

DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
January 29, 2010

The Executive Formulary Committee convened on Friday, January 29, 2010 in Conference Room 295 - CO Building 2. The meeting was called to order by Dr. Matthews, Chair at 9:53 a.m.

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

Introductions

No introductions were needed for the meeting.

Approval of Minutes of September 25, 2009

On a motion of Dr. Heidel, seconded by Ms. Chadwick, the minutes of the September 25th meeting were approved as previously distributed.

Conflict of Interest Disclosure Forms

Each Committee member in attendance of the meeting presented their conflict of interest disclosure form for review by the Committee. No conflicts were reported.

Adverse Drug Reaction Reports

The Executive Formulary Committee received ten adverse drug reaction reports. In the first case, a 40 year old African American male was admitted to a state hospital for treatment of schizoaffective disorder, bipolar type on July 21st. The patient has a history of substance abuse, marijuana. The patient has medical diagnoses of hypertension, anemia and has displayed choreic movements in the past. Upon admission, the patient was taking risperidone (Risperdal®) 3 mg in the

morning and 4 mg at bedtime, divalproex (Depakote®) ER 500 mg at bedtime and clonidine (Catapres®) 0.2 mg at bedtime. In addition, the patient reported receiving a risperidone (Risperdal®) Consta™ injection prior to admission. Labs were within normal limits, except for RBC 3.87 M/mm³, Hgb 12.0 g/dl, Hct 35%, RDW 14.7%, ALT 8 U/L and Alk Phos 35 U/L. His valproic acid level was 105.5 mcg/ml. The risperidone dose was changed to 4 mg at bedtime on August 14th and was continued until September 8th. In addition, aripiprazole (Abilify®) was started and increased to 30 mg/day on August 21st. Divalproex was increased to 2,500 mg/day on August 28th. On September 8th, the patient was observed to have an erection lasting most of the morning. Priapism was suspected and the patient was given terbutaline (Brethine®) 5 mg orally with instructions that he should be transported to the local emergency department if resolution of the erection is not obtained in 2 hours. Priapism did not resolve and the patient was transferred to a medical hospital and he was given terbutaline 10 mg orally and the treatment was successful. The patient was transferred back to the state hospital. The risperidone was discontinued and the patient continued on aripiprazole and divalproex. He had a subsequent episode of priapism on September 18th while off of risperidone. The patient received terbutaline 10 mg orally with resolution. The aripiprazole dose was reduced to 20 mg/day and the patient did not have any further episodes.

In the next adverse drug reaction report, a 67 year old male was admitted to a state hospital on April 13th with the diagnoses of schizoaffective disorder, bipolar type and dementia NOS, borderline intellectual functioning, glaucoma, hypothyroidism and hyperlipidemia. The patient was started on multivitamin/mineral, levothyroxine (Synthroid®) 25 mcg, simvastatin (Zocor®) 20 mg and divalproex (Depakote®) 1,500 mg/day. The divalproex was increased to 2,000 mg/day and paliperidone (Invega®) 3 mg was prescribed on June 1st and donepezil (Aricept®) 5 mg/day was added on June 2nd. The paliperidone was increased to 6 mg on June 10th but due to an increase in parkinsonian symptoms the dose was decreased to 3 mg/day on June 19th and was discontinued on June 26th. Lisinopril (Zestril®) 5 mg and fluticasone nasal spray (Flonase®) was started on June 19th. On July 6th the dose of donepezil was increased to 10 mg/day. Acetazolamide (Diamox®) 250 mg was initiated on July 13th for the treatment of normal pressure hydrocephalus as noted on MRI. Acetazolamide was initiated as a lumbar puncture and removal of 400 ml of CSF failed to improve patient's symptoms of normal pressure hydrocephalus (confusion, urinary and fecal incontinence and other neurologic symptoms). The patient was noted to be slightly more confused and lethargic. An ammonia level on July 16th was 42 mcg/dl. Sertraline (Zoloft®) 25 mg was started on July 17th and was increased to 50 mg on August 6th and then to 100 mg on August 18th for the treatment of depressive symptoms. Carbidopa/levodopa (Sinemet®) 25 mg/100 mg in the morning was started on July 25th and increased on the 27th to twice a day and again on the 29th to three times a day for the treatment of suspected Parkinson's disease. Divalproex was decreased to 500 mg in the morning and 1,000 mg at bedtime. In mid-August, the patient's oral intake began to decline and the patient stated he was not hungry. He had increased weakness and would rest on the floor and would slip from the recliner to the floor. He was sent to the medical clinic for further evaluation and was noted to have gapped metabolic acidosis secondary to acetazolamide. On August 13th, his CMP was within normal limits except BUN 25 mg/dl, CO₂ 16 mmol/L, Cl 109 mmol/L, potassium 3.5 mmol/L, sodium 139 mmol/L, creatinine 1.4 mg/dl, glucose 105 mg/dl. After consultation with a neurologist, the acetazolamide was discontinued on August 19th and the patient's metabolic acidosis normalized.

