

**DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES  
January 30, 2015**

The Executive Formulary Committee convened on Friday, January 30, 2015 in Room 125 - ASH Building 552. The meeting was called to order by Dr. Wright, Chair at 9:43 a.m.

Phillip Balfanz, M.D.	√	Jennifer Wright, M.D.	√
James Baker, M.D.	√	Valerie Kipfer, MSN, RN (non-voting)	√
Mary Bowers RN, BSN	Absent	Lilani Muthali, M.D. (non-voting)	√
Catherine Hall, Pharm.D.	√	Nina Muse, M.D. (non-voting)	Absent
Jeanna Heidel, Pharm.D.	√	Jay Norwood, MSN, RN (non-voting)	Absent
Marla Knight, Pharm.D., CGP, FASCP	√	Peggy Perry (non-voting)	Absent
Jeff Matthews, M.D.	√	Scott Schalchlin (non-voting)	Absent
Connie Millhollon, RN	√	Lauren Lacefield Lewis (non-voting)	Absent
Kenda Pittman, Pharm.D.	√	Kerry Raymond (non-voting)	Absent
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Archie Smith, M.D.	√	Vacant DADS Physician	
Robert L. Ward, D.O.	Absent		

**Guests Present:** Lisa Mican, Pharm.D., ASH; Manzoor Aman, Pharm.D. student, ASH

**Introduction and Other Information**

Dr. Smith was introduced as the new physician member representing a State Supported Living Center.

**Approval of Minutes of October 10, 2014**

On a motion of Dr. Heidel, seconded by Ms. Millhollon, the minutes of the October 10<sup>th</sup> meeting were approved as previously distributed.

**Conflict of Interest**

The Committee members present at the meeting completed their annual disclosure statements. None of the Committee members reported any conflicts of interest.

## Issues from the Clinical Directors' Meeting

Dr. Baker noted that there is no longer a formal clinical directors' meeting. Instead, a Medical Executive Committee (MEC) consisting of five clinical directors has been developed. Dr. Parsons is the chair of this Committee. The Medical Executive Committee will serve as the leadership group for our organization.

## Psychotropic Consent List

Dr. Richards presented the updated psychotropic consent list. The following changes were made:

- Added vortioxetine (Brintellix®) non-formulary to the Antidepressant section
- Deleted chloral hydrate (Noctec®) from the Anxiolytics/Sedatives/Hypnotics section as it is no longer available
- Added Abilify® Discmelt to the aripiprazole listing under the Antipsychotic section
- Added Versacloz® to the clozapine listing under Antipsychotics
- Added Focalin® XR to the dexamethylphenidate listing under the Stimulant section
- Added methylphenidate solution (Quillivant® XR) to the Stimulant section
- Added prazosin (Minipress®) to the Miscellaneous Drugs section

On a motion of Dr. Knight, seconded by Dr. Matthews, the recommended changes to the Psychotropic Consent List were approved. See Exhibit A.

Dr. Heidel questioned the use of melatonin and the need to obtain consent. She noted that melatonin is not listed in the electronic consent list. The Committee discussed whether or not melatonin requires consent. Melatonin is listed as a supplement in the Drug Formulary; therefore, the Committee does not believe it requires consent. However, facilities can obtain consent if desired.

## Psychotropic Audit Criteria & Guidelines – Mood Stabilizers

A Work Group consisting of Dr. Howe (North Texas State Hospital), Dr. Mican (Austin State Hospital), Dr. Richards (San Antonio State Hospital), Dr. Rivera (Terrell State Hospital), and Dr. Tobis (Kerrville State Hospital) revised the Mood Stabilizers Audit Criteria and Guidelines. Besides tertiary references, the following were used for references by the Work Group:

- Ng F, Mammen OK, Wilting I, Ferrier IN, Cassidy F, et al. The International Society for Bipolar Disorders (ISBD) consensus guidelines for the safety monitoring of bipolar disorder treatments. *Bipolar Disord.* 2009;11:559-595.
- Patsalos PN, Berry DJ, Bourgeois BFD, Cloyd JC, Glauser TA, Johannessen SI, et al. Antiepileptic drugs – best practice guidelines for therapeutic drug monitoring; A position paper by the subcommission on therapeutic drug monitoring, ILAE Commission on Therapeutic Strategies. *Epilepsia.* 49(7):1239-1276.
- Musenga A, Saracino MA, Sani G, Raggi MA.. Antipsychotic and Antiepileptic Drugs in Bipolar Disorder: The Importance of Therapeutic Drug Monitoring. *Current Medicinal Chemistry.* 2009;16:1463-1481.
- Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Beaulieu S, Alda M, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2013. *Bipolar Disorders.* 2013;15:1-44.

The Work Group recommended the addition of lactation risk to the guidelines. A lactation key was developed for inclusion into the Audit Criteria & Guidelines.

The Work Group recommended the following changes to the Mood Stabilizers Audit Criteria & Guidelines:

- Carbamazepine
  - Add “Tegretol® XR and Carbatrol®” to the header
  - Indications:
    - Change the first indication to “Bipolar disorder and other cyclic mood disorders”
    - Delete “Chronic Pain”
    - Delete “Acute mania”
  - Absolute contraindications add:
    - “Current bone marrow suppression”
    - “Concomitant use of MAO inhibitor or within 14 days of MAO Inhibitor use”
    - “Nefazodone”
    - “Concomitant use with NNRTI (HIV) agents”
  - Relative contraindication add:
    - “absence seizures”
    - “HLA-A\*3101”
  - Precautions:
    - Delete “Concomitant use of monoamine oxidase (MAO) inhibitors”
    - Add “Hepatic impairment”
    - Change “Coronary artery disease” to “Cardiovascular disease”
    - Change “Hyponatremia, dilutional” to “Hyponatremia”
  - Pregnancy and Breast-Feedings:
    - Change Pregnancy Category to “D”
    - Add Lactation Risk L2
  - Drug Interactions of Major Significance:
    - Delete “Coumadin”
    - Delete “hydantoin, succinimide, primidone, felbamate”
    - Add “phenytoin”
    - Delete “valproic acid”
    - Delete “tricyclic” from the antidepressant listing
    - Delete “Estrogens, including estramustine”
    - Add “rifampin, bedaquiline “
    - Delete “including furazolidone and procarbazine”
    - Delete “Propoxyphene”
    - Change “Contraceptives, oral estrogen” listing to “Oral estrogen and progestin”
    - Delete “(especially haloperidol and risperidone)” from the antipsychotic listing
    - Add the following:
      - “HIV Medication – NNRTI, protease inhibitors”
      - “Statins”
      - “guanfacine”
      - “cyclosporine”
      - “ketoconazole, itraconazole”
  - Age-Specific considerations add:
    - “Geriatric population maybe more sensitive to hyponatremia”
    - “Young children more susceptible to auto-induction of carbamazepine”
  - Side Effects Which Require Medical Attention add:
    - “Suicidal ideation”
    - “Myalgia, body weakness, malaise”
  - Patient Monitoring Parameters:
    - Change “CBC with platelets” to “CBC with differentials” and add “annually” to the requirement
    - Change electrolyte requirement to: “Electrolytes – baseline and 1 to 2 weeks after each dose increase, annually, and as clinically indicated” and make it a separate listing
    - Change hepatic function requirement to: “Hepatic function – baseline, monthly for first three months, annually and as clinically indicated”
    - Change pregnancy test to: “Pregnancy Test – baseline as appropriate and as clinically indicated”

- Add a requirement for a carbamazepine level at one week after initiation
    - Add the following:
      - “Consider HLA-A\*3101 genetic testing at baseline for those to be considered at high risk (most common in Asian, Native American, European, and Latin American descents)”
      - “Monitor for the emergence of suicidal ideation or behavior”
- Oxcarbazepine
  - Change indication to: “Bipolar disorder and other cyclic mood disorders”
  - Relative Contraindication add:
    - “Severe bone marrow suppression”
    - “HLA-B\*1502 allele”
    - “Severe renal or hepatic impairment”
  - Precautions
    - Change renal insufficiency to “Mild to moderate renal insufficiency”
    - Add “Mild to moderate hepatic insufficiency”
    - Add “Pregnancy/nursing mothers”
  - Add “Lactation Risk L3” to Pregnancy and Breast Feeding
  - Drug Interaction of Major Significance:
    - Change “Oral contraceptives” to “Oral estrogen and progestin products”
    - Add “carbamazepine, phenobarbital, primidone”
    - Add “Antipsychotics metabolized by 3A4 (aripiprazole, quetiapine, lurasidone, clozapine, haloperidol)”
    - Add “Clarithromycin, fentanyl, guanfacine, itraconazole, cyclosporine”
    - Add “Antidepressants metabolized by 3A4 (vilazodone, vortioxetine, MAO Inhibitors)”
    - Add “Apixaban, rivaroxaban”
    - Add “HIV medications: integrase inhibitors, maraviroc (Selzentry), cobicistat”
    - Add “Antigliptin medications: linagliptin (Tradjenta), saxagliptin (Onglyza)”
  - For Age-Specific considerations add: “Geriatric population maybe more sensitive to hyponatremia”
  - Side Effects Which Require Medical Attention add:
    - “Rash”
    - “Fever”
    - “Suicidal ideation”
  - Patient Monitoring Parameters to:
    - Add “CBC with differential – baseline and 1 to 2 weeks after each dose increase, annually, and as clinically indicated”
    - Change to “Electrolytes – baseline and 1 to 2 weeks after each dose increase, annually, and as clinically indicated”
    - Change to “Pregnancy test – baseline as appropriate and as clinically indicated”
    - Add “Hepatic function – baseline and annually”
    - Add “For patients with Asian descent, genetic test for HLA-B\*1502 at baseline (prior to the initiation of oxcarbazepine). May use results of previously completed testing.”
    - Add “Monitor for the emergence of suicidal ideation or behavior.”
- Gabapentin
  - Indication add:
    - “Treatment refractory anxiety disorders”
    - “Co-morbid anxiety in bipolar disorder (not as monotherapy)”
  - Relative Contraindications:
    - Add “creatinine clearance < 15 ml/min” to renal failure
  - Add “Lactation Risk L2” to Pregnancy and Breast Feeding
  - Drug Interactions of Major Significance:
    - Add “(aluminum or magnesium hydroxide) – when taken within 2 hours of the dose” to the Antacids listing
    - Delete “cimetidine”

- Delete “oral contraceptives”
    - Add “Hydrocodone (dose dependent)”
    - Add “Morphine”
    - Add “Concomitant CNS depressants”
  - Age-Specific Considerations add:
    - “Increased neuropsychiatric effects in children (emotional liability, hostility, thought disorder, hyperkinesia)”
    - “Clearance can be decreased in the elderly due to decrease in renal function.”
    - “Side effects such as peripheral edema, ataxia increase with age.”
  - Side Effects Which Require Medical Attention add:
    - “Dizziness”
    - “Ataxia”
    - “Peripheral edema”
    - “Rash, fever, lymphadenopathy”
  - Patient Monitoring Parameters:
    - Delete the word “test” from renal function
    - Add “Monitor for emergence of suicidal ideation or behavior”
  - Dosing add:
    - “Bioavailability decreases as the dose increases”
- Lamotrigine
  - Indication:
    - Change to “Bipolar disorders (not monotherapy for acute mania or monotherapy with an antidepressant) and other cyclic mood disorders”
    - Add “Lamotrigine has not been shown to be effective in preventing antidepressant induced mania” as a bullet
  - Relative Contraindications:
    - Delete “Age less than 16 years of age”
  - Precautions:
    - Delete “Photosensitivity”
    - Add “Suicidal ideations or behavior”
  - Add “Lactation Risk L2” to Pregnancy and Breast Feeding
  - Drug Interactions of Major Significance:
    - Delete “acetaminophen”
    - Add “primidone”
    - Add “Sertraline”
    - Add “Rifampin”
    - Add “oral estrogen containing contraceptives, oral estrogen replacement therapy”
  - Age-Specific Considerations:
    - Delete “Safety and efficacy in children <16 has not been established”
    - Add “Children and adolescents can have a higher incidence of rash.”
    - Add “Possible longer half-life in the elderly and patients with renal impairment.”
  - Side Effects Which Require Medical Attention:
    - Move “dizziness” to the headache listing
    - Add “blurred vision”
    - Add “ataxia”
    - Add “Fever, lymphadenopathy”
    - Add “Mental status changes, cognitive impairment”
    - Add “Aseptic meningitis”
  - Patient Monitoring Parameters:
    - Delete the word “test” from the Renal and Hepatic Function listings
    - Delete “yearly” from the Hepatic Function requirement
    - Add “CBC – baseline and as clinically indicated”
    - Add “Monitor for the emergence of suicidal ideation or behavior”
    - Add “Monitor for rash, especially during the first two months of therapy”

