receptors located in the respiratory passages, lungs, and pleura by dampening their activity and thereby reducing the cough reflex at its source. It begins to act within 15 to 20 minutes and its effect lasts for 3 to 8 hours. It has no inhibitory effect on respiratory center in the recommended dosage. Benzonatate is indicated for the symptomatic relief of cough. The recommended oral dose of benzonatate for adults and children over 10 years old is 100 mg three times a day or every 4 hours as needed. If necessary, up to 600 mg daily may be given. Release of the benzonatate from the capsule in the mouth can produce a temporary local anesthesia of the oral mucosa and choking could occur. Therefore, the capsules should be swallowed whole without chewing.

Following discussion, on motion of Dr. Becker, seconded by Dr. Ward, the request to add benzonatate (Tessalon® Perles) to the formulary was approved. The Formulary Drug Check List was completed.

bupropion XL (Wellbutrin XL®) - presented by Dr. Mican (developed by Jennifer Almarez, pre-pharmacy student and Mina Mehvar, Pharmacy Intern)

Bupropion is a weak inhibitor of the neuronal uptake of norepinephrine, serotonin, and dopamine, and does not inhibit monoamine oxidase. While the exact mechanism of action of bupropion for the treatment of depression is unknown, the primary mechanism is thought to be secondary to norepinephrine and dopamine reuptake inhibition. Peak plasma concentration of the XL formulation is reached in approximately 5 hours after the dose. For the IR (immediate release) the peak plasma concentration is reached in 1.5 hours and for the SR (sustained release) the peak concentration occurs in 3 hours. Bupropion is indicated for the treatment of major depressive disorder, and prevention of seasonal major depressive episodes in patients with a diagnosis of seasonal affective disorder. The initial starting dose is 150 mg once daily in the morning without regard to meals. The usual adult target dose is 300 mg once a day (maximum recommended dose is 450 mg/day). Current data does not suggest a lower rate of adverse events with the XL formulation versus other formulations. Based on a study completed in a managed care population, persistence of use was higher with once daily bupropion XL than twice daily bupropion. Bupropion XL is available generically.

Following discussion, on motion of Dr. Becker, seconded by Dr. Hood, the request to add bupropion XL (Wellbutrin XL®) to the formulary was approved. The Formulary Drug Check List was completed.

cetirizine (Zyrtec®) - presented by Dr. Mican (developed by Jennifer Almarez, pre-pharmacy student and Angela Campbell, Pharm.D.)

Cetirizine is an active, human metabolite of hydroxyzine. It selectively binds peripheral histamine H1 receptors, competitively inhibiting the actions of histamine with no measureable affinity for histamine H2 receptors in *in vitro* studies. Unlike similar first generation H1-antagonists, cetirizine has a hydrophilic, carboxyl tail that effectively decreases CNS penetration resulting in minimal anticholinergic effects. While the mechanisms are unclear, cetirizine has also been shown to interfere with late phase inflammatory mediators. Cetirizine is indicated for the treatment and management of symptoms of seasonal/perennial allergic rhinitis and chronic urticaria in adults and children as young as 6 months of age. For adults and children over 6 years old, the initial recommended dose is 5 mg or 10 mg as a single dose depending on symptom severity. Cetirizine is contraindicated in patients with hypersensitivity to cetirizine or hydroxyzine. The most commonly reported adverse reaction in adults older than 12 years is somnolence. Cetirizine is available generically and is a commonly used non-formulary agent.

Following discussion, on motion of Dr. Becker, seconded by Ms. Chadwick, the request to add cetirizine (Zyrtec®) to the formulary was approved. The Formulary Drug Check List was completed.

The Committee discussed the addition of the combination of cetirizine and pseudoephedrine (Zyrtec D®) to the formulary. Pseudoephedrine is already on the Formulary. **Following discussion, on motion of Dr. Ward, seconded by Ms. Chadwick, the request to add cetirizine/pseudoephedrine (Zyrtec-D®) to the formulary was approved.** The Formulary Drug Check List was completed

esomeprazole (Nexium®) - presented by Dr. Mican (developed by Mina Mehvar, Pharmacy Intern and Lisa Mican Pharm.D.)

Esomeprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H^+/K^+ - ATPase in the gastric parietal cell. The S- and R-isomers of omeprazole are protonated and converted in the acidic compartment of the parietal cell forming the active inhibitor, the achiral sulphenamide. Esomeprazole is the S-isomer of omeprazole. By acting specifically on the proton pump, esomeprazole blocks the final step in acid production, thus reducing gastric acidity. The effect is dose-related up to a daily dose of 20 mg to 40 mg and leads to inhibition of gastric acid secretion. Esomeprazole is indicated for the treatment o gastroesophageal reflux disease (GERD), risk reduction of NSAID- associated gastric ulcer, *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence and pathological hypersecretory conditions including Zollinger-Ellison Syndrome. The cost of esomeprazole is 2.25 to 2.39 times more expensive than lansoprazole (Prevacid®), 12.8 to 29 times more expensive than omeprazole (Prilosec®) and is 1.9 times more expensive than pantoprazole (Protonix®). It was noted that some of the Medicare Part D plans used at the State Supported Living Centers will pay for esomeprazole but not other proton pump inhibitors.

Following discussion, on motion of Dr. Becker, seconded by Ms. Chadwick, the request to add esomeprazole (Nexium®) to the formulary was approved as a reserve drug. The Formulary Drug Check List was completed. The reserve criteria will be for patients who have Medicare Part D coverage for esomeprazole.

guaifenesin/codeine (Robitussin AC®) - presented by Dr. Richards (developed by Sonya Guerrero, Pharmacy Student and Robyn Howard, Pharmacy Student)

Codeine works as an antitussive through suppression of the cough reflex by directly affecting the cough center in the medulla. It also appears to have a drying effect on respiratory tract mucosa and apparently increases the viscosity of bronchial secretions. Guaifenesin works by thinning bronchial secretions and increasing sputum volume, thereby promoting lower respiratory tract drainage and removal of mucus. Codeine/guaifenesin is indicated for cough due to minor throat and bronchial irritation. The dose is 5 to 10 ml (codeine 10 to 20 mg/guaifenesin 100 to 200 mg) orally every 4 to 6 hours, not to exceed 60 ml/24 hours.

Following discussion, on motion of Dr. Becker, seconded by Ms. Millhollon, the request to add guaifenesin/codeine (Robitussin AC®) to the formulary was approved. The Formulary Drug Check List was completed. Due to the potential abuse issue with the codeine, it was recommended that unit dose cups be utilized if possible and if not available that oral syringes be used to measure the dose to be administered.

levalbuterol (Xopenex®) - presented by Dr. Mican (originally developed by Sharon Tramonte, Pharm.D. and updated by Mina Mehvar, Pharmacy Intern and Lisa Mican, Pharm.D.)

Levalbuterol is the (R)-enantiomer of (racemic) albuterol. It is an inhaled $beta_2$-adrenergic agonist. Activation of $beta_2$-adrenergic receptors on airway smooth muscle leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic AMP. This increase in cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation. Levalbuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Levalbuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway. While it is recognized that $beta_2$-adrenergic receptors are the predominant receptors on bronchial smooth muscle, data indicate that there is a population of $beta_2$-receptors in the human heart that comprise between 10% and 50% of cardiac beta-adrenergic receptors. The precise function of these receptors has not been established. However, all beta-adrenergic agonist drugs can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or electrocardiographic changes. Results from an *in vitro* study of binding to human beta-adrenergic receptors demonstrated that levalbuterol has approximately 2-fold greater binding affinity than racemic albuterol and approximately 100-fold greater binding affinity than (S)-albuterol. Levalbuterol is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease. In comparing the cost of levalbuterol to albuterol, levalbuterol inhaler is 113 times more expensive than albuterol inhaler and the levalbuterol inhalation solution is 10.9 times more expensive than the albuterol solution.

