

**DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES**  
**September 25, 2009**

The Executive Formulary Committee convened on Friday, September 25, 2009 in Conference Room 240 - CO Building 2. The meeting was called to order by Dr. Matthews, Chair at 9:40 a.m.

Janet Adams, MSN, RN, CNS	Absent	Julie Graves Moy, M.D., M.Ph. (non-voting)	√
Emilie A. Becker, M.D. (for a specific agenda item)	√	Nina Muse, M.D. (non-voting)	Absent
Rosha Chadwick, R.Ph. (via phone)	√	Kenny Dudley (non-voting)	Absent
Catherine S. Hall, Pharm.D.	√	Barry Fredrickson (non-voting)	Absent
Jeanna Heidel, Pharm.D.	√	Mike Maples (non-voting)	Absent
J. Brett Hood, M.D.	Absent	Bob Burnett (non-voting)	Absent
Jeff Matthews, M.D.	√	Julie McRae, MS, RN, CDDN (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.	Absent	Vacant Center Position	
Robert L. Ward, D.O.	√		

**Guest Present: Staci Kurlmel, Pharmacy student; Ashley Smith, Pharm.D., Resident**

**Introductions**

Dr. Julie Graves Moy was introduced as the new Medical Director/Medical Services Coordinator for DADS.

**Approval of Minutes of June 12, 2009**

On a motion of Ms. Millhollon, seconded by Dr. Heidel, the minutes of the June 12<sup>th</sup> meeting were approved as previously distributed.

## Adverse Drug Reaction Reports

The Executive Formulary Committee received one adverse drug reaction report. In this case, a fourteen year old male was admitted to a state hospital for the treatment of bipolar depression. His medical diagnoses include GERD and migraine headaches. Upon admission, the patient reported taking oxycodone (Oxycontin®) 2 tablets per day five times a week. He was taking no other prescribed or OTC medications prior to admission. The baseline labs were within normal limits. He was started on lamotrigine (Lamictal®) 25 mg once daily in the morning for the treatment of bipolar depression. The patient's only other medication was omeprazole (Prilosec®) once daily in the morning which was started two days after initiation of the lamotrigine. Nine days after initiation of the lamotrigine, it was noted that the patient had a generalized rash and the lamotrigine was discontinued. Lithium was initiated for mood stabilization when the lamotrigine was discontinued. The rash continued to worsen after the lamotrigine was discontinued. Two days later, the patient was noted to have a spreading erythematous rash on his upper and lower extremities including chest, back, neck, face and ears. The patient denied fever, chest tightness, or trouble breathing and vital signs were stable. A CBC and CMP were obtained and were within normal limits. Hydrocortisone cream and PRN oral diphenhydramine (Benadryl®) were ordered. Later in the day, the patient's rash was noted to be raised and tender to the touch and he complained of a sensation of "rocks" in his throat. Epinephrine injection was administered. The patient was sent to a medical hospital for evaluation. The medical hospital reported no findings of signs/symptoms of Stevens - Johnson syndrome. The medical hospital recommended continuing to monitor. The next day, the patient's lithium was discontinued until the patient became medically stable. The rash eventually resolved and the patient was discharged on lithium.

## New Drug Applications

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

### **cycloserine (Seromycin®) - presented by Dr. Smith (developed by Regina Tabor with assistance by Staci Kurlmel)**

Cycloserine is a broad spectrum antibiotic that may be bactericidal or bacteriostatic, depending on its concentration at the site of the infection and the susceptibility of the organism. Cycloserine works by blocking the formation of peptidoglycans which causes the walls of the bacteria to become weak and it eventually results in the death of the bacteria. Cycloserine is an analog of the amino acid D-alanine. It interferes with an early step in bacterial cell wall synthesis in the cytoplasm by competitive inhibition of two enzymes, L-alanine racemase, which forms D-alanine from L-alanine, and D-alanylalanine synthetase, which incorporates D-alanine into the pentapeptide necessary for peptidoglycan formulation and bacterial cell wall synthesis. Cycloserine is indicated in the treatment of active pulmonary and extrapulmonary tuberculosis (including renal disease) when the causative organisms are susceptible to this drug and when treatment with the primary medications (streptomycin, isoniazid, rifampin, and ethambutol) has proved inadequate. Like all antituberculosis drugs, cycloserine should be administered in conjunction with other effective chemotherapy and not as the sole therapeutic agent. The initial adult dose is 250 mg twice daily at 12-hour intervals for the first two weeks. The usual dosage is 500 mg to 1 gram daily in divided doses monitored by blood levels for 18 – 24 months. A daily dosage of 1 gram should not be exceeded. Cycloserine can cause peripheral neuropathy so concomitant administration of pyridoxine 100 mg daily is recommended for prevention.