- Dosing add:
  - “Titrate dose per manufacturer’s package insert to minimize risk of significant side effects.”
  - “If therapy lapses for greater than 5 half-lives, the labeling recommends re-titrating the medication to minimize the incidence of rash.”
  - “The medication should be discontinued gradually (over at least two weeks) unless significant adverse effects (e.g., rash) or other serious adverse events exist.”
  
- Lithium
  - Indication:
    - Change to “Bipolar disorders or other cyclic mood disorders”
    - Change to “Augmentation of antidepressant therapy for major depressive disorders”
    - Delete “Acute mania.”
  - Relative Contraindications:
    - Change to “Severe cardiovascular disease”
    - Delete “Goiter or hypothyroidism”
    - Delete “Psoriasis”
    - Change to “Severe renal insufficiency”
    - Delete “Concomitant use of diuretics”
    - Add “Severe hyponatremia”
  - Precautions:
    - Change to “Dermatological conditions (Psoriasis, acne, hair loss and other skin eruptions)”
    - Delete “Severe acne”
    - Add “Goiter”
    - Add “Concomitant use of thiazide diuretics”
    - Add “Concomitant use of ACE Inhibitors, ARBs”
    - Add “Concomitant use of NSAIDs”
    - Add “Gastrointestinal symptoms (nausea, diarrhea, vomiting)”
    - Add “Syncope episodes”
    - Add “Neurological symptoms (tremors, ataxia, dysarthria, parkinsonism)”
  - Add “Lactation Risk L4” to Pregnancy and Breast Feeding
  - Drug Interactions of Major significance:
    - Change to “Thiazide diuretics”
    - Change to “Non-steroidal and anti-inflammatory drugs (except sulindac, low dose aspirin)”
    - Add “ACE Inhibitors, ARBs”
    - Add “Serotonergic agents”
    - Add “Topiramate”
  - Age-Specific Considerations:
    - Change to “Monitoring of skeletal development and calcium levels in children if chronic lithium therapy is advised.”
  - Side Effects Which Require Medical Attention:
    - Change to “Thyroid disorders (hypothyroidism, hyperthyroidism)”
    - Change “Trembling” to “Tremors”
    - Add “Parathyroid disorders”
    - Add “Renal Impairment”
    - Add “Cardiac conduction abnormalities”
    - Add “Dermatological conditions (acne, hair loss)”
    - Add “Cognitive impairment”
    - Add “Mental status changes (disorientation, confusion)”
  - Patient Monitoring Parameters:
    - Change to: “Comprehensive Metabolic Panel (BUN, creatinine, glucose, calcium and electrolytes) – baseline, 3 months, annually and as clinically indicated. Caution: BUN:serum creatinine ratio > 20 maybe an indication of dehydration.”
    - Change to “Lithium Levels – one week (i.e., 5-7 days) after initiation or dosage change, 3 months after initiation, and as clinically indicated; for maintenance treatment every 6 months, and as clinically indicated”
    - Delete “Calcium and phosphate, in children under 12, prior to initiation and as clinically

- indicated”
      - Add “Weight – baseline, every 6 months and as clinically indicated”
      - Add “trough” so that it reads “Usual trough therapeutic level”
- Topiramate
  - Indication:
    - Delete “Cyclic mood disorders”
    - Add “Treatment resistant bipolar disorder (adjunct only)”
    - Add “Weight loss or prevention of weight gain from antipsychotic or divalproex therapy”
    - Add “Alcohol dependence”
  - Relative Contraindications:
    - Add “Glaucoma”
    - Add “Metabolic acidosis”
  - Precautions:
    - Delete “Parasthesias”
    - Change to “Moderate or severe renal impairment”
    - Add “Concomitant valproate therapy”
    - Add “Hyperammonemia”
    - Add “Hypothermia or hyperthermia”
  - Pregnancy and Breast-Feeding:
    - Change FDA Pregnancy Category to “D”
    - Add “Lactation Risk L3”
  - Drug Interactions of Major Significance:
    - Change to “Estrogen containing oral contraceptives (only significant if topiramate dose  $\geq$  200 mg/day)”
    - Change to “carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide)”
    - Add “Lithium”
  - Age-Specific Considerations:
    - Add “Oligohidrosis, hypothermia, kidney stones, metabolic acidosis are more common in children”
  - Side Effects Which May Require Medical Attention:
    - Add “Eye pain, visual disturbances”
    - Add “Oligohidrosis”
    - Add “Hypothermia or hyperthermia”
    - Add “Cognitive dysfunction”
    - Add “Hyperammonemia”
    - Add “Paresthesia”
    - Add “Metabolic acidosis”
    - Add “Kidney stones (severe flank or back pain)”
  - Patient Monitoring Parameters:
    - Change to “Comprehensive Metabolic Panel (renal and hepatic function, serum bicarbonate) – baseline, 3 months, annually and as clinically indicated”
    - Add “Eye Exam – baseline and annually”
    - Add “Monitor for the emergence of suicidal ideation or behavior”
    - Add “If used for weight loss, monitor weight baseline, quarterly and as clinically indicated”
- Valproic acid, divalproex sodium
  - Indication:
    - Change to “Bipolar disorder and other cyclic mood disorders”
    - Delete “Acute mania”
  - Absolute Contraindications:
    - Add “Severe hepatic dysfunction”
    - Add “Known mitochondrial disorders caused by mutations in mitochondrial DNA polymerase gamma”
    - Add “Urea cycle disorders”