Following discussion, on motion of Dr. Ward, seconded by Dr. Becker, the request to add levalbuterol (Xopenex®) to the formulary was denied.

megestrol (Megace®) - presented by Dr. Richards (developed by Regina Tabor, RPh)

Megestrol is a synthetic derivative of the naturally occurring steroid hormone progesterone. Several investigators have reported on the appetite enhancing properties of megestrol and its possible use in cachexia. The precise mechanism by which megestrol produces effects in anorexia and cachexia is unknown at the present time. Megestrol is indicated for the treatment of anorexia, cachexia, or an unexplained, significant weight loss in patients with a diagnosis of acquired immunodeficiency syndrome (AIDS). In the Hospital setting it is being used as adjunctive therapy in the treatment of tuberculosis. The initial dose in the treatment of HIV-related cachexia is 800 mg/day. Doses of 400 and 800 mg/day were found to be clinically effective.

Following discussion, on motion of Dr. Becker, seconded by Dr. Ward, the request to add megestrol (Megace®) to the formulary was approved. The Formulary Drug Check List was completed.

Olanzapine pamoate (Zyprexa® Relprevv™)

At the previous meeting, the request to add olanzapine pamoate to the Formulary was tabled until additional information could be obtained from the outpatient clinics. Dr. Becker contacted the medical directors in order to determine if the clinics would use olanzapine pamoate. The overall response was that it would not be used due to the observation period required for the drug. Dr. Richards contacted the hospital clinical directors and a couple responded that they thought that the drug should be available for use for those patients that required a long acting

injection and who have responded to olanzapine. Currently a couple of hospitals have used olanzapine pamoate. The question arose regarding the observation requirement and who could complete the observation. The credentials of the individual completing the observation are vague. One hospital is using licensed vocational nurses to complete the observation. The issue of court compelled patients was discussed. As part of the Risk Evaluation and Mitigation Strategy (REMS), patients must sign consent for each injection. If a patient is court compelled the question arose as to whether or not they are required to sign consent for the injection. Dr. Heidel noted her facility has used it in court compelled patients and the manufacturer has accepted the court order instead of the consent. The Committee discussed that due to the requirements needed to use this drug, that the use of this drug would be limited.

Following discussion, on motion of Dr. Becker, seconded by Dr. Ward, the request to add olanzapine pamoate (Zyprexa® Relprevv™) to the formulary was approved as a reserve drug. The Formulary Drug Check List was completed. The following criteria were established for the use of olanzapine pamoate:

1. Written approval by the Hospital Clinical Director and the local mental health authority clinical director prior to initiation of therapy with olanzapine pamoate
2. Compliance with the Risk Evaluation and Mitigation Strategy (REMS)

For the written approval, the Committee will develop a standardized form that can be used to indicate approval. Once approved, the prescriber can communicate this approval to the pharmacy by adding the approval information in the medication order.

New Gen Medication Monitoring Tool for Clinical Directors

Dr. Race discussed the tools that the clinical directors are now receiving to use as quality control measures. The clinical directors are being provided with data that shows the cost of new gen medications by unit as well as by doctors. In addition, they are receiving data to show the comparison with the other hospitals. This data can assist the clinical directors in monitoring the cost of new gen medications. Currently 65% to 75% of patients in the hospitals are on new gen medications. New gen medications account for approximately 75% of the drug budget for the Hospital Section. This data is being provided to the clinical directors and it will be up to the clinical directors to decide how the data is used at their facility. This information is being obtained from WORx™, so eventually, the State Supported Living Centers may consider using the same information. The Committee endorsed the sharing of this data with the clinical directors as a monitoring tool.

Asenapine (Saphris®) Review

Asenapine was added to the Formulary about six months ago. Since it was a newly marketed drug, the Committee is reviewing its adverse drug reactions and medication errors within the agencies. Dr. Richards contacted the pharmacy directors to obtain this information. It appears that asenapine has had limited use within the State Hospitals and State Supported Living Centers. One medication error was reported. In this case, it appears that iloperidone (Fanapt®) was being confused with asenapine. Adverse drug reactions reported include possible drug rash and neutropenia (MedWatch to be submitted in the near future). A couple of patients have had the drug discontinued due to lack of effect. With the minimal use of asenapine, the Committee recommended that it be reviewed for adverse drug reactions and medication errors in six months.