A 53 year old African American male with a history of bipolar disorder, seizures and diabetes was transferred to a state hospital on July 16th after becoming very aggressive, agitated and combative despite six weeks of treatment. Upon admission, he was taking metformin (Glucophage®) 1,500 mg, glipizide (Glucotrol®) 10 mg, insulin NPH/regular 70/30 15 units, lisinopril (Zestril®) 2.5 mg, escitalopram (Lexapro®) dose unknown, carbamazepine (Tegretol®) 600 mg and risperidone (Risperdal®) 2 mg daily. The escitalopram and insulin were not continued. Instead the patient was started on sitagliptin (Januvia®) 100 mg, insulin glargine (Lantus®) 10 units and an insulin sliding scale. A basic metabolic panel completed on July 17th showed a low sodium level of 128 mmol/L. On July 21st the ammonia level, iron panel and TSH were within normal limits. The carbamazepine level was 5.6 mcg/ml on July 27th. On August 5th, the insulin glargine was increased to 15 units. On August 20th, the serum sodium was 125 mmol/L and a CBC obtained on August 21st showed Hgb 9.8 g/dl and Hct 28.8%. As a result of the unexplained anemia and persistent hyponatremia, the carbamazepine was tapered and divalproex was initiated. On August 22nd, the patient was found unresponsive at 7:19 am with a FBS of 27 mg/dl. Glucagon 1 mg IM was administered and EMS was contacted for transport to a medical hospital. The patient reported a possible postictal state with hypoglycemic episode. Serum sodium drawn after the hypoglycemic episode was 124 mmol/L. Upon return from the medical hospital, the patient was on risperidone 2 mg, carbamazepine 600 mg, metformin 1,500 mg and insulin glargine 10 units. Fluid restrictions were implemented. On September 10th, levetiracetam (Keppra®) was initiated with the hopes of tapering and discontinuing carbamazepine. The sodium level continued to fall and the patient complained of feeling weak and tired. Sodium chloride 1 gm three times a day was added to his drug regimen. On September 26th the sodium was 118 mmol/L and the patient needed more assistance walking, was more confused, lethargic, unable to follow simple commands, and oriented to person only. The patient was sent back to the medical facility for further evaluation and

treatment. The dose of carbamazepine was further reduced and eventually discontinued on October 3rd and fluid restriction continued. On October 5th, the serum sodium was 132 mmol/L. Oral sodium chloride which was discontinued in the medical facility was resumed at 1 gram twice a day. The patient was more alert and more active. The patient continued to be more alert with normal gait and ambulating with good coordination. The sodium chloride was increased to 1 gram three times a day and fluid restriction was continued. Sodium levels improved significantly with the discontinuation of carbamazepine.

A 26 year old Ethiopian male was re-admitted to a state hospital on October 11th after being out about four days. Diagnoses at admission include schizoaffective disorder bipolar type, alcohol abuse and cannabis abuse. In addition, the patient had a right eye injury. The patient continued on fluphenazine (Prolixin®) and carbamazepine (Tegretol®), which had been initiated during the previous hospitalization. The patient had multiple episodes of agitation and aggression during his stay necessitating changes to his medication regimen and administration of emergency medications. Notable additions to the patient's medication regimen included clonazepam (Klonopin®) 1 mg twice a day started on October 14th and increased to 2 mg twice a day on the 19th and quetiapine (Seroquel®) 300 mg twice a day initiated on October 20th. The patient had tolerated all medications administered until October 20th at 12:40 pm when the patient was noted to have difficulty breathing (labored respirations), not responding to verbal commands, dilated pupils, blood pressure was 120/70 mmHg, pulse 127 beats/minute, RR 20 breaths/minute, and oxygen saturation 43%. The patient was transferred to a local medical hospital. At the time of transfer, the patient's vitals were blood pressure 112/65 mmHg, pulse 110 beats/minutes, temperature 95.9 degrees, RR 20 breaths/minute and oxygen saturation 86%. Emergency medication administered during the previous 36 hours included:

October 19th

12:50 am – lorazepam (Ativan®) 2 mg oral

11:18 am – lorazepam 2 mg IM

11:28 am – olanzapine (Zyprexa®) 10 mg IM

October 20th

2 am – ziprasidone (Geodon®) 20 mg IM and lorazepam 2 mg IM

9:45 am – quetiapine 300 mg oral

1:20 pm – quetiapine 300 mg oral

4:25 pm – olanzapine Zydis™ 15 mg oral and lorazepam 2 mg oral

At the medical hospital, the patient was intubated and then placed on a ventilator. Oxygen was administered and the patient was extubated once his condition was stabilized. Upon return to the state hospital, the patient was placed on fluphenazine 5 mg twice a day and diphenhydramine 50 mg at bedtime. The patient was also noted to have hyponatremia and SIADH which is why the carbamazepine was discontinued.