- Relative Contraindications:
    - Change to “Mild to moderate hepatic disease/impairment”
    - Add “Hyperammonemia”
  - Precautions add:
    - “Pancreatitis”
    - “Concomitant topiramate use”
    - “Polycystic ovarian syndrome”
    - “Use of concomitant medication that can cause blood dyscrasias (e.g., carbamazepine, clozapine, etc.)”
    - “HIV or CMV infection”
    - “Brain atrophy (e.g., Cerebellar atrophy)”
  - Add “Lactation Risk L4” to Pregnancy and Breast Feeding
  - Drug Interactions of Major Significance:
    - Change to “Aspirin (for doses > 81 mg/day)”
    - Add “primidone” to the phenobarbital listing
    - Add “Amitriptyline, nortriptyline, desipramine, fluoxetine”
    - Add “Topiramate”
    - Add “Rifampin”
    - Add “Carbapenem antibiotics”
    - Add “Ethosuximide”
    - Add “Zidovudine”
  - Age-specific Considerations:
    - Add “Women of child-bearing age (e.g., polycystic ovarian syndrome)”
  - Side Effects Which Require Medical Attention:
    - Add “pancreatitis” to the “Nausea, vomiting, diarrhea, abdominal discomfort or anorexia” listing
    - Add “Signs/symptoms of infection (e.g., fever, sore throat, malaise, etc.)”
    - Add “Ataxia, gait disturbances, dysarthria”
    - Add “Sedation”
    - Add “Alopecia”
    - Add “Peripheral edema”
    - Add “Rash”
    - Add “Oligomenorrhea, signs/symptoms of hyperandrogenism”
    - Add “Suicide ideation”
  - Patient Monitoring Parameters:
    - Change to “CBC – with differential and platelet count – baseline then one (1) to two (2) weeks after each dosage increase, every 3 months for the first year of treatment, then annually and as clinically indicated”
    - Change to “Comprehensive Metabolic Panel (hepatic function, serum creatinine, BUN and electrolytes) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated” and remove the individual hepatic function, serum creatinine and BUN and electrolytes listing
    - Change to “Pregnancy Test – baseline as appropriate and as clinically indicated”
    - Add “Weight – baseline, quarterly for the first year of treatment, then annually and as clinically indicated”
    - Add “Monitor for the emergence of suicidal ideation”
    - Add “trough” so that it reads “Usual therapeutic trough level”
    - Change “For divalproex extended release (Depakote® ER) it is 85 – 125 mcg/ml (trough) for the treatment of acute mania. A lower therapeutic trough level may be needed with divalproex extended release for maintenance treatment. For extending release products, a trough level is considered to be 18 to 24 hours after the last dose”
- 
- Verapamil – Delete this listing due to lack of support for its use in clinical guidelines

In reviewing the psychotropic audit criteria, the Committee noted that the elements in the comprehensive metabolic panel meet the requirements for hepatic function monitoring.

On a motion of Dr. Heidel, seconded by Dr. Pittman, the recommended changes to the Mood Stabilizers Psychotropic Audit Criteria were approved. See Exhibit B.

### **Psychotropic Audit Criteria & Guidelines - Antidepressants**

The Antidepressant Audit Criteria and Guidelines have not been reviewed.

### **Psychotropic Audit Criteria & Guidelines – Chemical Dependence Adjunct**

The Chemical Dependence Adjunct Audit Criteria and Guidelines have not been developed.

### **Hepatitis C Treatment Guidelines**

Over the past several months, a few facilities have had patients/individuals that have had pharmacotherapy recommendations for the treatment of hepatitis C. The recommended treatments for hepatitis C cost around \$90,000 and payment for the treatment is a major concern in all areas of healthcare. The Texas Department of Criminal Justice (TDCJ) and their Correctional Managed Care are in the process of determining guidelines for treatment. The following draft guidelines are being considered by this agency:

If criteria is not met, therapy will be deferred until later date.

- Severe bridging fibrosis or cirrhosis (greater than or equal to F3);
- Extra-hepatic manifestations present;
- Liver transplant recipient;
- Hepatitis B co-infection; or
- On therapy at the time of incarceration

No longer recommended/use the following regimens:

- Peginterferon + ribavirin
- Peginterferon + ribavirin + 1<sup>st</sup> generation DAAs (telaprevir or oceprevir)

The TDCJ guidelines are scheduled to have their final review for approval in March.

The Infectious Diseases Society of America and the American Associations for the Study of Liver Diseases guidelines propose that because all patients cannot receive treatment immediately due to cost, priority should be given to those with the most urgent need.

The recommendations include the following:

- 1<sup>st</sup> tier = Patients with:
  - Advanced fibrosis
  - Compensated cirrhosis
  - Liver transplant recipients
  - Severe extrahepatic hepatitis
- 2<sup>nd</sup> tier = Patients with high risk for:
  - Liver-related complications or
  - Severe extrahepatic complications
- Also consider anticipated reduction in transmission versus likelihood of reinfection, such as:
  - Men who have high-risk sex with men

- Active injection drug users
- Incarcerated persons
- Those on hemodialysis

Dr. Pittman noted that a State Supported Living Center had an individual that required treatment for hepatitis C. Since the individual had Medicare Part D, the facility had a retail pharmacy fill the prescription. In order to qualify through their Medicare Part D Plan, the facility had to complete a questionnaire which was approved by their plan.

Dr. Richards noted that SASH had a patient that needed treatment for hepatitis C. The hospital bought the first month of treatment and then applied for the patient assistance program. The patient was accepted so the remaining two months of therapy was provided through the patient assistance program.

Dr. Baker noted that based on current funding, DSHS should not use general revenue for the payment of these drugs as this is not our primary mission.

The Committee discussed several options for treating patients with hepatitis C. These included:

- Treat everyone who meets the 1<sup>st</sup> tier criteria established by the Infectious Diseases Society of America
- Do not provide treatment
- Only treat if outside funding for the patient can be obtained (e.g., Medicare Part D, patient assistance programs)
- Only write a prescription to start therapy upon discharge so that another entity is financially responsible
- Consider treatment on a case by case basis approved by someone within DSHS. The Committee expressed concern that it isn't within the scope of this Committee to make this approval. The Committee can develop clinical guidelines for determining use.