Rosiglitazone (Avandia®) Removal from Formulary

At the last meeting, it was recommended that rosiglitazone be removed from the Formulary. No facility requested that the drug remain on Formulary. Therefore, rosiglitazone will be removed from the Formulary.

The Joint Commission – Multi-dose vials

The Joint Commission published an update on expiration dates for multi-dose vials. USP and APIC now recommend that opened or punctured multi-dose vials be used for no more than 28 days unless the manufacturer specifies otherwise. Therefore, The Joint Commission requires a 28-day expiration date for multi-dose vials from the date of opening or puncture, unless the manufacturer specifies otherwise. The Joint Commission bases the 28-day time frame on the fact that manufacturers are required by law to test the effectiveness of the bacteriostatic agent used in the multi-dose vial for a period of 28 days. It was noted that for multi-dose vials that utilize flip tops that once the flip top is removed, the 28 day expiration dating will need to be enforced whether or not the vial has been punctured. This information was previously distributed to the State Hospital Pharmacy Directors.

Non-Formulary Process

Prior to the implementation of WORx, the non-formulary process required that a Non-Formulary Drug Justification form be completed for each new medication order. The request had to be approved by the Clinical Director and the Pharmacy Director. It was up to the pharmacy personnel to identify which products were non-formulary and initiate the non-formulary process. During this time, it was believed that the data was incomplete. With the implementation of WORx™, the number of non-formulary medication orders and their identification are obtained through a separate reporting mechanism. This information is aggregated and presented to this Committee. With this mechanism, the Committee is reviewing reliable data; however, the approval process is not being used. With the old system, it was reported that it was rare that a non-formulary request was disapproved. With the implementation of computerized prescriber order entry in CWS, the State Hospital physicians are notified immediately when a non-formulary drug is requested and a justification is required. However, the justification entered does not have to justify the prescribing of the product as entering a single letter will let the prescriber complete the justification process. In WORx™, the pharmacist has to enter a justification for validating or entering a medication order for a non-formulary drug.

Dr. Richards noted that reports have been developed for WORx™ that can identify patients receiving non-formulary drugs by date range as well as physician specific reports. The original intent was to have the physician specific report substitute for the non-formulary approval process. However, in attempting to use it, it became quite cumbersome to run the reports on a routine basis.

The Committee recommended that each facility be encouraged to run the physician specific report on a monthly basis and share it with the clinical/medical director. The clinical/medical director is encouraged to use the report as part of the privileging and/or evaluation process of the physician. In addition, it was recommended that the summary sheet for the "Quarterly Non-Formulary Drug Reports Received" be shared with the pharmacy directors and clinical/medical directors.

New Dosage Strengths

It was recommended to add pantoprazole (Protonix®) 40 mg suspension packets, enoxaparin (Lovenox®) 150 mg injection and ferrous sulfate 160 mg to the Formulary. On a motion of Ms. Millhollon, seconded by Ms. Chadwick, the recommendation to add these dosage strengths to the Formulary was approved.

It was requested that the non-formulary status of the fenofibrate products be reviewed. At the time of addition to the Formulary, it was recommended that the fenofibrate nanocrystallized products not be added due to costs. Fenofibrate micronized and fenofibrate products were added to the Formulary. This has lead to confusion as to what products are or are not on Formulary. An updated price listing of the fenofibrate products was reviewed by the Committee. Due to the changes in pricing, on a motion of Dr. Ward, seconded by Ms. Chadwick, it was recommended that all fenofibrate products be added to Formulary.

Possible TAC Change

The Committee is still pursuing the option of changing the TAC regarding the requirements for the completion of an evaluation for movement disorders for typical and atypical antipsychotics. At this time, a Work Group has not been formed.

FDA Drug Safety Communications

The FDA has issued the following safety communications that may have impact on our facilities.