A 21 year old female was admitted to a state hospital on August 24th for the treatment of bipolar disorder. The diagnosis was later changed to major depressive disorder. The patient had no significant medical condition except for periodic migraine headaches and chronic back pain. The patient has a history of substance abuse including Ecstasy and methamphetamines and reported her last use as being approximately one week prior to admission although a urine drug screen was positive for amphetamines. The patient was not noted to be on any medications prior to admission. On August 24th, the patient was administered aripiprazole (Abilify®) 10 mg and trazodone (Desyrel®) 75 mg. On August 25th at 12:50 am the patient received clonazepam (Klonopin®) 2 mg for insomnia. On August 25th, the patient's labs were within normal limits except for BUN 5 mg/dl, total protein 5.2 g/dl, albumin 3.2 g/dl, HDL 32 mg/dl, RBC 4.0 M/mm³. Later that morning, the patient fell and became nonresponsive when approaching the medication cart. Her skin was cool and clammy. Blood pressure was 73/38 mmHg, pulse 88 beats/minute and respiratory rate was 14 breaths/min. The patient was not responding to stimuli, so EMS was called for transportation to a medical facility. Tests from the medical facility showed a positive urine drug screen (amphetamines), troponin I 0.04 ng/ml, CK-MB 0.5 ng/ml, total CK 25 IU/L. Her EKG was irregular and had bradycardia. In addition, she was noted to have hypotension during her hospitalization. The patient was administered fluids and the aripiprazole was discontinued. The patient continued on trazodone and was also given sertraline (Zoloft®). The patient was diagnosed with vasovagal reflex likely due to initiation of a new psychotropic medication and arrhythmia possible due to amphetamine use. The patient returned to the state hospital on August 26th in the afternoon. The patient again complained of feeling badly at 10:10 pm on the same day she returned to the state hospital. Trazodone 50 mg was administered and the patient reported to be feeling better after about 10 minutes. The patient did not experience any other syncopal episode at the state hospital. The patient was discharged on sertraline and hydroxyzine (Atarax®).

A 43 year old male was admitted to a state hospital on August 27th for the treatment of schizophrenia. The patient also had diabetes and heart disease and is status post coronary artery bypass graph (CABG). A CBC was obtained on August 20th with the plan to start clozapine (Clozaril®). However, the patient became toxic on lithium resulting in discontinuation of all psychiatric medication. On September 8th, clozapine was initiated and titrated to a dose of 150 mg/day on September 21st. On September 21st, the patient showed signs suggestive of myocarditis (tachycardia, fever, one plus edema, positive jugular distension, ESR 117 mm/hour (normal is 0 to 20), brain natriuretic peptide (BNP) 539 pg/ml (normal is 0 to 100) and EKG changes). The clozapine was discontinued. The patient had increased monitoring and did recover from the episode.

A 58 year old African American male was admitted to a state hospital from a state supported living center on September 17th with a diagnosis of schizophrenia, undifferentiated type. The patient has mild mental retardation and several medical conditions including chronic constipation, atrial fibrillation and sick sinus syndrome with pacemaker placement, heart failure/cardiomyopathy with 20% EF, allergic rhinitis, hypertension, GERD and anemia. The patient developed pancytopenia and severe neutropenia during his stay. At the time of admission, he was being treated with several medications including quetiapine (Seroquel®) 275 mg/day, divalproex (Depakote®) ER 500 mg/day, ziprasidone (Geodon®) 160 mg/day, thiothixene (Navane®) 5 mg/day, lisinopril (Zestril®) 40 mg daily, omeprazole (Prilosec®) 20 mg daily, diphenhydramine 100 mg/day, warfarin (Coumadin®) 2.5 mg daily, spironolactone (Aldactone®) 25 mg daily, loratadine (Claritin®) 10 mg daily, trazodone 100 mg at bedtime and polyethylene glycol powder (MiraLax®) 17 g daily. Admission labs obtained on September 18th showed valproic acid level of 67.6 mcg/ml, ammonia 25 mcg/dl, and the complete metabolic panel was within normal limits. The CBC with differential showed the following: WBC 3.2 K/mm³, RBC 4.09 M/mm³, hemoglobin 12 g/dl, hematocrit 36.2%, RDW 16.8%, ANC 1.8 K/mm³ and lymphocytes 0.8 K/mm³. The patient's protime was 11.6 seconds (normal is 8.8 – 10.4) and INR 1.23. Similar CBC and valproic acid level labs were observed on September 21st except the ANC dropped to 1.3 K/mm³. At that time, the thiothixene was discontinued and the ziprasidone dose was decreased to 120 mg/day and then discontinued on September 22nd. The trazodone was also discontinued on September 22nd. Warfarin was titrated to 4 mg due to subtherapeutic INR and enoxaparin (Lovenox®) 40 mg at bedtime was initiated temporarily due to the subtherapeutic INR (discontinued on October 1st). Quetiapine was increased to 300 mg/day on September 18th and again on September 22nd to 400 mg/day. On September 23rd a follow up CBC with differential showed WBC 3.0 K/mm³, RBC 4.41 M/mm³, hemoglobin 13 g/dl, hematocrit 38.7%, RDW 16.9%, platelet 110 K/mm³, ANC 1.5 K/mm³, absolute lymphocyte 0.9 K/mm³ with similar indices found on a repeat CBC on September 24th. Quetiapine was further increased to 500 mg/day on September 23rd and 600 mg on September 24th. CBC with differential on September 28th showed WBC 2.3 K/mm³, RBC 4.08 M/mm³, hemoglobin 12.3 g/dl, hematocrit 35.8%, RDW 16.7%, platelet 91 K/mm³, and ANC 0.2 K/mm³ (nadir). The RBC, WBC and platelet morphology were normal. Additional labs included valproic acid level 81.3 mcg/ml, INR 4.9 and protime 41.3 seconds. The divalproex was discontinued on September 28th and the warfarin dose was decreased to 3.5 mg. On October 1st a fecal occult blood was negative. On October 5th, the valproic acid level was 10.1 mcg/ml, WBC 3.0 K/mm³, RBC 4.27 M/mm³, hemoglobin 12.6 g/dl, hematocrit 37.5%, RDW 16.2%, platelet 103 K/mm³, and ANC 0.6 K/mm³. Again the RBC, WBC, and platelet had normal morphology and the protime was 18.1 seconds and INR was 2. The quetiapine dose was subsequently decreased to 500 mg/day. There was marginal improvement in the CBC with the discontinuation of divalproex and the dose reduction of quetiapine. The last CBC obtained prior to transfer back to the state supported living center was obtained on October 15th and showed WBC 2.7 K/mm³, RBC 3.72 M/mm³, hemoglobin 10.8 g/dl, hematocrit 32.3%, RDW 16.1%, ANC 1.1 K/mm³, and absolute lymphocyte 0.09 K/mm³. Records indicated the patient had a similar reaction to a previous exposure to divalproex at the supported living center, however, divalproex was reinitiated prior to transfer to the state hospital due to behavioral exacerbations.