The Committee expressed concern about starting treatment for a patient who may get discharged prior to completing treatment and who may not complete the entire course of therapy.

After much discussion, the Committee suggested tabling any decision regarding the use of these medications. The Committee recommended waiting to see how Texas Medicaid approaches the situation and obtaining data on the number of patients/individuals diagnosed with hepatitis C within the State Hospitals and State Supported Living Centers.

### **Antipsychotic Tier Schedule**

With the addition of clozapine suspension to the Formulary at the previous meeting, the Committee recommended that the Antipsychotic Tier Schedule be updated. The following changes were made to the Antipsychotic Tier Schedule:

- Increase the relative cost for aripiprazole to 8 dollar signs
- Increase the relative cost of asenapine to 5 dollar signs
- Increase the relative cost of fluphenazine decanoate LAI to 2 dollar signs
- Increase the relative cost of lurasidone to 8 dollar signs
- Increase the relative cost of perphenazine to 3 dollar signs
- Decrease the relative cost of quetiapine to 1 cent sign
- Increase the relative cost of thiothixene to 1 dollar sign
- Change the clozapine listing to "Clozapine Tablets, Oral Disintegrating Tablets"
- Change the relative cost of clozapine tablets to a range of 2 dollar signs to 7 dollar signs to reflect the difference in costs between tablets and oral disintegrating tablets
- Increase the relative cost of iloperidone to 11 dollar signs
- Increase the relative cost of paliperidone to 10 dollar signs
- Increase the relative cost of paliperidone palmitate LAI to 11 dollar signs
- Increase the relative cost of risperidone microspheres LAI to 10 dollar signs
- Decrease the relative cost of ziprasidone to 1 dollar sign

- Add clozapine suspension to the Tier 3 listing with the relative cost of 15 dollar signs
- Increase the relative cost of quetiapine ER to 7 dollar signs
- Increase the relative cost of thioridazine to 2 dollar signs

On a motion of Dr. Matthews, seconded by Dr. Heidel, the revised Antipsychotic Tier Schedule was approved. See Exhibit C.

### **New Drug Applications**

The Committee did not receive any new drug applications.

### **Drug Deletions**

No drugs were being considered for deletion at this time.

### **New Dosage Strengths**

The Committee did not consider any dosage strength addition to the Formulary.

### **Quetiapine (Seroquel®, Seroquel® XR) Purchases**

Dr. Richards reviewed the State Hospital purchases and returns of Seroquel® and Seroquel® XR from October through December. During this time, only Rio Grande State Center purchased \$1,221.25 worth of Seroquel® XR. During this time frame, five patients had orders for Seroquel® XR. At this time, no one at Rio Grande State Center is receiving Seroquel® XR. The Committee will continue to monitor the purchases to determine if this trend continues.

### **Adverse Drug Reaction Reports**

The Executive Formulary Committee discussed several adverse drug reaction reports received from the field.

In the first case, a 53 year old African American male with the diagnosis of dementia NOS, paranoid schizophrenia, antisocial personality disorder, esophageal reflux, and history of cervical cord decompression, discectomy and fusion, hyponatremia and seizures was admitted to a state hospital. The patient was transported to the emergency room multiple times for recurrent symptomatic hyponatremia and hypotension despite fluid restriction and demeclocycline 300 mg BID. On September 4, 2014, demeclocycline was increased to 300 mg TID with weekly follow-up. On September 23, 2014, his ANC dropped to 0.8 K/mm<sup>3</sup>. The demeclocycline was discontinued. On October 2, 2014 the ANC rebounded to 2.2 K/mm<sup>3</sup>.

In June 2014, a 52 year old male began to have meal refusals and weight loss (April 2014 weight was 117.5 lbs. and September 2014 weight was 104.6 lbs., height 62"). Lacosamide (Vimpat®) had been added to his drug regimen on April 16, 2014 at a low dose of 50 mg BID. The dose was increased to 200 mg BID by May 7<sup>th</sup>. Tremors and tics were noted on the right side (head and shoulders). A referral to neurology was made and on September 22<sup>nd</sup>, the neurologist started propranolol 40 mg BID for the abnormal movements. The "athetoid" or abnormal movements increased significantly by September 29<sup>th</sup> and were described as head shaking as if he was saying "no." Meal refusals continued. On September 29<sup>th</sup>, he was sent to the hospital with fever and unresponsiveness. A CT scan of the head showed nothing notable. His UA showed a probable UTI. He was treated with Bactrim® DS BID for 7 days. On September 30<sup>th</sup>, he was admitted to the facility Infirmery and a PICC line was placed for fluids and nutrition. At the same time, an order was given to taper the lacosamide rapidly over 7 days then discontinue. On October 1<sup>st</sup>, the propranolol was discontinued (after the dose was reduced to 20 mg BID on September 24<sup>th</sup> due to low blood pressure). Over the next 6 days, the abnormal head movements and meal refusals improved steadily. On

October 7<sup>th</sup>, the PICC line was discontinued because meal refusals had stopped and the abnormal head movements had ceased. Dr. Knight noted that lacosamide can cause head shaking.

A 64 year old Hispanic male presented with massive asymmetrical swelling of his tongue on the morning of November 6, 2014. He had no hives, wheezing or rash. He was started on lisinopril 5 mg two weeks prior at the suggestion of a cardiologist due to mild aortic regurgitation. He was transported to the emergency room. Lisinopril was discontinued and he was treated with epinephrine, diphenhydramine, Solu-Medrol®, and fresh frozen plasma. He also developed swelling in his feet that was treated with furosemide 20 mg. His blood pressure was elevated after the first unit of fresh frozen plasma. The patient was started on prednisone 20 mg for 4 days, then 10 mg for 4 days, amlodipine 5 mg for hypertension and ranitidine 150 mg BID. By 5 pm on the same day, the patient was feeling better and ready for supper. Tongue and leg swelling resolved.