**Following discussion, on motion of Dr. Heidel, seconded by Ms. Millhollon, the request to add cycloserine (Seromycin®) to the formulary as a reserved drug was approved.** The reserve criteria shall be: "when recommended by a consultant physician or prescribed by an infectious disease specialist at the Texas Center for Infectious Disease Hospital." The Formulary Drug Check List was completed.

**paliperidone palmitate (Invega® Sustenna™) - presented by Dr. Richards (developed by Dr. Stephen Saklad)**

Paliperidone palmitate is a long acting injectable atypical antipsychotic. The commercial product is a racemic mixture of paliperidone palmitate enantiomers wet-milled into nano particles that have an increased surface area resulting in an increased rate of drug absorption and bioavailability. The nano particles sustained release profile provides a therapeutic effect throughout the four-week intramuscular dosing interval. Paliperidone palmitate nano particle suspension dissolves slowly after IM injection due to its lipophilic character, then is hydrolyzed rapidly to paliperidone and absorbed into the systemic circulation. Following a single IM dose, the plasma concentrations of paliperidone gradually rise to reach maximum plasma concentrations ( $C_{max}$ ) at a median time to maximum concentration ( $T_{max}$ ) of 13 days. The release of the drug from the depot injection site begins the first day and lasts for as long as 126 days. Following IM injection of single doses (39 mg to 234 mg) in the deltoid muscle, on average, a 28% higher  $C_{max}$  was observed compared with injection in the gluteal muscle. In a multi-dose study, deltoid administration of 156 mg of paliperidone palmitate yielded higher  $C_{max}$  than did gluteal administration after the second injection; the difference was less after the fourth injection. The  $T_{max}$  and the cumulative exposure after four injections (area under the curve [AUC] from time zero to infinity [AUC $_{\infty}$ ]) did not differ between the two injection sites. Paliperidone palmitate is indicated for acute treatment of schizophrenia in adults and maintenance treatment of schizophrenia in adults. Paliperidone palmitate utilizes a loading dose strategy for initiating this product. The initial dosing consists of paliperidone palmitate 234 mg IM in the deltoid muscle on day 1 and 156 mg IM in the deltoid muscle one week later. The first maintenance dose is administered one month after the day 8 injection and can be administered in the deltoid or gluteal muscle. The usual recommended monthly maintenance dose is 117 mg. The maintenance dose can range from 39 to 234 mg. Adjustment of the maintenance dose may be made with each monthly dose. However, when such dose adjustments are made, the prolonged-release characteristics of paliperidone palmitate extended-release injectable suspension should be considered, since the pharmacokinetic time to the new steady state and subsequent clinical effects of the dose adjustment may not be evident for several months. Based upon the half-lives reported previously, the time to 90% of steady state should be in the range of 82 to 162 days. Mean paliperidone plasma levels were lower during the initiation of treatment in overweight patients ( $>25 \text{ mg/m}^2$ ) compared to patients with normal BMI ( $<25 \text{ mg/m}^2$ ) prior to the third injection on day 36. As a result, it is recommended that a longer needle (1.5 inch) in the deltoid muscle be used for heavier ( $\geq 90 \text{ kg}$ ) individuals. The paliperidone palmitate product is equipped with two different size needles (22 G x 1 1/2"; 23 G x 1"). As with all long acting injections, tolerability to paliperidone, risperidone, or risperidone long-acting injection should be established prior to initiation of paliperidone palmitate therapy.

**Following discussion, on motion of Dr. Ward, seconded by Dr. Heidel, the request to add paliperidone palmitate (Invega® Sustenna™) 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.

Similar to the current use of risperidone long acting injection (Risperdal® Consta™), it is suggested that inpatient facilities obtain prior approval from the patient's local mental health authority prior to initiating therapy with paliperidone palmitate.