Ortho-McNeil-Janssen and the FDA notified healthcare professionals of changes to the Warnings section of the prescribing information for tramadol (Ultram®), a centrally acting synthetic opioid analgesic indicated for the management of moderate to moderately severe chronic pain. The strengthened Warnings information emphasizes the risk of suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs and also warns of the risk of over dosage. Tramadol-related deaths have occurred in patients with previous histories of emotional disturbances or suicidal ideation or attempts, as well as histories of misuse of tranquilizers, alcohol, and other CNS-active drugs. Tramadol may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs that cause central nervous system depression. Serious potential consequences of over dosage with tramadol are central nervous system depression, respiratory depression and death. Tramadol has mu-opioid agonist activity, can be abused and may be subject to criminal diversion.

The FDA is revising the prescription and over-the-counter (OTC) labels for a class of drugs called proton pump inhibitors to include new safety information about a possible increased risk of fractures of the hip, wrist, and spine with the use of these medications. Proton pump inhibitors work by reducing the amount of acid in the stomach. Esomeprazole (Nexium®), dexlansoprazole (Dexilant®), omeprazole (Prilosec®), omeprazole/sodium bicarbonate (Zegerid®), lansoprazole (Prevacid®), pantoprazole (Protonix®), rabeprazole (Aciphex®), and naproxen/esomeprazole (Vimovo®) are available by prescription to treat conditions such as gastroesophageal reflux disease (GERD), stomach and small intestine ulcers, and inflammation of the esophagus. Prilosec® OTC, Zegerid® OTC, and Prevacid® 24HR are sold over-the-counter (OTC) for the treatment of frequent heartburn. The new safety information is based on the FDA's review of several epidemiological studies that reported an increased risk of fractures of the hip, wrist, and spine with proton pump inhibitor use. Some studies found that those at greatest risk for these fractures received high doses of proton pump inhibitors or used them for one year or more. The majority of the studies evaluated individuals 50 years of age or older and the increased risk of fracture primarily was observed in this age group. While the greatest increased risk for fractures in these studies involved people who had been taking prescription proton pump inhibitors for at least one year or who had been taking high doses of the prescription medications (not available over-the-counter), as a precaution, the "Drug Facts" label on the OTC proton pump inhibitors (indicated for 14 days of continuous use) also is being revised to include information about this risk. Healthcare professionals and users of proton pump inhibitors should be aware of the possible increased risk of fractures of the hip, wrist, and spine with the use of proton pump inhibitors, and weigh the known benefits against the potential risks when deciding to use them.

The FDA has added a *Boxed Warning* to the label for propylthiouracil, a drug used to treat hyperthyroidism, to include information about reports of severe liver injury and acute liver failure, some of which have been fatal, in adult and pediatric patients using this medication. The new warning also states that for patients being started on treatment for hyperthyroidism it may be appropriate to reserve use of propylthiouracil for those who cannot tolerate other treatments such as methimazole (Tapazole®), radioactive iodine or surgery. In addition, due to the occurrence of birth defects that have been observed with the use of methimazole during the first trimester of pregnancy, propylthiouracil may be the treatment of choice during and just before the first trimester of pregnancy. Propylthiouracil has been shown to be effective in reducing thyroid hormone levels and decreasing symptoms associated with hyperthyroidism. However, to help patients understand the known benefits and potential risks of this medication, as part of a

Risk Evaluation and Mitigation Strategy (REMS), the FDA is requiring that a *Medication Guide* be given to every patient filling a prescription for propylthiouracil. The recommendations in the *Boxed Warning* and the requirement of a *Medication Guide* are based on FDA's review of post-marketing safety reports of propylthiouracil as well as meetings with the American Thyroid Association, the National Institute of Child Health and Human Development, and the pediatric endocrine clinical community. Healthcare professionals should be aware of this new safety information in the drug label and follow the recommendations outlined above.

The FDA notified healthcare professionals and patients regarding an update to the Warnings, Information for Patients, and Dosage and Administration sections of the Prescribing Information of naltrexone extended release injection (Vivitrol®) in order to strengthen language regarding the risk of injection site reactions based on postmarketing reports that had been received prior to June 2009. The FDA requires that a Medication Guide, which communicates this and other important information about treatment, be provided to all patients. Healthcare professionals should also counsel patients about the risks and benefits of naltrexone extended release injection before an initial prescription, including those risks and benefits set forth in the new Medication Guide and Prescribing Information, and should ensure that patients understand these risks.

Quarterly Non-Formulary Drug Justification Report

For the third quarter of fiscal year 2010, all facilities reported use of non-formulary agents. The following were the top non-formulary agents that were prescribed:

Quetiapine extended release (Seroquel XR®)
Cetirizine (Zyrtec®)
Esomeprazole (Nexium®)
Propoxyphene with acetaminophen (Darvocet®)
Levalbuterol (Xopenex®)
Brompheniramine/phenylephrine (Dimetapp®)

For the top non-formulary requests, cetirizine was added to the Formulary. In addition, benzonatate, bupropion XL, guaifenesin/codeine and megestrol were also added. Esomeprazole was added as a reserve drug. Levalbuterol was declined at this meeting due to cost. Previously, quetiapine extended release and propoxyphene with acetaminophen were declined.

Drug Formulary Sectional Review- Dermatologicals

Dr. Mican provided the review on the agents in the Dermatological Section. See Attachment B.

In reviewing the Scabicides and Pediculicides, Dr. Mican suggested the following minor changes to the Formulary listing of products:

- Add Acticin® as a brand name for permethrin 5% cream
- Add Pronto® instead of A-200® as a common trade name for pyrethins/piperonyl butoxide
- Include the strength for the listing of RID®/Pronto® - pyrethins 0.33%/piperonyl butoxide 4%

No formulary additions or deletions were recommended.

For the corticosteroids, Dr. Mican noted that products from each potency groups are included in the formulary.

- Ultra-High Potency – betamethasone dipropionate augmented formulations; clobetasol
- High Potency – betamethasone dipropionate non-augmented formulations; fluocinonide
- Medium Potency – betamethasone valerate; fluocinolone; triamcinolone
- Low Potency – desonide; hydrocortisone

Dr. Mican made the following recommendations for the corticosteroid section:

- Add betamethasone dipropionate 0.05% lotion
- Make augmented betamethasone dipropionate as a reserve drug using the same criteria as for clobetasol since both are ultra-high potency
- Delete clobetasol shampoo from the Formulary due to cost as compared to the topical scalp solution

The following minor formulary listing changes were recommended:

- Add Cormax® and Clobex® as common branded names for clobetasol
- Change clobetasol scalp application 0.05% to solution, topical scalp application
- Add Lokara® as a common branded name for desonide
- Add Derma-Smooth/FS® as a common brand name for fluocinolone for body and scalp oil and Capex® as a branded name for the shampoo
- List the corticosteroids by potency

On a motion of Ms. Chadwick, seconded by Dr. Ward, the recommendations for the corticosteroid section were approved.

For the local anesthetics, Dr. Mican made the following recommendations:

- Delete benzocaine lotion from the Formulary as it is no longer available
- Add benzocaine paste 20% (Orabase-B®) to the Formulary
- Add lidocaine 5% patch (Lidoderm®) to the Formulary

On a motion of Dr. Ward, seconded by Ms. Millhollon, the recommendations for the local anesthetics section were approved.

Dr. Mican did not have any recommendations for the emollient section, the skin protectants, tar-containing agents, or rubs and liniments

For the ointment and lotion bases, Dr. Mican recommended to add Vaseline topical lip therapy. On a motion of Dr. Ward, seconded by Ms. Millhollon, the recommendation was approved.

For the keratolytics, Dr. Mican recommended the addition of urea 10%, 20% and 40% cream, 10% and 40% lotion and 10% shampoo to the Formulary. On a motion of Ms. Chadwick, seconded by Dr. Becker the recommendation was approved.