On June 16, 2014, a 21 year old female was reported to have a heart rate of 140 beats/minute. On June 18<sup>th</sup>, the patient's heart rate was reported as 140 beats/minute in the morning. The patient's olanzapine oral disintegrating tablet (ODT) medication order was rewritten to hold the evening dose if the heart rate was greater than 110 beats/minute. That evening the heart rate was reported to be 128 beats/minute and the dose was held. On June 26<sup>th</sup>, an elevated heart rate of 126 beats/minute was reported and the olanzapine dose was held. The prescriber decreased the daily dose of olanzapine ODT. On June 27<sup>th</sup>, the patient was seen by the Internist who assessed the patient as having a "med-related tachycardia." On July 1<sup>st</sup> and July 2<sup>nd</sup>, both the morning and evening doses of olanzapine were held due to reports of a heart rate in the 130's beats/minute. On July 21<sup>st</sup>, the heart rate was reported as 152 beats/minute, and the olanzapine ODT dose was held. On July 22<sup>nd</sup>, the olanzapine ODT dose was discontinued. The patient had been on olanzapine ODT since October 30, 2013. On September 19<sup>th</sup> the prescriber documented in the medical record: "her pulse has also been normal since switching off Zyprexa and the rest of her vital signs stable."

A 45 year old male patient was started on pyrazinamide and rifampin on October 6, 2014. On October 23<sup>rd</sup>, the patient's serum creatinine started to trend upwards. His serum creatinine increased to as high as 3.76 mg/dl. He developed mild volume overload with increased blood pressure and pedal edema. He was transferred from our facility to a more acute hospital where a kidney biopsy was performed and it was confirmed allergic acute interstitial nephritis. Pyrazinamide and rifampin were discontinued. He was started on prednisone 70 mg and his serum creatinine began to trend downward.

A 56 year old female was admitted to the psychiatric hospital on September 11, 2014 with risperidone as a home medication for psychosis along with multiple other medical medications for hypertension, diabetes, and hyperlipidemia. All medical medications remained the same for the duration of her hospitalization. Psychotropic medications ordered at the time of admission include risperidone 1 mg twice daily, oxcarbazepine 600 mg twice daily and doxepin 25 mg at bedtime. An EKG on September 12<sup>th</sup> showed QTc of 513 msec. Doxepin was discontinued September 15<sup>th</sup> and risperidone was discontinued September 16<sup>th</sup> and chlorpromazine 150 mg per day was prescribed. Two follow-up EKGs were within normal limits (September 17<sup>th</sup> QTc 430 msec and September 19<sup>th</sup> QTc 426 msec). Risperidone was restarted on September 19<sup>th</sup> at 3 mg bedtime. Doxepin was not restarted. A repeat EKG on September 29<sup>th</sup> showed QTc 504 msec and risperidone was again discontinued. On October 22<sup>nd</sup>, an EKG was done before discharge and her QTc was 423 msec on same admission medical medications plus oxcarbazepine 600 mg twice daily, and chlorpromazine 350 mg total daily dose. Risperidone was thought to be responsible for the severe elevation on QTc > 500 confirmed upon on rechallenge.

## **Drug Formulary Sectional Review - Nasal/Mouth/Throat Agents**

### **Otic Agents**

### **Ophthalmic Agents**

Dr. Hall provided the review on the agents in the Nasal/Mouth/Throat section. See Attachment D. The only change that Dr. Hall recommended was that the "Nasal" section be separated from the mouth and throat section. On a motion of Dr. Matthews, seconded by Dr. Pittman the recommendation to separate the nasal products was approved.

Dr. Hall provided the review on the agents in the otic section. See Attachment E. Dr. Hall did not recommend any changes to this section.

Dr. Hall provided the review on the agents in the ophthalmic section. See Attachment F. Dr. Hall recommended that the “Lubricants” section be deleted and that the entry in this section be placed in the “Miscellaneous Ophthalmics” section. On a motion of Dr. Matthews, seconded by Ms. Millhollon, the recommendation to delete the lubricant section was approved.

Dr. Hall provided a brief review on glaucoma. The following are key points for glaucoma.

- World’s leading cause of irreversible blindness
- Asymptomatic until severe – only 10-50% know they have it
- Two broad categories
  - Open angle
    - > 80% cases
    - Increased resistance to aqueous outflow through trabecular meshwork
  - Closed angle
    - Iris obstructs access to drainage pathway
- Glaucoma can occur in individuals whose IOPs are within normal range
  - Population-based studies found IOP < 22 mm Hg in 25%-50% of individuals with glaucoma
- Risk factors for open-angle glaucoma
  - Older age, family history, black, systemic/topical corticosteroids, increased IOP
    - Many with increased IOP never develop glaucoma
- No symptoms until disease is advanced
  - Changes in appearance of optic nerve head and retinal nerve fiber layer
    - Retinal ganglion cell (RGC) loss → progressive deterioration of visual fields
  - Anyone with family history who has not had dilated funduscopic exam of optic nerve head in past 2 years should be referred
- Decreased IOP only proven method to treat glaucoma
  - American Academy of Ophthalmology recommends decreasing IOP toward a target range of values
  - If clinician observes optic nerve changes or visual field loss, target will need to be decreased.

Prostaglandin analogues (e.g., latanoprost, travoprost, tafluprost, unoprostone, bimatoprost) are first line treatment for glaucoma.

### **Supported Living Centers – Anticonvulsant Use**

At the last meeting, it was noted that many individuals at the Supported Living Centers are on three or more anticonvulsants for the treatment of seizure disorders. It was suggested that this data be brought back to the Committee for discussion. This data has not been obtained.

### **DSHS/DADS 2015 Drug Formulary - Website**

The 2015 Drug Formulary is posted at the following website:

<http://www.dshs.state.tx.us/mhprograms/Formulary.shtm>

## **FDA Drug Safety Communications**

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

The FDA is warning that the antipsychotic drug ziprasidone (marketed under the brand name, Geodon®, and its generics) is associated with a rare but serious skin reaction that can progress to affect other parts of the body. A new warning has been added to the ziprasidone drug label to describe the serious condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS may start as a rash that can spread to all parts of the body. It can include fever, swollen lymph nodes, and inflammation of organs such as the liver, kidney, lungs, heart, or pancreas. DRESS also causes a higher-than-normal number of eosinophils in the blood. DRESS can lead to death. Patients who have a fever with a rash and/or swollen lymph glands should seek urgent medical care. Health care professionals should immediately stop treatment with ziprasidone if DRESS is suspected.