A 14 year old white female was admitted to a state hospital on September 24th for suicidal ideation. Her diagnoses include bipolar disorder with psychotic features, anxiety disorder NOS and history of cannabis abuse. She has no known medical conditions. Prior to admission, she was taking risperidone (Risperdal®) 5 mg/day, divalproex (Depakote®) ER 1,000 mg, benztropine (Cogentin®) 4 mg/day, clonazepam (Klonopin®) 1.5 mg/day and hydroxyzine 50 mg every 6 hours as needed. The patient reported to the admitting physician that she had experienced breast leakage (possible galactorrhea) three weeks prior to admission while menstruating. Labs completed on September 25th were significant for negative serum pregnancy test, negative HIV and normal TSH. Serum prolactin level was 135.8 ng/ml (normal 2.8 – 29.2 ng/ml). The risperidone dose was decreased on September 25th to 2 mg/day and was further decreased to 1 mg/day on September 27th with the last dose being taken on September 27th. Quetiapine (Seroquel®) was initiated for psychosis and mood stabilization. A repeat prolactin level was obtained on October 5th and it was still elevated at 60.1 ng/ml. An additional prolactin level was obtained on October 12th was 16.5 ng/ml. The patient did not

experience any additional episodes of galactorrhea during her hospitalization.

Another 14 year old female was admitted to a state hospital on July 13th for the treatment off bipolar disorder, attention deficit hyperactivity disorder, oppositional defiant disorder and polysubstance abuse. She had no known medical conditions. Medications prior to admission include risperidone (Risperdal®) 4 mg/day, oxcarbazepine (Trileptal®) 300 mg/day and mixed amphetamine salts (Adderall®) XR 30 mg daily. Labs completed on July 14th were significant for negative serum pregnancy test, negative HIV, and normal TSH. All other labs were within normal limits. The risperidone dose remained unchanged. The oxcarbazepine and mixed amphetamine salts XR were discontinued on July 16th. Divalproex (Depakote®) ER was initiated on July 17th. On July 20th a screen for chlamydia was negative. Another pregnancy test was obtained since the patient had amenorrhea for four months. The second pregnancy test was also negative. On July 22nd, a prolactin level was obtained and it was 82.3 ng/ml (normal 2.8 – 29.2 ng/ml). Upon further questioning, the patient admitted to having galactorrhea in addition to the amenorrhea. The risperidone was tapered and quetiapine (Seroquel®) was initiated. A follow up prolactin level obtained on August 3rd was 18.6 ng/ml.

A 29 year old African American male was admitted to a state hospital on August 22nd for the treatment of schizophrenia, paranoid type. The patient has a history of alcohol and cannabis abuse as well as sickle cell anemia. After admission, the patient was noted as receiving risperidone (Risperdal®) 1 mg at 6:50 pm and a second dose at 8 pm. The patient refused the 8 am dose the next day due to a complaint of having a prolonged erection. The patient was sent to the medical clinic for further evaluation of prolonged erection and admission physical at 9:05 am. The physical exam notes indicate that the patient had an erection for approximately 10 hours so the patient was transferred to a local medical hospital for further evaluation and treatment. According to the records from the medical hospital, the risperidone was discontinued and the patient was given morphine and ketorolac (Toradol®) IV and was started on terbutaline (Brethine) 2.5 mg three times a day as needed for priapism. The patient was returned to the state hospital. Olanzapine (Zyprexa®) was started and the patient did not have any further episodes of priapism while hospitalized.