Dr. Richards presented the psychotropic audit criteria and guidelines for paliperidone palmitate. Since there have been changes in the indications and class effect warnings for the atypical antipsychotics, the current audit criteria and guidelines were updated. See Attachment B. The following changes were made:

- Added "not paliperidone" to the bipolar disorder indication
- Added "irritability associated with autistic disorders in children and adolescent (5 to 16 years old) – risperidone" and "adjunct for patients on antidepressants for major depressive disorder"

(aripiprazole)” to the indication section

- Removed “olanzapine” from the diabetes mellitus listing under Precautions and from the hyperglycemia listing under Side Effects Which Require Medical Attention
- Changed Age-Specific Considerations to: “Risperidone and aripiprazole have approved specific indications for designated ages in children. The safety and efficacy have not been established in children under the age of 18 for all other medications. Conservative dosing is advised in the elderly.”

On a motion of Dr. Ward, seconded by Dr. Morgan, the psychotropic audit criteria and guidelines for the atypical antipsychotics were approved.

### **epoetin alfa (EpoGen®, Procrit®) - presented by Staci Kurlmel, pharmacy student**

Epoetin alfa, a biosynthetic form of the glycoprotein hormone erythropoietin, is a hematopoietic agent that principally affects erythropoiesis. Erythropoietin is a hormone that is instrumental in the production of red cells from the erythroid tissues in the bone marrow. Reticulocytes are released from the bone marrow into the bloodstream, where they mature into erythrocytes followed by a rise in hemoglobin and hematocrit levels. Epoetin alfa is approved by the FDA for use in anemia of chronic renal failure; anemia, zidovudine adverse reaction; and anemia, due to chemotherapy (neoplastic disease, non-myeloid, metastatic). A non-FDA approved indication is: anemia, hepatitis C (patients treated with ribavirin plus interferon alfa, or ribavirin plus peginterferon alfa). The dose is dependent on the diagnosis. Renal failure patients with hemoglobin greater than 12 g/dL and receiving epoetin alfa may have an increased risk of death and serious cardiovascular events; therefore for this patient population the target hemoglobin levels is between 10 to 12 g/dL.

**Following discussion, on motion of Dr. Ward, seconded by Dr. Heidel, the request to add epoetin alfa (EpoGen®, Procrit®) to the formulary as a reserved drug was approved.** The reserve criteria shall, be “when recommended by a consultant physician or prescribed by an infectious disease specialist at the Texas Center for Infectious Disease Hospital.” The Formulary Drug Check List was completed.

### **Quetiapine extended release (Seroquel XR®) - presented by Dr. Hall**

Quetiapine extended release was previously considered for addition to the Formulary at the May 2008 meeting. Quetiapine extended release is indicated for schizophrenia; depressive episode associated with bipolar disorder; manic or mixed episodes associated with bipolar I disorder, as either monotherapy or adjunct therapy to lithium or divalproex; and maintenance treatment of bipolar I disorder as adjunct to lithium or divalproex. Quetiapine extended release is administered once a day. In a study completed by Chengappa et al (2003), it was determined that it is clinically feasible to switch patients on twice a day dosing with immediate release quetiapine to once a day (at bedtime) dosing with the immediate release product. Currently, a large portion of patients receive the immediate release product once a day. At this time, the quetiapine extended release product is less expensive than the immediate release product. The patent for the immediate release quetiapine expires in 2011 and at that time it is expected that competition of the immediate release generic product will result in a lowering of pricing of the immediate release tablet and an increase in the pricing of the extended release product.

**Following discussion, on motion of Dr. Heidel, seconded by Ms. Millhollon, the request to add quetiapine extended release (Seroquel XR®) to the formulary was denied; based on a lack of clear evidence for any clinical advantage of the extended release quetiapine over the immediate release product.**

## **Conflict of Interest Draft Policy**

A draft of the Conflict of Interest Policy was distributed to the Committee for their review. The policy would require Committee members to complete a Disclosure Form on an annual basis and as needed as their situation changes. In addition, individuals submitting a New Drug Application and those that are completing a drug monograph will need to submit a Disclosure Form with each application or monograph, unless they are on the Committee. Furthermore, the Policy recommends that each facility Pharmacy and Therapeutics Committee or similarly functioning committee adopt a similar policy. The Committee recommended some minor changes to the draft policy.

On a motion of Dr. Ward, seconded by Ms. Millhollon, the revised Conflict of Interest Policy was approved. Dr. Richards will distribute this information to the field. See Attachment C.

After the policy was approved, individuals that had developed monographs for this meeting were questioned about their conflicts of interest. Dr. Hall and Ms. Kurlmel were questioned verbally and Dr. Saklad and Ms. Tabor were previously requested to complete a Disclosure Form. After reviewing their information, no conflicts of interest in the preparation of the monographs were detected.