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

For the first quarter of fiscal year 2015, all facilities reported use of non-formulary agents. The DADS facilities submitted 863 non-formulary requests and the DSHS facilities had 500 requests. The following were the top non-formulary agents that were prescribed:

Saccharomyces boulardii capsule (Florastor®)  
Fiber-Stat laxation solution packets  
Meningococcal conjugate vaccine (Menactra®)  
Magnesium oxide (Mag-Ox®)

## **Sectional Review for Next Meeting**

The following section will be reviewed at the next meeting:

Psychotropic Agents

## **Other Issues**

The following information was shared with the Committee members:

USA Today reports that “deaths from prescription painkillers have decreased for the first time since 1999, while heroin deaths have surged, suggesting some addicts may have turned to illicit drugs as new federal and state restrictions made prescription narcotics harder to get,” according to data from the Centers for Disease Control and Prevention revealed today by the White House Office of National Drug Control Policy. The data show that “abuse of prescription opioids...fueled a surge in overdose deaths, which quadrupled from 4,030 deaths in 1999 to 16,917 deaths in 2011.” The data also indicate that in 2012, “deaths from prescription painkillers dropped 5% to 16,007.”

The Wall Street Journal reports the FDA plans to survey 3,000 pharmacists and consumers to find out if physical characteristics of tablets such as shape, size and color have any impact on patient adherence. The agency wants to conduct the study that with a focus on generics as they make up about 85 percent of all medicines prescribed in the country. There is also a variability in physical characteristics of generic medicines, and patients refilling their prescriptions may end up getting a supply that appears different from what they had taken before.

The Huffington Post reported that research “presented at a meeting of the Canadian Cardiovascular Congress shows an association between having a mental disorder – including schizophrenia, depression,

anxiety and bipolar disorders – and an increased risk of heart disease or stroke.” Researchers analyzed information from the Canadian Community Health Survey. The investigators “found that the likelihood of having heart disease or a stroke was doubled for people who had a mental disorder during any point of their lives.” Additionally, the investigators “found that the likelihood of having heart disease was doubled and the likelihood of having had a stroke was tripled among people on psychiatric medications, which include antidepressants, mood-stabilizing drugs and antipsychotics.”

Medscape reports that at the 27th European College of Neuropsychopharmacology Congress, the first phase of “a newly proposed psychotropic drug reclassification system, complete with app, has been unveiled in the hope that it will reduce confusion over contradictory-sounding terminology.” The Nomenclature Project “was developed by the ECNP in collaboration with the American College of Neuropsychopharmacology (ACNP), the International College of Neuropsychopharmacology, the International Union of Basic and Clinical Pharmacology, and the Asian College of Neuropsychopharmacology.” The new system “shifts away from the current symptom-based terminology to terminology that focuses on the pharmacologic target, such as serotonin or dopamine, and mode of action.” At the American Psychiatric Association’s annual meeting in 2015, David Kupfer, MD, the ACNP representative to the task force putting together the new system, will present further information. Further plans to meet with the Food and Drug Administration and the American Medical Association are in development.

TIME reports that for the past 10 years, certain antidepressants have carried boxed warnings cautioning that the medications “may increase the risk of suicidal thoughts and behaviors in children and young adults.” Now, however, “many experts say...that the warnings overstate the real risk and may deter doctors from prescribing them to people who could benefit from being on antidepressants,” particularly people with severe depression who are in a higher risk category for suicide. Recently in the *New England Journal of Medicine*, a perspective piece called for removal of boxed warnings, while a companion critique questioned the data suggesting that boxed warnings could be removed. After speaking to 17 experts in the field of psychiatry, Time revealed that “11 said the warnings should be removed; two think the media has overblown the suicide risk posed by antidepressants, resulting in more panic than is necessary; and four support the box’s place on” the medicines. Currently, the Food and Drug Administration has no plans “to revisit the warning.”

Medwire News reports that according to a meta-analysis published online Nov. 5 in *JAMA Psychiatry*, atypical antipsychotics appear to “benefit patients with acute schizophrenia across the full spectrum of symptom severity, as well as highly symptomatic patients with predominantly negative symptoms.” Researchers arrived at that conclusion after analyzing the results from “three pivotal clinical trials comparing two atypical antipsychotics against placebo” and three clinical trials of patients who had predominantly negative symptoms of schizophrenia.

The NPR “Shots” blog reported that a 150-patient study found that the “pop bottle method,” in which people put a tablet in their mouth and lean their heads back as if gulping liquids from a soda bottle, helped about 60 percent of participants get a large vitamin tablet down comfortably. The second technique, called the “lean forward method,” is particularly helpful for swallowing capsules. It works by placing a capsule on the tongue, taking “a medium sip of water,” and then leaning the head forward while swallowing. Ninety percent of participants found that technique useful.

Recent changes to the CredibleMeds® lists of medications that prolong the QT interval and/or cause torsades de pointes (TdP) include:

**Hydroxyzine (Atarax®, Vistaril® and many other brand names)** is an antihistamine that is used to treat allergies, anxiety and other conditions. It has been added to the list of drugs with **Conditional Risk of TdP** because it is associated with TdP in patients with conditions such

as low serum potassium or magnesium, extremely slow heart rate or concomitant use of drugs known to cause TdP and/or prolong the QT interval.

**Metoclopramide (Reglan® and many other brand names)** is an anti-emetic that is used to treat nausea, vomiting and other conditions. It has been added to the list of drugs with **Conditional Risk of TdP** because it is associated with TdP in patients with conditions such as concomitant use of drugs known to cause TdP and/or prolong the QT interval.

Hydroxyzine and metoclopramide have also been added to the list of [Drugs to be Avoided by Patients with Congenital Long QT Syndrome](#) (CLQTS) if at all possible.