New Drug Applications

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

asenapine (Saphris®) - presented by Dr. Richards (developed by Dr. Stephen Saklad)

Asenapine is an atypical antipsychotic. It is a member of the chemical class dibenzo-oxepino pyrroles and is only distantly related to the chemical structures of other marketed antipsychotic agents. The mechanism of action remains unknown. It is thought that the efficacy of asenapine in schizophrenia is due to the combination of antagonist activity at central D₂ and 5-HT_{2a} receptor systems. The absolute bioavailability of sublingual asenapine is 35%. Doubling the dose from 5 mg to 10 mg BID, yields a less than linear (1.7 times) increase in AUC and C_{max}. Due to extensive first-pass metabolism, oral asenapine has <2% bioavailability. Swallowing the sublingual tablet will significantly decrease bioavailability. Intake of water within the first several (2 to 5) minutes after administration of an asenapine sublingual dose will result in a decrease in asenapine absorbed. Eating and drinking should be avoided for 10 minutes after sublingual administration. Asenapine is rapidly distributed into a large volume of distribution (20-25 L/kg) and is highly bound (95%) to plasma proteins, primarily albumin and α₁-acid glycoprotein. Asenapine's primary metabolic pathways are UGT1A4 (direct glucuronidation) and CYP1A2 (oxidation). Asenapine shares this pair of metabolic pathways with clozapine (Clozaril®) and olanzapine (Zyprexa®). In addition, CYP3A4 and CYP2D6 are minor metabolic pathways. Asenapine is a weak inhibitor of CYP2D6 and does not cause induction of CYP1A2 or CYP3A4. The terminal half-life is approximately 24 hours and steady-state is observed within 3 days after multiple-dose twice daily dosing. Asenapine is indicated for the acute treatment of schizophrenia and manic or mixed episodes associated with Bipolar I Disorder in adults. For schizophrenia, the dose is 5 mg twice a day administered sublingually. For bipolar disorder, the initial dose is 10 mg twice a day administered sublingually.

Following discussion, on motion of Dr. Ward, seconded by Ms. Millhollon, the request to add asenapine (Saphris®) to the formulary was approved. The Formulary Drug Check List was completed. Since this is a newly marketed drug, it will need to be reviewed in six months for adverse events and medication errors.

Dr. Richards presented the psychotropic audit criteria and guidelines for asenapine. Since there have been changes in

the indications, the current audit criteria and guidelines were updated. See Attachment B. On a motion of Dr. Heidel, seconded by Dr. Hood, the psychotropic audit criteria and guidelines for the atypical antipsychotics were approved.

bupivacaine (Marcaine®) and bupivacaine with epinephrine - presented by Dr. Richards (developed by Regina Tabor)

Bupivacaine is a local anesthetic. Local anesthetics block the generation and conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: 1) pain, 2) temperature, 3) touch, 4) proprioception, and 5) skeletal muscle tone. Bupivacaine is hepatically metabolized via glucuronidation and is renally eliminated. The onset is 4 to 7 minutes and the elimination half life is 3.5 hours in adults. The duration of action can be prolonged through the addition of epinephrine. Bupivacaine is indicated for the production of local or regional anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures. Since lidocaine (Xylocaine®) is somewhat less cardiotoxic than lipophilic local anesthetics such as bupivacaine and because there have been occurrences of numerous fatalities associated with the cardiovascular toxicity of bupivacaine, it was recommended that this drug not be added to the Formulary.

Due to the lack of a second on the motion to add bupivacaine, the drug was not added to Formulary.

glucosamine - presented by Dr. Heidel (developed by Phuong (Peter) Tran, pharmacy student)

Glucosamine is an amino-sugar that is naturally produced in humans. It is used in the synthesis of glycolipids, glycoproteins, hyaluronic acid, proteoglycans, and glycosaminoglycans, which are the major structural components of cartilage. The synthesis of proteoglycans inhibits the deterioration of cartilage brought about by osteoarthritis and helps maintain the balance between cartilage catabolic and anabolic processes. Glucosamine is extensively metabolized in the liver and is rapidly desulfated to smaller molecules and ultimately to carbon dioxide, water and urea. The elimination half life is 70 hours. Glucosamine's reported uses include: chronic venous insufficiency, inflammatory bowel disease, knee injury recovery, osteoarthritis and joint structure support, rheumatoid arthritis and other inflammatory conditions, and temporomandibular joint disorders. Since glucosamine is a nutraceutical, it is not approved by the FDA. The usual dose for osteoarthritis is 500 mg three times a day.