## **Anticonvulsant Lab Monitoring**

Dr. Matthews noted that the audit criteria that is published on our website does not include anticonvulsant agents unless the anticonvulsant is used as a mood stabilizer. Since there are several anticonvulsants that are not used in the treatment of a mental illness and clinicians are not necessarily aware of their monitoring, it was recommended that suggested guidelines for the use of these agents might be beneficial for clinicians. Ideally, it would be advantageous to find an independent website that would provide this information and update recommendations on a routine basis. Dr. Moy will research this issue and if needed, will form a Work Group to develop suggested guidelines on the use of anticonvulsants.

## **NGM List – Addition Process**

Dr. Becker was present for this portion of the meeting. Dr. Becker noted that it has become the responsibility of her office to determine which drugs should be on the NGM (New Generation Medication) list. In the past, drugs were just added once they were marketed regardless of their Formulary status. As a result, Dr. Becker proposed that the Executive Formulary Committee determine the drugs that are placed on the NGM list based on the Formulary status of the medication.

On a motion of Dr. Ward, seconded by Dr. Heidel, it was recommended that the Executive Formulary Committee be responsible for determining which drugs are included on the NGM list based on the Formulary status of the agent.

The Committee discussed the issue of having quetiapine extended release (Seroquel XR®) on the NGM list, since the request to add quetiapine extended release to the Formulary was denied earlier in the meeting. On a motion of Dr. Ward, seconded to Dr. Heidel, it was recommended that a memo regarding the potential removal of the quetiapine extended release from the NGM list in the future be distributed.

Paliperidone palmitate (Invega® Sustenna™) was added to the NGM list as it was added to the Formulary.

## **Medication Information Websites**

At the last meeting, it was noted that many facilities utilize websites to provide patient information to facilitate sharing information and obtaining consent. Committee members were requested to submit websites that they use in their practice. The following are websites that were submitted:

National Institute of Mental Health

<http://www.nimh.nih.gov/health/index.shtml>

Medline Plus

<http://www.nlm.nih.gov/medlineplus/druginformation.html>

Drugs.com

[http://www.drugs.com/drug\\_information.html](http://www.drugs.com/drug_information.html)

RxList The Internet Drug List

<http://www.rxlist.com/script/main/hp.asp>

WebMD

<http://www.webmd.com/>

MayoClinic.com

<http://www.mayoclinic.com/>

### **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 notified healthcare professionals that it is taking several actions to reduce the risk of overdose in patients using pain medications that contain propoxyphene because of data linking propoxyphene and fatal overdoses. The FDA will require manufacturers of propoxyphene-containing products to strengthen the label, including the boxed warning, emphasizing the potential for overdose when using these products and to provide a medication guide to patients stressing the importance of using the drugs as directed.

The FDA notified healthcare professionals and patients that it has required the manufacturers of the smoking cessation aids varenicline (Chantix®) and bupropion (Wellbutrin®, Zyban® and generics) to add new Boxed Warnings and develop patient Medication Guides highlighting the risk of serious neuropsychiatric symptoms in patients using these products. These symptoms include: changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. The added warnings are based on the continued review of postmarketing adverse event reports for varenicline and bupropion received by the FDA. These reports included those with a temporal relationship between the use of varenicline or bupropion and suicidal events and the occurrence of suicidal ideation and suicidal behavior in patients with no history of psychiatric disease. Healthcare professionals should advise patients to stop taking varenicline or

bupropion and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior.

The FDA notified healthcare professionals that a Boxed Warning is being added to the prescribing information for promethazine products, describing the risks of severe tissue injury, including gangrene, requiring amputation following intravenous administration of promethazine. The Boxed Warning will remind practitioners that due to the risks of intravenous injection, the preferred route of administration is deep intramuscular injection and that subcutaneous injection is contraindicated. Perivascular extravasation, unintentional intra-arterial injection and intraneuronal or perineuronal infiltration of the drug may result in irritation and tissue damage. Healthcare professionals should be alert for signs and symptoms of potential tissue injury including burning or pain at the site of injection, phlebitis, swelling, and blistering.

The joint panel of the FDA's Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and Anesthetic and Life Support Drugs Advisory Committee held hearings on the issue of acetaminophen liver toxicity and how to prevent it. The panel voted to require the "block box" warning on prescription product labels. A proposal to ban the prescription combinations of acetaminophen failed. The advisory panel recommended that the FDA consider the following:

- Require a single dose of acetaminophen in liquid products for children in order to avoid confusion (36 to 1 vote in favor)
- Lower the maximum recommended daily and single doses (21 to 16 and 24 to 13 in favor, respectively)
- Make the current 500 mg extra-strength version available by prescription only (26 to 11 in favor)
- Sell acetaminophen in smaller packages with fewer pills, as done in the U.K. - an attempt to prevent massive intentional overdosing as a suicide attempt (20 – 17 against)

The FDA does not have to follow the recommendations made by the Advisory Panel.

### **Update Formulary Indications**

Previously, Dr. Morgan requested that the audit criteria indications for the atypical antipsychotics be updated to reflect the current FDA indications for bipolar and depression as appropriate. The atypical audit criteria was previously updated with the addition of paliperidone palmitate (Invega® Sustenna™) to the Formulary and the indications were updated.

The indications for valproic acid (Depakene®)/divalproex (Depakote®) and the other anticyclic medications have not yet been addressed.

### **New Dosage Strengths**

The following dosage strengths were recommended to be added to the Formulary:

- Brimonidine
  - Solution, ophthalmic: 0.1%
- Tizanidine
  - Capsule: 2 mg, 4 mg
- Calcipotriene

- Solution, topical: 0.005%
- Donepezil
  - Tablet, oral disintegrating: 10 mg

On a motion of Dr. Heidel, seconded by Ms. Millhollon, the recommendation to add these dosage strengths to the Formulary was approved.

### **Quarterly Non-Formulary Drug Justification Report**

For fiscal year 2009, the following were the top non-formulary agents that were prescribed:

Quetiapine extended release (Seroquel XR®)  
 Cetirizine (Zyrtec®)  
 Levalbuterol (Xopenex®)  
 Lansoprazole (Prevacid®)  
 Propoxyphene with acetaminophen (Darvocet®)  
 Esomeprazole (Nexium®)  
 Omega-3 fish oil  
 Melatonin  
 Celecoxib (Celebrex®)  
 Bupropion XL (Wellbutrin XL)

The Committee discussed the possibility of considering: cetirizine, levalbuterol and bupropion XL for formulary addition sometime in the future. Only the USP Verified products for the fish oil are on formulary, so this list represents those that are not USP Verified.

All facilities did report their non-formulary drug list in the fourth quarter.

### **Drug Formulary Sectional Review-**

### **Agents for Migraine**

Dr. Hall provided the review on the agents used for the treatment of migraines. In her review, she recommended adding the following drugs that are currently on Formulary to the Migraine Section: See Attachment D.

- Aspirin
- Ibuprofen
- Amitriptyline
- Topiramate

In Dr. Hall's review, she noted that during the past three months all but one purchase from the wholesaler has been for sumatriptan. Over time, most patients who have a history of migraines, have had their therapy individualized to their unique situation and when they are admitted to the facility, most pharmacies will obtain their particular medication through the non-formulary process. As a result, Dr. Hall did not recommend adding any other triptan to the formulary.

However, in Dr. Hall's review, it was noted that the combination product of acetaminophen/aspirin/caffeine (Excedrin®) which is indicated in the acute treatment of migraines is not on formulary. Therefore, it was recommended to add this combination product to the formulary. A monograph was not completed.

On a motion, by Dr. Heidel, seconded by Dr. Ward, the recommendations made by Dr. Hall were

approved.

### **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 guanfacine extended release (Intuniv®) has been approved by the FDA in the treatment of attention-hyperactivity disorder (ADHD) in children and adolescents aged 6 to 17 years.

Eli Lilly and Company has announced that Humulin® 50/50 insulin will be discontinued. It is estimated that fewer than 3,000 people in the U.S. currently use the product.

The FDA has approved benzyl alcohol 5% lotion (Ulesfia®) for the treatment of head lice in patients  $\geq 6$  months old. Lice exposed to benzyl alcohol lose the ability to close their respiratory spiracles; the lotion vehicle then obstructs their airways and causes them to asphyxiate. Benzyl alcohol has no ovicidal activity. This product may be a viable option for those cases of hard-to-treat lice.

### **Next Meeting Date**

The next meeting was scheduled for January 29, 2010.

### **Adjourn**

There being no further business, the meeting was adjourned at 1:45 p.m.



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**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®) Guidelines
- Attachment C – Conflict of Interest Policy
- Attachment D – Agents for Migraine Sectional Review

Minutes Prepared by:

Ann L. Richards, Pharm.D., BCPP