[Bloomberg News](#) reports that, according to a study released by the Tufts Center for the Study of Drug Development, “it costs drug makers \$2.56 billion to bring a new medicine to market, on average,” which is “more than double the price of 11 years ago,” according to a study released today. The researchers say the higher cost “comes from clinical trials that are larger and more complex, as well as more drugs that fail in development.” Joseph DiMasi, director of economic analysis at the Boston-based center, said in a statement, “Drug development remains a costly undertaking despite ongoing efforts across the full spectrum of pharmaceutical and biotech companies to rein in growing R&D costs.”

[HealthDay](#) reports that according to a study published in the December issue of the journal *Anesthesiology*, “the proportion of women dependent on drugs such as narcotic painkillers or heroin during pregnancy has more than doubled in the past decade and a half.” The research “covers a class of drugs known as opioids, which include prescription painkillers such as oxycodone (Oxycontin®) and Vicodin®; morphine and methadone; as well as illegal drugs such as heroin.” Researchers arrived at the study’s conclusion after analyzing “national hospitalization data on nearly 57 million deliveries between 1998 and 2011.”

The [Fox News](#) website reports that according to a study published in the journal *Psychology of Addictive Behaviors*, adolescents “prescribed sleep and anti-anxiety drugs may be up to 12 times more likely to abuse them compared to teens who have never received these prescriptions.” Investigators arrived at that conclusion after surveying “more than 2,700 middle and high school students online from the Detroit area twice annually from 2009 to 2012.” The study authors suggested that “substance abuse assessments, in addition to strict limitations on prescription refills, may help reduce the number of teens that abuse prescription” medicines. The piece also points out that a 2011 survey conducted by the Substance Abuse and Mental Health Services Administration found that three percent of US teens abuse sleep and anti-anxiety medicines.

The [New York Times](#) reported that the FDA issued a new rule that “changed how drug companies are required to present the risks of taking medicine during pregnancy and while breast-feeding.” The current system, described as “confusing and outdated” by physicians, used “letters of the alphabet to denote risk, with X being the most dangerous.” The new system, which will be implemented in June, “breaks the risk into three parts — pregnancy, lactation and fertility — and requires companies to give a summary of the risk,” including information “on existing human studies and on adverse reactions caused when the drug was taken during pregnancy or lactation.” Dr. Sandra Kweder, deputy director of the FDA’s Office of New Drugs in the Center for Drug Evaluation and Research, said of the rule, “It requires that more information about drugs will be provided than ever before, and in a manner that speaks directly to the concerns that doctors and their patients are likely to have.”

[HealthDay](#) reports that according to a study (12/5) published online in the *American Journal of Psychiatry*, a publication of the American Psychiatric Association, improper medication “treatment is given to nearly 40 percent of people who suffer their first episode of schizophrenia.” In the study of 404 patients suffering from their first episode of schizophrenia, 159 patient received medication “treatment that was inconsistent with recommendations for first-episode patients,” such as being prescribed more than one antipsychotic or

being prescribed “an antidepressant without justification” or a “psychotropic medication other than an antipsychotic.”

HealthDay reports that taking methylphenidate, a “medication for attention-deficit/hyperactivity disorder (AD/HD), might reduce the risk of young patients accidentally injuring themselves.” Researchers found that “when several thousand children and teens were taking methylphenidate...they were a little less likely to end up in the” emergency department “than when they weren’t taking the” medication.

Medwire News reports that according to a study published Nov. 30 in BMC Psychiatry, about “a quarter of patients with schizophrenia receive antipsychotic polypharmacy, despite a lack of evidence for the approach.” After analyzing “data on 4156 patients with schizophrenia who belonged to an employer-based health plan,” investigators “found that 968 (23.3%) patients received two or more antipsychotic drugs within 90 days of each other during one-year follow-up.”

The Wall Street Journal reports that Alkermes announced positive results from its phase 2 study of ALKS 3831, its investigational schizophrenia treatment. The article emphasizes that Alkermes’ experimental treatment was as effective as the established antipsychotic olanzapine (Zyprexa) and, crucially, patients had 37% less weight gain on average than those using the established treatment. The Journal says Alkermes plans to ask the FDA for a meeting to move to a late-stage study in 2015.

The Hill reports that the FDA announced the agency is “looking to identify drugs that impair drivers’ ability and increase their risk of being involved in a motor vehicle accident.” The draft guidance, which will help “drugmakers assess the risk psychoactive drugs pose to drivers and other people who share the road with them,” recommends that “manufacturers use a systematic approach to identify which drugs should be evaluated to determine what effects they would have on drivers.”

Reuters reports that Richter, a Hungarian pharmaceutical company, and Actavis announced today that a Phase III trial of Cariprazine (RGH-188), an antipsychotic medication tested to prevent relapse for schizophrenia patients, yielded positive results. In a statement, the companies reported that use of the treatment was associated with a 55% reduction in the risk of relapse when compared to placebo.

Forbes (1/27) contributor Luke Timmerman wrote about an experimental depression treatment, called NRX-1074, that in a 140-participant study “helped push patients out of a major depressive state within 24 hours of getting a single intravenous shot.” According to the National Institute of Mental Health, “about 6.7 percent of US adults are estimated to experience a major depressive episode – defined as depression that interferes with the ability to work, sleep, study, eat, and enjoy life.”

### **Next Meeting Date**

The next meeting was scheduled for April 17, 2015.

### **Adjourn**

There being no further business, the meeting was adjourned at 1:35 p.m.

Approved: Jennifer Wright, M.D.  
Jennifer Wright, M.D., Chairman

Attachments

- Attachment A – Psychotropic Consent List
- Attachment B – Psychotropic Audit Criteria & Guidelines – Mood Stabilizers
- Attachment C – Antipsychotic Tier Schedule
- Attachment D – Nasal/Mouth/Throat Agents Sectional Review
- Attachment E – Otic Agents Sectional Review
- Attachment F – Ophthalmic Agents Sectional Review

Minutes Prepared by:

Ann L. Richards, Pharm.D., BCPP