Following discussion, on motion of Dr. Ward, seconded by Dr. Heidel, the request to add glucosamine to the formulary as a supplement was approved. Since it is a supplement, only USP verified products will be considered formulary. The Formulary Drug Check List was completed.

fondaparinux (Arixtra®) - presented by Dr. Heidel (developed by Phuong (Peter) Tran, pharmacy student)

Fondaparinux is a synthetic pentasaccharide that binds to antithrombin III, thus selectively inhibits factor Xa. Neutralization of factor Xa interrupts the blood coagulation cascade and inhibits thrombin formation and thrombus development. Fondaparinux has no known effect on platelet aggregation and does not inactivate thrombin; therefore, it does not affect bleeding time or fibrinolytic activity at the recommended dose. Peak concentration after subcutaneous injection is 3 hours. Fondaparinux is FDA approved for the treatment of deep vein thrombosis (DVT), treatment of pulmonary embolism (PE), venous thromboembolism (VTE) prophylaxis after major orthopedic surgery (knee replacement, hip replacement, and hip fracture), extended VTE prophylaxis after hip fracture surgery and VTE prophylaxis after abdominal surgery. A non-FDA indication is prophylaxis of DVT in patients with a history of heparin-induced thrombocytopenia (HIT). For the treatment of DVTs, the dose for patients ≥ 50 kg is 2.5 mg daily subcutaneously. For acute DVT/PE the dose for patients < 50 kg is 5 mg daily subcutaneously, for patients between 50 – 100 kg it is 7.5 mg daily subcutaneously and for patients > 100 mg the dose is 10 mg daily subcutaneous.

Based on its use, it was originally recommended to be added to formulary as a reserve drug with the reserve criteria being restricted to TCID. However, based on the fact that enoxaparin (Lovenox®) is not on the reserve drug list, the Committee recommended that fondaparinux be added to Formulary. **Following discussion, on motion of Dr. Heidel, seconded by Dr. Hood, the request to add fondaparinux (Arixtra®) to the formulary was approved.** The Formulary Drug Check List was completed.

Quetiapine extended release (Seroquel XR®)

Since the last meeting, another request to add quetiapine extended release to the Formulary was submitted. At the September 2009 meeting the request to add quetiapine extended release to the Formulary was denied due to the lack of clear evidence for any clinical advantage of the extended release quetiapine over immediate release product. Since that time, there has not been any evidence to indicate that quetiapine extended release offers any clinical advantage to the immediate release product and the patent for the immediate release quetiapine will expire in 2011, therefore the request to add this drug was not discussed any further.

Anticonvulsant Guidelines

At the last meeting, the issue of recommending anticonvulsant guidelines was discussed. Dr. Moy indicated that the Healthcare Guidelines developed as a result of the settlement with the state supported living centers contain minimum guidelines that could be used for anticonvulsants. The Committee agreed that using these guidelines would be appropriate.

Update Formulary Indications

The indications for valproic acid (Depakene®)/divalproex (Depakote®) and the other anticyclic medications have not yet been updated in the psychotropic audit criteria and guidelines.

New Dosage Strengths

It was recommended to add calcium citrate 315 mg/vitamin D 250 units to the Formulary. On a motion of Dr. Heidel, seconded by Dr. Ward, the recommendation to add this dosage strengths to the Formulary was approved.

Psychotropic Consent List

Dr. Richards presented an updated version of the psychotropic consent list. The following are changes since the last approval in March 2009:

- Added to the Antipsychotic list
 - Asenapine (Saphris®)
 - Iloperidone (Fanapt®) – *nonformulary*
 - Olanzapine pamoate (Zyprexa® Relprevv™) – *nonformulary*
 - Paliperidone palmitate (Invega® Sustenna™)
 - Quetiapine extended release (Seroquel XR®) – *nonformulary*
- Added to the miscellaneous drugs
 - Guanfacine ER (Intuniv®) – *nonformulary*

On a motion of Dr. Ward, seconded by Dr. Heidel the revised psychotropic consent list was approved.

DSHS/DADS Drug Formulary 2010

The following changes were made to the Psychotropic Dosage Guidelines and Reserve Drugs listed in the Drug Formulary:

- Changes to the Antipsychotics Table
 - Added asenapine (Saphris®) with the suggested maximum adult dose of 20 mg/day

- Added iloperidone (Fanapt®) – nonformulary with the suggested maximum adult dose of 24 mg/day
- Added olanzapine pamoate – nonformulary with the suggested maximum adult dose of 300 mg per 2 weeks or 405 mg per 4 weeks
- Added paliperidone palmitate (Invega® Sustenna™) with suggested maximum adult dose of 234 mg per 4 weeks
- Changed the suggested child (< 12 y/o) dose for risperidone to 6 mg/day based on the updated package insert
- In the Mood Stabilizers Table, changed the plasma level for valproic acid from 50 to 150 mcg/ml to 50 to 125 mcg/ml based on MicroMedex™ and the Therapeutic Serum Concentrations of Some Anticonvulsants Table
- Changes to the Miscellaneous Drugs Used for Psychotropic Purposes Table
 - Added atomoxetine (Strattera®) with the suggested maximum adult dose of 100 mg/day; for children and adolescent 1.4 mg/kg (≤ 70 kg) & 100 mg/day (> 70 kg)
 - Added guanfacine (Tenex®) with the suggested adult, child and adolescent dose of 4 mg/day. The child and adolescent doses were based on the guanfacine monograph's Tourette's dosing
 - Added guanfacine extended release (Intuniv®) nonformulary with the suggested adult, child and adolescent dose of 4 mg/day. The extended release product has not been studied in children less than 6 years old.
- Changes to the Reserve Drugs
 - Added cycloserine (Seromycin®)
 - Added epoetin alfa (Epogen®, Procrit®)
 - Added linezolid (Zyvox®)
- Changes to Therapeutic Serum Concentrations of Some Anticonvulsants
 - Changed phenobarbital from 10 to 40 mcg/ml to 15 to 40 mcg/ml based on MicroMedex™
 - Changed valproic acid for seizure disorder from 50 to 150 mcg/ml to 50 to 100 mcg based on MicroMedex™