For the Miscellaneous Dermatologicals section, Dr. Mican had recommended that pimecrolimus (Elidel®) and tacrolimus (Protopic®) be deleted or moved to the reserve section due to the potential risk of cancer. The Committee discussed that the use of these products are minor within the agencies and that they are rarely prescribed without consultation with a dermatologist. Therefore, the recommendation was not approved.

Sectional Review for Next Meeting

A decision regarding the next sectional review will be made at a later date.

Other Issues

The following information was shared with the Committee members:

A recent study published May 20 in the British Medical Journal suggested that diabetics who take metformin (Glucophage®) over the long term should get their vitamin B-12 levels checked regularly to see if they are developing a vitamin deficiency. In this study, researchers observed that patients on metformin treatment for type 2 diabetes had a hazard ratio of 5.5 relative to placebo for developing vitamin B12 deficiency while on metformin. It was noted that the decrease was not a transitory phenomenon, but persists and grows over time. The authors suggested that in order to prevent a vitamin B-12 deficiency, regular measurement of vitamin B-12 concentrations during long term metformin treatment should be considered.

A recent GAO study showed that nearly all of the herbal dietary supplements tested in a Congressional investigation contained trace amounts of lead and other contaminants, and some supplement sellers made illegal claims that their products can cure cancer and other diseases. The levels of heavy metals (mercury, cadmium and arsenic) did not exceed thresholds considered dangerous. About half of them did contain pesticide residues that appeared to exceed legal limits.

After analyzing data from eight published cohorts, Dutch researchers determined that valproic acid (Depakene®) or divalproex (Depakote®) in the first trimester of pregnancy significantly increased the risk of six types of birth defect. These included spina bifida, atrial septal defect, cleft palate, hypospadias, polydactyly and craniosynostosis. While valproic acid/divalproex was associated with a higher relative risk of these six birth defects, the absolute risk of having a baby with any of the defects remains small.

In a new study, the diabetes drug rosiglitazone (Avandia®) may have led to thousands of heart problems that could have been prevented if patients had been using a different medication. In the near future, the FDA is scheduled to evaluate the safety of rosiglitazone. Rosiglitazone was removed from the Formulary earlier in this meeting.

Two studies published in the June issue of Ophthalmology have raised red flags about visual problems linked to selective serotonin reuptake inhibitors (SSRIs) in elderly patients and to long-term use of amantadine (Symmetrel®) by patients with Parkinson's disease. For SSRIs, it found that these drugs were associated with an increase in cataract risk by up to 39% in people older than 65 years. For amantadine, it showed corneal damage linked to the use of amantadine is dependent on the cumulative dose received.

A new case-controlled study published in the *Canadian Medical Association Journal (May 31)* showed that pregnant women who take antidepressants have a 68% increased risk of miscarriage compared with those who do not take the medications. SSRIs and SNRIs, especially paroxetine and venlafaxine, were associated with an increased risk, as were higher daily doses of either antidepressant. According to the

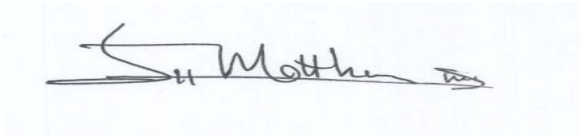
authors, up to 3.7% of women will use antidepressants at some time during their first trimester of pregnancy. Analyzing data on 5,124 women between the ages of 15 and 45 from the Quebec Pregnancy Registry who had clinically verified miscarriages between 1998 and 2003, investigators found that 5.5% of the women had taken antidepressants during their pregnancy, compared with 2.7% of the matched control patients. Several limitations in the study were reported, but the data add to the growing body of literature that indicates increased caution when using antidepressants during pregnancy.

Next Meeting Date

The next meeting was scheduled for October 15, 2010.

Adjourn

There being no further business, the meeting was adjourned at 2:05 p.m.



Approved: _____
Jeff R. Matthews, M.D., Chairman

Attachments
Attachment A – New Drug Applications
Attachment B - Dermatological Agents Sectional Review

Minutes Prepared by:
Ann L. Richards, Pharm.D., BCPP