On a motion of Dr. Ward, seconded by Dr. Morgan the revised Psychotropic Dosage Guidelines and Reserve Drugs were approved.

The 2010 DSHS/DADS Drug Formulary was presented to the Committee for approval. All changes completed in this meeting will be included in the Formulary. In the 2010 Drug Formulary, a generic category for birth control pills was added. In addition, in the alphabetical listing a generic line item for antivirals for the treatment of HIV was added. On a motion of Dr. Ward, seconded by Dr. Hood, the 2010 Drug Formulary was approved.

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 Alerts

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

The FDA approved class labeling revisions for the atypical antipsychotic agents olanzapine (Zyprexa®) and ziprasidone (Geodon®) to warn of a temporal relationship with the development of leukopenia/neutropenia; agranulocytosis has also been reported. Patients with risk factors for leukopenia/neutropenia, such as preexisting low white blood cell count (WBC) or a history of drug-induced leukopenia/neutropenia, should have frequent monitoring of complete blood count (CBC) during the first few months of treatment. Antipsychotic therapy should be discontinued at the first sign of a clinically significant decline in WBC that cannot be attributed to other causes. Patients with clinically significant neutropenia should be carefully monitored for fever or other signs of infection and treated promptly if symptoms occur. Antipsychotic therapy should be discontinued for severe neutropenia (absolute neutrophil counts < 1,000 mm³) and WBC should be monitored until recovery.

FDA has reported new safety information on an interaction between clopidogrel (Plavix®) and omeprazole (Prilosec®/Prilosec OTC®). Data show that when clopidogrel and omeprazole are taken together, the

effectiveness of clopidogrel is reduced. Patients at risk for heart attacks or strokes who use clopidogrel to prevent blood clots will not get the full effect of this medicine if they are also taking omeprazole. Separating the dose of clopidogrel and omeprazole in time will not reduce this drug interaction. Other drugs that are expected to have a similar effect and should be avoided in combination with clopidogrel include: cimetidine (Tagamet®), fluconazole (Diflucan®), ketoconazole (Nizoral®), voriconazole (Vfend®), etravirine (Intelence®), felbamate (Felbatol®), fluoxetine (Prozac®), fluvoxamine (Luvox®), and ticlopidine (Ticlid®).

Healthcare professionals were notified of changes to the Warnings and Overdosage sections of the Prescribing Information for desipramine (Norpramin®). The new safety information states that extreme caution should be used when this drug is given to patients who have a family history of sudden death, cardiac dysrhythmias, and cardiac conduction disturbances; and that seizures precede cardiac dysrhythmias and death in some patients.

The FDA has issued a warning about the increased risk of neural tube defects and other major birth defects, such as craniofacial defects and cardiovascular malformations, in babies exposed to valproic acid (Depakene®) and divalproex sodium (Depakote®) during pregnancy. Healthcare practitioners should inform women of childbearing potential about these risks, and consider alternative therapies, especially if using valproic acid or divalproex to treat migraines or other conditions not usually considered life-threatening. Women of childbearing potential should only use valproic acid or divalproex if it is essential to manage their medical condition. Those who are not actively planning a pregnancy should use effective contraception, as birth defect risks are particularly high during the first trimester, before many women know they are pregnant.

The FDA has requested that all diclofenac containing products be updated due to potential for elevations in liver tests during treatment with all products containing diclofenac. Elevations of one or more liver tests may occur during therapy with diclofenac. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continued therapy. Borderline elevations (i.e. less than 3 times the upper limit of normal range) or greater elevations of transaminases occurred in about 15% of diclofenac-treated patients. Of the markers of hepatic function, ALT (SGPT) is recommended for the monitoring of liver injury. Physicians should measure transaminases periodically in patients receiving long-term therapy with diclofenac, because severe hepatotoxicity may develop without a prodrome of distinguishing symptoms. The optimum times for making the first and subsequent transaminase measurements are not known. Based on clinical trial data and postmarketing experiences, transaminases should be monitored within 4 to 8 weeks after initiating treatment with diclofenac. However, severe hepatic reactions can occur at any time during treatment with diclofenac. If abnormal liver tests persist or worsen, if clinical signs and/or symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, abdominal pain, diarrhea, dark urine, etc.), diclofenac should be discontinued immediately. To minimize the possibility that hepatic injury will become severe between transaminase measurements, physicians should inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and “flu-like” symptoms), and the appropriate action patients should take if these signs and symptoms appear.

The FDA Advisory Panel has recommended that product labeling for aripiprazole (Abilify®) be changed to more adequately warn of the risk of excessive weight gain in pediatric patients. The FDA does not have to accept the recommendations of the Advisory Panel.

Quarterly Non-Formulary Drug Justification Report

For the first 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®)
- Melatonin
- Propoxyphene with acetaminophen (Darvocet®)
- Levalbuterol (Xopenex®)
- Brompheniramine/phenylephrine (Dimetapp®)
- Esomeprazole (Nexium®)

The Committee plans on considering: cetirizine, levalbuterol and bupropion XL for formulary addition sometime in the

future.

Drug Formulary Sectional Review-

**Muscle Relaxants
Miscellaneous CNS (dementia agents)
Endocrine**

Dr. Hall provided the review on the agents used as muscle relaxants. In her review, she did not make any recommendations for change. See Attachment C.

Dr. Hall provided the review on the Miscellaneous CNS agents (dementia agents). In her review, Dr. Hall recommended the addition of the rivastigmine (Exelon®) Transdermal patch as it has less nausea and vomiting as compared to the oral formulation that is on Formulary. See Attachment D.

Dr. Hall presented the following information on the drugs used to treat dementia.

Drug	*MOA	FDA Indication	Dosage Forms/Dosing	Metabolism and T1/2
Donepezil (Aricept)	Acetylcholinesterase inhibitor	Alzheimer's dementia: mild to severe	tablet: QD oral disintegrating tablet: QD	CYP2D6/3A4 70 hours
Galantamine (Razadyne)	Acetylcholinesterase inhibitor; also modulates nicotinic acetylcholine receptor	Alzheimer's dementia: mild to moderate	24 hour capsule: QD oral solution: BID tablet: BID	CYP2D6/3A4 6 to 8 hours
Memantine (Namenda)	NMDA receptor antagonist (blocks the action of glutamate)	Alzheimer's dementia: moderate to severe	tablet: BID oral solution: BID	57-82% excreted in urine as unchanged drug 60-80 hours (terminal)
Rivastigmine (Exelon)	Acetylcholinesterase inhibitor	Alzheimer's and Parkinson's dementia: mild to moderate	capsule: BID oral solution: BID transdermal patch: QD	Non P450 2 hours

*MOA = mechanism of action

On a motion of Dr. Ward, seconded by Dr. Hood, the request to add rivastigmine (Exelon®) Transdermal patch to the Formulary was approved. The Formulary Check List was completed.

Dr. Hall provided the review on the endocrine agents. In her review, she did not make any recommendations for change. However, previously in the meeting, it was recommend to have a "generic" entry in the Drug Formulary for birth control pills. See Attachment E.

Sectional Review for Next Meeting

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

Other Issues

It was noted that ziprasidone (Geodon®) has received FDA approval for the indication for maintenance treatment of bipolar I disorder as an adjunct to lithium or valproate.

The FDA recently approved olanzapine pamoate (Zyprexa® Relprevv), a long acting injection for the treatment of schizophrenia. This product is currently nonformulary. It requires increased monitoring secondary to the post-injection delirium/sedation syndrome and enrollment in the Zyprexa Relprevv Patient Care Program by the prescriber, healthcare facility, patient and pharmacy. The Committee will investigate the requirements to enroll in their Patient Care Program.

The field has received notice that Endo Pharmaceutical plans to discontinue the distribution of molindone (Moban®) due to the inability to obtain a supplier of molindone hydrochloride. Healthcare professionals that currently have patients on molindone should be planning to transition the patients to another product.

Aripiprazole (Abilify®) has received a FDA indication for the treatment of irritability associated with autistic disorder in pediatric patients (ages 6 to 17 years).

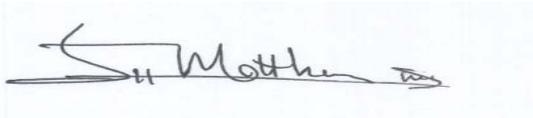
Due to budget issues, the Committee discussed alternative methods for on-site meetings. Three members participated by phone and the rest were in one location for the meeting. The individuals participating by phone, strongly suggested that the meetings occur in person as many interactions and benefits are lost over the phone lines. Since this Committee serves both the DADS and DSHS agencies and the community, videoconferencing does not appear to be a viable option. Since this Committee only meets four times a year, the cost of meeting in person is minimal. The Committee agreed that the nature of this Committee's business suggests that meeting in person is more beneficial.

Next Meeting Date

The next meeting was scheduled for April 9, 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 – Risperidone (Risperdal®, Risperdal® Consta™), olanzapine (Zyprexa®), paliperidone (Invega®, Invega® Sustenna™), quetiapine (Seroquel®), ziprasidone (Geodon®), aripiprazole (Abilify®) and asenapine (Saphris®) Guidelines

Attachment C – Agents for Muscle Relaxants Sectional Review

Attachment D – Agents for Miscellaneous CNS (dementia) Sectional Review

Attachment E – Agents for Endocrine Sectional Review

Minutes Prepared by:

