

DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
January 29, 2016

The Executive Formulary Committee convened on Friday, January 29, 2016 in Room 125 - ASH Building 552. The meeting was called to order by Dr. Wright, Chair at 9:45am.

Phillip Balfanz, M.D.	Absent	Lilani Muthali, M.D. (non-voting)	√
Mary Bowers RN, BSN	Absent	Nina Muse, M.D. (Acting Medical Director)	√
Catherine Hall, Pharm.D.	√	Peggy Perry (non-voting)	Absent
Jeanna Heidel, Pharm.D.	√	Scott Schalchlin (non-voting)	Absent
Marla Knight, Pharm.D., CGP, FASCP	Absent	Lauren Lacefield Lewis (non-voting)	Absent
Jeff Matthews, M.D.	Absent	Kerry Raymond (non-voting)	Absent
Mark Messer, D.O.	√	Vacant Center Position	
Connie Millhollon, RN	√	Vacant Center Position	
Kenda Pittman, Pharm.D.	√	Vacant DADS Nursing Director (non-voting)	
Ann L. Richards, Pharm.D.	√	Vacant DADS Physician	
Archie Smith, M.D.	√	Vacant DSHS Nursing Director (non-voting)	
Jennifer Wright, M.D.	√		

Guests Present:

Lisa Mican, Pharm.D., Austin State Hospital; Michelle Bastanjoo, Pharmacy Student ASH; Michelle Ding, Pharm.D., Resident ASH; Thomas Maestri, Pharm.D., Pharmacy Resident ASH; Karen Hardwick, PhD, DADS; Isaac Pan, Pharm.D., Resident SASH

Introduction and Other Information

Ms. Valerie Kipfer has departed DADS and her position is vacant. Dr. Pittman noted that Dr. Murry has returned to Austin State Supported Living Center and is interested in serving in the open DADS physician position.

Approval of Minutes of October 30, 2015

On a motion of Dr. Heidel, seconded by Ms. Millhollon, the minutes of the October 30th meeting were approved as previously distributed.

Conflict of Interest

Committee members in attendance of the meeting completed their annual disclosure of conflict of interest. The review of these statements did not reveal any conflicts of interest. Members not in attendance will be asked to complete their statements for presentation at the next meeting.

Issues from the Medical Executive Committee

Dr. Muse attended the meeting briefly to indicate that the Medical Executive Committee did not have any issues for this Committee.

Adverse Drug Reaction Reports

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

An 80 year old African American male was admitted to the psychiatric hospital in November of 2015. He has a diagnosis of schizoaffective disorder and also multiple medical problems including Type 2 Diabetes, GERD, *H. pylori* infection, and hypertension. Admission labs related to the adverse event were unremarkable. In addition, his EKG one day after admission indicated left ventricular hypertrophy and the QTc was within normal limits at 391 msec. A chest x-ray prior to admission noted an ectatic aorta. Medications prescribed prior to the adverse event include vitamin B12 and D3, omeprazole (Prilosec®) 20 mg twice daily for *H. pylori*, metronidazole (Flagyl®) 500 mg three times daily for *H. pylori*, doxycycline (Vibramycin®) 100 mg twice daily for *H. pylori*, bismuth subsalicylate (Pepto-Bismol®) 524 mg four times daily for *H. pylori*, divalproex (Depakote®) 500 mg at bedtime for mood stabilization, mirtazapine (Remeron®) 15 mg daily, metformin (Glucophage®) 500 mg twice daily with meals for diabetes, PEG 3350 (Miralax®) 17 Gm twice daily for constipation, and lisinopril (Prinivil®) 20 mg daily for hypertension. A PSA level one week after admission was elevated at 22.6 ng/mL and finasteride (Proscar®) 5 mg in the morning was prescribed for presumed BPH with the first dose initiated the day after the first day of diastolic hypotension. The diastolic hypotension would occur almost every other day with systolic blood pressure in the 90-100's mmHg and diastolic blood pressure in the 50's mmHg. The day prior to the adverse event the patient refused most of his medications and received only one metronidazole and bismuth subsalicylate dose at noon as well as a dose of metformin and bismuth subsalicylate that evening. Three weeks after admission and the day of the adverse event, the patient refused all oral medications prescribed. A dose of aripiprazole (Abilify®) 9.75 mg IM was administered at 8:08 pm for refusal of court ordered mirtazapine 15 mg po in the evening. Approximately 30 minutes after the aripiprazole short-acting IM injection, the patient experienced a syncopal episode with loss of consciousness for 10 seconds with hypotension (blood pressure 106/51 mmHg) and he was transferred to a local medical hospital for treatment. The syncopal event with hypotension was thought to be due to aripiprazole short-acting IM and it was discontinued without further syncope reported.

A 44 year-old biological female who was admitted to the psychiatric hospital April of 2014 for the treatment of schizophrenia. Her only medical diagnosis is a Vitamin D insufficiency (vitamin D level 25 ng/ml on 8/1/15) with no reported history of seizures prior to 9/6/15. Prior to admission, she had taken clozapine (Clozaril®) with good response and during this current psychiatric hospitalization from 12/11/14 – 02/13/15 without reported seizures. Clozapine was discontinued on 2/13/15 after a brief trial due to slurred speech; however, she was also prescribed clonazepam (Klonopin®) at the time. A comprehensive metabolic panel on 4/20/15 was within normal limits and CBCs around the time of the event were also within normal limits. Clozapine was reinitiated on 5/4/15 with a dose of 12.5 mg po in the evening. The dose was slowly titrated over the next two months. Based on a clozapine level of 380 ng/ml on 6/29/15 while prescribed clozapine 200 mg po in the morning and 250 mg po in the evening; the dose was further titrated to 300 mg po in the morning and 400 mg po in the evening on 7/31/15. Due to the lower than expected lab level and history of cheeking medication, it was suspected that she may not be receiving the full intended, prescribed dose. Clozapine was switched to the ODT formulation FazaClo® on 8/7/15 at the same 700 mg total daily dose. The clozapine level was 592 ng/ml on 8/17/15. On 9/2/15, the morning dose was increased to 350 mg ODT and the evening dose remained 400 mg ODT. She was found in her room on 9/6/15 lying on the floor with a painful lump on her head after having what looked like a tonic seizure and was transported to a local medical hospital where a CT was performed. The results were within normal limits. Scheduled medications at the time of the event were clozapine (FazaClo®) ODT 350 mg in the morning and 400 mg in the evening (750 mg total daily dose) for psychosis, atenolol (Tenormin®) 12.5 mg taken at 10:00 am and 6:00 pm daily for tachycardia, and risperidone LAI 50 mg IM every two weeks at bedtime for delusions/hallucinations. On 9/7/15, clozapine ODT was tapered to 300 mg ODT twice daily and atenolol was discontinued after two falls that day without loss of consciousness. On 9/18/15, she was observed to have a 3 minute seizure. A clozapine level on 9/21/15 was 597 ng/ml. An EEG was obtained and indicated potential epileptic activity bilaterally in a multifocal pattern with diffuse slowing and disorganization of the background rhythm indicating encephalopathy. The neurologist recommended adding an anticonvulsant or discontinuing clozapine; however, the patient began refusing all oral medication so clozapine was discontinued and an anticonvulsant was not prescribed. No further seizures were observed off of clozapine.

On the morning of 11/12/15, it was reported that 67 year old African-American female was making unusual tongue movements. Dental exam was negative. By 2:00 pm, her tongue was noted to be swollen almost to the point of occluding her airway. Diphenhydramine (Benadryl®) IM was administered with no effect and she was sent to the Emergency Room by ambulance. At the hospital, she was admitted to ICU and intubated. She was given methylprednisolone (Solu Medrol®), diphenhydramine and levofloxacin (Levaquin®). Chest x-ray showed no acute abnormalities. A urinary tract infection was diagnosed at admission as well as normocytic anemia of chronic disease. The angiotensin converting enzyme (ACE) inhibitor (lisinopril), which she had been on since 2008, was discontinued at admission and possible angioedema, bradykinin-mediated, was tentatively diagnosed. CBC was unremarkable with the exception of the slight anemia noted above. CMP was unremarkable. Urine culture showed >100,000 gram positive flora. Previous to this incident, she had been treated with levofloxacin for a UTI (10/31/15) and dehydration. The tongue swelling had decreased significantly by the next morning and she was moved to a telemetry unit. Her hypertension medication was changed to a calcium channel blocker, amlodipine

(Norvasc®) and she was normotensive. She was discharged from the hospital on 11/17/2015 on a tapering dose of prednisone with instructions to continue the amlodipine for hypertension. Final diagnosis was angioedema due to ACE inhibitor.

A 48 year old female patient developed a rash that was first noticed on day 33 of hospitalization. It was a macular, papular rash described as erythematous and petechial that spread to the majority of the body; it was most pronounced on the chest and trunk. It was non-itchy except when scratched, non-painful, and non-scaly. Valproic acid (Depakene®) was discontinued that day and the penicillin VK was discontinued the following day (day 34 of hospitalization). Prior to the rash being noted, the patient had a few medication adjustments that occurred. On hospital day 10, valproic acid 500 mg BID was initiated, the dose was increased to 750 mg BID on hospital day 23 and then again to 1,000 mg BID on hospital day 31. Of note, the patient has been previously treated with valproic acid in the past with good outcomes. The patient was seen in the dental clinic during her hospitalization and penicillin VK 500 mg four times a day was initiated on hospital day 28. Patient was treated with diphenhydramine 25 mg three times a day on hospital day 35 and methylprednisolone (Medrol® dose pack) starting with 24 mg in divided doses and tapering down by 4 mg each day for six days which would be completed on hospital stay day 41. She refused the Medrol® dose pack. The rash began to improve and was last mentioned in a progress note on hospital stay day 45. Instead of re-challenging with valproic acid, the patient was started on lithium citrate on day 43 of hospitalization.

A 45 year old white male was admitted to the hospital for treatment of psychosis and mood disorder on 10/15/2015. Medications taken prior to admission included lisinopril (Prinivil®) 20 mg BID, trazodone (Desyrel®) 50 mg Q PM, divalproex (Depakote®) 1,500 mg daily, and clonidine 0.1 mg BID. All medications were continued with the exception of trifluoperazine (Stelazine®), which was changed to perphenazine (Trilafon®) 16 mg. In addition, the following medications were added: Terbinafine (Lamisil®) 1% cream, olanzapine (Zyprexa®) 10 mg tab PRN, Mylanta® 30 ml PRN, lactulose PRN, carbamide peroxide otic. Amoxicillin (Amoxil®) 500 mg TID was added on October 19th. On October 20th, perphenazine 4 mg BID was added for total dose of 20 mg BID. On October 22nd, nicotine gum 2 mg every 4 hours PRN and ibuprofen (Motrin®) 600 mg BID with meals were added. His sodium prior to admission was 128 mEq/L. On admission, he had abnormal labs including, sodium 126 mEq/L. He was diagnosed with hyponatremia and placed on fluid restrictions. By October 23rd, his sodium level was up to 136 mEq/L. On October 26th, he was sent to the ER with hypotension and bradycardia. His sodium at this time was 129 mEq/L. He was admitted for observation and IV fluids. He was given 3 liters of normal saline. Sodium returned to 136 mEq/L on October 27th. Perphenazine was discontinued due to potential risk for causing QT prolongation and bradycardia. Amoxicillin and clonidine were also discontinued and lisinopril was increased to 40 mg per day. On October 29th, he was discharged back to the psychiatric hospital with diagnosis of hypotension, bradycardia from drug effects and dehydration. He was started on quetiapine (Seroquel®), which he reports he did well on in the past. On November 14th, he had no further issues with bradycardia and hypotension.

A 54 year old black male was admitted to the hospital for psychiatric treatment and competency restoration on August 26th. His medical history includes hypertension, pulmonary problems, asthma, heart disease, hyperlipidemia, mitral and tricuspid regurgitation, and left ventricular hypertrophy. He has a history of cannabis abuse for 7 years, most recently 1 year ago. He has a history of sleep apnea and has a sleep study pending. Medications at admission included

risperidone (Risperdal®) 8 mg po PM for psychosis
benztropine (Cogentin®) 1 mg po BID for EPS
spironolactone (Aldactone®) 50 mg po Q-AM for hypertension
nifedipine (Procardia®) SL 60 mg po Q-AM for hypertension
metoprolol (Toprol®) XL 50 mg PO BID for Hypertension
atorvastatin (Lipitor®) 20 mg po Q-PM for high cholesterol
ipratropium/albuterol (Duoneb®) solution q4h cough
modafinil (Provigil®) 200 mg po Q-AM for obstructive sleep apnea
fluticasone (Flonase®) 2 sprays Q-AM
minoxidil orally, dose not reported
fluticasone/salmeterol (Advair®) Inhaler

On October 8th, the patient continued to have problems staying awake in class. At times, he stated that the risperidone was the cause of his sedation. He was encouraged to switch to aripiprazole (Abilify®), but preferred to stay on risperidone. The dose was lowered to 6 mg daily. On October 14th, the patient complained of difficulty breathing and was started on oxygen, which brought up his oxygen saturation to around 70%. He was transported to the ER and admitted to the medical hospital for respiratory arrest. During his stay, he was intubated on two occasions, but he was eventually weaned off and stable for 2-3 days before being transferred back to this facility. Final diagnosis at discharge was COPD, obstructive sleep apnea and possible narcolepsy. On October 26th, he was returned to this hospital where he was continued on BiPAP, with recommendation to avoid benzodiazepines. Pulmonary consultation pending for atrial fibrillation and pericardial effusion. Advair® and Combivent® were continued for COPD; nifedipine, minoxidil, spironolactone and metoprolol extended release

for hypertension; and atorvastatin continued for hyperlipidemia. Risperidone and benztropine were discontinued on October 27th and it was suggested that the patient be placed in a skilled nursing facility due to severe debilitation. On October 28th, the patient states he is using the BiPAP and he showed improvement with daytime hypersomnolence and the minoxidil dose was decreased. On October 29th, the patient was dramatically improved with O₂Sat on room air at 93%. He was still drowsy, but greatly improved and transfer to skilled nursing facility was no longer recommended. Minoxidil was discontinued on November 15th.

Drug Formulary Sectional Review-

Dementia/Miscellaneous CNS Agents Migraine Agents Nutritional/Nutritional Supplements

Dr. Hall and Dr. Pan provided the sectional review on these agents. Ms. Debra Gregg, Assistant Director at San Antonio State Hospital assisted in the review of the drug products.

The following is a summary of indications for the agents used to treat dementia:

- Donepezil – mild, moderate, severe Alzheimer Disease
- Rivastigmine – mild, moderate, severe Alzheimer Disease; dementia related to Parkinson Disease
- Galantamine – mild, moderate Alzheimer Disease
- Memantine – mild, moderate, severe Alzheimer Disease

The Committee noted that donepezil 23 mg tablet is listed as being on Formulary. The Committee decided to review the purchase history of donepezil 23 mg.

The Committee reviewed clinical pearls for using these agents including:

- Cholinesterase inhibitors
 - Due to GI issues: slow titration, give with food and if need be implement dose reduction
 - GI bleed: Avoid NSAIDs
 - Insomnia: morning dosing
 - Monitor for bradycardia
- Memantine
 - Immediate release (IR) can be given once daily due to very long half -life (no head-to-head trial comparison between IR once daily and XR cap)

No changes were recommended for the dementia or miscellaneous CNS agents.

Dr. Pan provided a review of the agents used to treat migraine and cluster headache. NSAIDs and the combination of acetaminophen/aspirin/caffeine are used first line for the treatment of mild to moderate migraines. For moderate to severe migraines, the triptans are the treatment of choice. Ergots are less used due to the availability of the triptans.

Prophylactic treatments for migraines include:

- Beta Blockers
 - Formulary drugs listed in the migraine section
 - Propranolol
 - Metoprolol
 - Atenolol
- Antidepressants
 - Formulary drug listed in the migraine section
 - Fluoxetine
- Anticonvulsants
 - Formulary drugs listed in the migraine section
 - Divalproex
 - Valproate
 - Topiramate
- Other Agent
 - Formulary drug listed in the migraine section
 - Verapamil
 - Used for prevention of cluster headache

Dr. Pan noted that in 2012, the American Academy of Neurology rated fluoxetine as a Category U (inadequate or conflicting data to support or refute). Therefore, it was suggested that fluoxetine be removed from the migraine section. The American Academy of Neurology does list amitriptyline and venlafaxine as Level B (probably effective) as a migraine preventive.

On a motion of Dr. Messer, seconded by Dr. Pittman, the recommendation to remove fluoxetine from the migraine and add amitriptyline and venlafaxine to the migraine section was approved.

Dr. Hall reviewed the nutritional agents by sections. For the vitamins, it was noted that products get added to the market frequently and others get removed. With this ongoing change, it is difficult to keep the formulary up to date on these products. Therefore, it was recommended that specific dosage strengths not be listed but instead, only the dosage form. In addition, all these products would be considered to be on Formulary. However, for the fat soluble vitamins A, D, E and K, it was recommended that the specific dosage products be listed and only these would be considered formulary.

The following changes were recommended:

- Delete leucovorin (Wellcovorin®) from the vitamin section
- Delete nicotinamide from the niacin listing
- Delete phytonadione injection
- Delete Vitamin A 50,000 units as not available
- Delete Vitamin A injection
- For Vitamin D listings, identify if the product is D2 or D3
- Delete Vitamin E tablet: 200 units, 400 units and 2,000 units as they are no longer available

On a motion of Dr. Messer, seconded by Dr. Pittman, the recommended changes to the vitamin section were approved.

For the minerals, trace elements and electrolytes; it was noted that the products in this section changes frequently. As a result, it was recommended that only the dosage form be listed in the Formulary and not specific dosage strengths. All products falling within the dosage form listed would be considered Formulary. For the calcium and iron listings, it was recommended that the percent of the element be included within the listing. Other recommendations for this section include:

- Delete dosage forms no longer commercially available
- Keep the specific product listings for potassium chloride
- For potassium chloride delete the following:
 - Liquid, oral: 15% (30 mEq/15ml) as not available
 - Crystals for oral suspension, extended release: 20 mEq/packet as not available
 - Powder for oral suspension (per packet): 15 mEq as not available
 - Controlled release (wax matrix) 500 mg (6.7 mEq) as not available
- Delete potassium phosphate powder for oral solution: 250 mg elemental phosphorus/14.2 mEq potassium per packet as not available
- For the combination products, only list dosage forms not specific dosage strengths
- For listings involving calcium and iron, adding the percent of the element
- Delete Filibon® as the trade name for multivitamins, prenatal

On a motion of Dr. Messer, seconded by Dr. Pittman, the recommended changes were approved.

For the nutritional supplement section, it was recommended that the table of certification processes and product lines be listed prior to the listings of products. In addition, it was recommended that only the dosage forms be listed and not specific dosage strengths. Thus, any product within that dosage line would be considered to be on Formulary. On a motion of Dr. Messer, seconded by Dr. Pittman, the recommended changes to the nutritional supplement section were approved.

In discussing vitamin D, it was noted that the normal range for vitamin D, 25-OH is 30-100 ng/ml. Dr. Smith noted that even though the normal range extends to 100 ng/ml, one wouldn't supplement with vitamin D to reach levels greater than 50 ng/ml. And that just because someone has a level < 30 ng/ml, one may choose not to provide vitamin D supplements, especially if the level is only slightly below 30 ng/ml. On a motion of Dr. Smith, seconded by Dr. Pittman, it was recommended that the ideal vitamin D level be researched.

Psychotropic Consent List

Dr. Richards presented the proposed psychotropic consent list. It was suggested to add the following drugs to the list:

Antidepressant

Levomilnacipran (Fetzima®) *nonformulary*

Anxiolytics/Sedatives/Hypnotics

Suvorexant (Belsomra®) *nonformulary*

Zolpidem (Ambien® CR) *nonformulary*

Antipsychotics

Aripiprazole lauroxil (Aristada®) *nonformulary*

Brexpiprazole (Rexulti®)

Molindone (Moban®) *nonformulary*

Paliperidone palmitate (Invega® Trinza™) *nonformulary*

Later in the meeting, aripiprazole lauroxil and brexpiprazole were considered for addition to the Formulary with brexpiprazole being added to the Formulary. Molindone is being produced again but is not currently available through our wholesaler.

It addition, it was recommended to add the following trades names to the consent list:

- Depakote® Sprinkles to divalproex sodium
- Dexedrine® ER to dextroamphetamine

The following drugs/products currently FDA approved or on the market were not added to the psychotropic consent list as the products are currently not being used or are nonformulary:

- Bupropion (Forfivo® XL)
- Trazodone ER (Oleptro®)
- Zolpidem sublingual (Intermezzo®)
- Naltrexone patch (Vivitrol®)
- Cariprazine (Vraylar®)
- Aptensio® XR - trade name for methylphenidate

On a motion of Dr. Heidel, seconded by Dr. Smith, the proposed psychotropic consent list was approved. See Attachment A.

Drug Deletion

The following items were recommended for deletion at the October meeting.

Generic Name	Brand Name	Dosage forms to be deleted	Dosage forms still available
Amoxicillin	Amoxil®, Polymox®	Powder for oral suspension: 50 mg/ml	Capsule: 250 mg, 500 mg Powder for oral suspension: 125 mg/5 ml, 250 mg/5 ml Tablet: 500 mg, 875 mg Tablet, chewable: 125 mg, 250 mg
Amoxicillin-Clavulanate	Augmentin®	Tablet: 200 mg (contains clavulanate 28.5 mg), 400 mg (contains clavulanate 57 mg)	Suspension, oral: 400 mg (contains clavulanate 57 mg) per 5 ml, 600 mg (contains clavulanate 42.9 mg) per 5 ml Tablet: 250 mg (contains clavulanate 125 mg), 500 mg (contains clavulanate 125 mg), 875 mg (contains clavulanate 125 mg) Tablet, chewable: 125 mg (contains clavulanate 31.25 mg), 250 mg (contains clavulanate 62.5 mg) Tablet, extended release: 1000 mg (contains clavulanate 62.5 mg)
Nafcillin	Unipen®	Capsule: 250 mg Powder for injection: 4 g Solution: 250 mg/5 ml Tablet 500 mg	Powder for injection: 500 mg, 1 g, 2 g, 10 g
Penicillin G Benzathine	Bicillin®	Injection: 300,000 units/ml	Injection: 600,000 units/ml
Penicillin G Benzathine – Penicillin G Procaine	Bicillin C-R®	Penicillin G Benzathine 150,000 units – Penicillin G Procaine 150,000 units	Penicillin G Benzathine 900,000 units – Penicillin G Procaine 300,000 units
Penicillin G Procaine	Wycillin®	Injection (suspension): 300,000 units/ml, 500,000 units/ml	Injection (suspension): 600,000 units/ml
Penicillin V Potassium	Pen-Vee K®, V-Cillin K®	Tablet: 125 mg	Powder for oral solution: 125 mg/5 ml, 250 mg/5 ml Tablet: 250 mg, 500 mg
Cefazolin	Kefzol®, Ancef®	Powder for injection: 250 mg	Injection: 500 mg, 1 g Powder for injection: 500 mg, 1 g, 5 g, 10 g, 20 g
Cephalexin	Keflex®	Powder for oral suspension: 100 mg/ml Tablet: 1 g	Capsule: 250 mg, 500 mg Powder for oral suspension: 125 mg/5 ml, 250 mg/5 ml Tablet: 250 mg, 500 mg
Azithromycin	Zithromax®	Powder for oral solution: 400 mg/5 ml	Powder for oral solution: 200 mg/5 ml Tablet: 250 mg, 500 mg, 600 mg

Tetracycline		Capsule: 100 mg Suspension, oral 125 mg/5 ml Tablet: 250 mg, 500 mg	Capsule: 250 mg, 500 mg
Gentamicin		Infusion, premixed in D5W: 60 mg, 80 mg, 100 mg	Infusion, premixed in NS: 40 mg, 60 mg, 80 mg, 90 mg, 100 mg, 120 mg Injection: 10 mg/ml, 40 mg/ml Injection, intrathecal (preservative free): 2 mg/ml
Vancomycin	Vancocin®	Powder for oral solution: 1 g, 10 g Powder for injection: 2 g	Powder for injection: 1 g, 5 g, 10 g
Erythromycin base	Eryc®, E-Mycin®, Ery-Tab®, E-Base®, PCE®	Tablet, enteric coated: 250 mg, 333 mg, 500 mg Tablet, polymer coated particles: 333 mg, 500 mg	Capsule, delayed release: 250 mg Tablet, film coated: 250 mg, 500 mg
Erythromycin ethylsuccinate	EryPed®, EES®	Suspension, oral (drops): 100 mg/2.5 ml Tablet, chewable: 200 mg	Granules/Powder for oral suspension: 200 mg/5 ml, 400 mg/5 ml Suspension, oral: 200 mg/5 ml, 400 mg/5 ml Tablet: 400 mg
Griseofulvin	Fulvicin®	Microsize: Capsule: 125 mg, 500 mg Tablet: 250 mg Ultramicrosize: Tablet: 165 mg, 330 mg	Microsize Suspension, oral: 125 mg/5 ml with 0.2% alcohol Tablet: 500 mg Ultramicrosize: Tablet: 125 mg, 250 mg
Nystatin	Mycostatin®	Powder for oral suspension: 50 million units, 1 billion units, 2 billion units, 5 billion units Troche: 200,000 units	Suspension, oral: 100,000 units/ml Tablet, oral: 500,000 units
Isoniazid		Tablet: 50 mg	Injection: 100 mg/ml Syrup: 50 mg/5 ml Tablet: 100 mg, 300 mg
Thiabendazole	Mintezol®	Suspension, oral: 500 mg/5 ml Tablet, chewable: 500 mg	None
Nitrofurantoin	Macrochantin®	Capsule: 50 mg, 100 mg Capsule, extended release: 100 mg	Capsule, macrocrystal: 25 mg, 50 mg, 100 mg Capsule, macrocrystal/ monohydrate: 100 mg Suspension, oral: 25 mg/ml

The field did not provide any feedback on the suggested deletions. On a motion of Ms. Millhollon, seconded by Dr. Heidel, the products were deleted from the Formulary.

New Dosage Strengths

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

Dexmethylphenidate (Focalin®, Focalin® XR) Purchases

The following is a summary of dexmethylphenidate purchases for the State Hospitals and State Supported Living Centers for the past quarter (October through December):

Facility Type	Item Quantity	Total
State Hospitals	4	\$2,790.02
State Supported Living Centers	6	\$2604.88
Grand Total	10	\$5394.90

The Committee decided that the amount of dexmethylphenidate purchased does not warrant consideration for addition to Formulary at this time. If purchases or orders for the drug increase, then this decision will be reconsidered.

CMS Quality Measure – Smoking Cessation

For 2016, CMS is measuring the number of patients who are tobacco product users that were referred to or refused evidence-based outpatient counseling and received or refused a prescription for FDA-approved cessation medication at discharge. The list of FDA approved cessation medication includes the following:

- Bupropion (Zyban®)
- Varenicline (Chantix®) - *nonformulary*
- Nicotine gum
- Nicotine inhaler – *nonformulary*
- Nicotine lozenges - *nonformulary*
- Nicotine nasal spray - *nonformulary*
- Nicotine patches

The Formulary includes bupropion (generic forms) and nicotine gum and patches. The Committee noted that at this time, this data is only being measured. State Hospitals are currently smoke-free; therefore patients are placed on cessation medication upon admission. The Formulary does offer numerous types of products used for smoking cessation. If someone insists on using a nonformulary medication, then the product can be purchased through the normal process.

On a motion of Dr. Messer, seconded by Dr. Smith, it was recommended that patients be offered smoking cessation medication and counseling while hospitalized, then upon discharge a seven day supply of medication be provided and as appropriate, referral to a community treatment program for smoking cessation.

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.

New Drug Applications

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

Aripiprazole lauroxil (Aristada®) - presented by Isaac Pan, Pharm.D., Pharmacy Resident

Aristada™ is a long-acting injectable form of aripiprazole that can be given monthly and every 6 weeks. It is not the same as Abilify Maintena®. Aristada™ is available in the following strengths:

- 441 mg/1.6 ml

- 662 mg/1.6 ml
- 882 mg/1.6 ml

All three dosage strengths can be administered monthly. The 882 mg dose can also be administered every 6 weeks. When initiating Aristada™, oral aripiprazole needs to overlap with the injection for 21 days. Aristada™ is aripiprazole lauroxil and is a pro-drug of aripiprazole. Following an injection and slow dissolution, aripiprazole lauroxil is converted by enzyme mediated hydrolysis to N-hydroxymethyl aripiprazole, which subsequently undergoes water-mediated hydrolysis to aripiprazole. Steady state is reached after the 4th monthly injection. The combination of the 21 day oral aripiprazole overlap with the initiation of the injection leads to therapeutic levels within 4 days. The mean elimination half-life is 29.2 days to 34.9 days. One possible advantage of Aristada™ is the potential to have higher aripiprazole levels.

Following discussion, on motion of Dr. Pittman, seconded by Dr. Smith, it was recommended to table the decision regarding the addition of Aristada™ to formulary. Aristada™ will be reviewed in 6 months.

Brexpiprazole (Rexulti®) - presented by Thomas Maestri, Pharm.D., Pharmacy Resident

Brexpiprazole is an atypical antipsychotic. It is indicated for use in the treatment of schizophrenia and for use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD). The mechanism of action of brexpiprazole is unknown. The efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D₂ receptors, and antagonist activity at serotonin 5-HT_{2A} receptors. For the treatment of schizophrenia, the starting dose is 1 mg/day, with a recommended dose of 2-4 mg/day and a maximum dose of 4 mg/day. For use in major depressive disorder, the starting dose is 0.5-1 mg/day, with a recommended dose of 2 mg/day and a maximum of 3 mg/day.

Following discussion, on motion of Dr. Pittman, seconded by Dr. Hall, the recommendation to add brexpiprazole (Rexulti®) to the Formulary was approved. It was recommended that the maximum dose be set at 4 mg/day, that it be added to the atypical antipsychotic audit criteria and considered a Tier 2 drug.

Since brexpiprazole is a new drug on the market, its packaging was evaluated for potential medication errors and no issues were found at this time. Brexpiprazole will be reviewed in six months for medication errors and adverse drug reactions.

Hydroxyzine – QTc Interval Follow Up & Audit

Dr. Pan reviewed the findings of the hydroxyzine – QTc Interval Audit. See Attachment C for the detailed results. Seventeen facilities participated in the audit and 220 patients were evaluated. The following is a brief overview of the results:

- 116 patients had a baseline EKG
 - 37 patients had a follow-up EKG
 - 30 patients had a hydroxyzine dose reported at the time of the follow-up EKG.
- Indications
 - 46.4% for anxiety
 - 27.7% for insomnia
 - 19.1% for other (mainly allergy or skin conditions)
- Contraindications
 - 100% had none or not reported
- Relative Contraindication
 - 80.9% had none or not reported
- Precautions
 - 92.3% had none or not reported
- Adverse Events
 - 74.1% had none or not reported
 - 5% reported “other”
 - 4.5% had worsening confusion or agitation
 - 4.1% had constipation

Number of concurrent QTc prolonging drugs	Results
0	29 (13.2%)
1	70 (31.8%)
2	83 (37.7%)
3	29 (13.2%)
4 or more	6 (2.7%)
Not reported	3 (1.4%)

Dr. Pan highlighted the following points:

- There was no statistically difference between change in QTc and hydroxyzine; the effect size of hydroxyzine on QTc change is estimated to be small
- There was no correlation between hydroxyzine dose and QTc change (p=0.812)

Based on the findings of this audit and the lack of action taken by the FDA, it was recommended that the current guidelines on maximum doses for hydroxyzine be kept. If the FDA makes other recommendations regarding hydroxyzine dosing or if adverse drug reactions are reported, then this issue will be re-evaluated.

DSHS/DADS Drug Formulary - Website

The DSHS/DAD Drug Formulary is posted at the following website:

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

FDA Drug Safety Communications

Since the last meeting, the FDA has not published any Drug Safety Communications that would have impact in our facilities.

Medical Director for Behavioral Health

Dr. Muse briefly attended the meeting but did not have any issues to report.

Quarterly Non-Formulary Drug Justification Report

For the first quarter of fiscal year 2016, all facilities reported use of non-formulary agents. The DADS facilities submitted 967 non-formulary requests and the DSHS facilities had 362 requests. The following were the top non-formulary agents that were prescribed:

Saccharomyces boulardii capsule (Florastor®)
 Fiber-Stat Natural solution packets
 SilvaSorb Gel
 Guanfacine ER (Intuniv®)

Sectional Review for Next Meeting

The following sections will be reviewed at the next meeting:

Respiratory Agents
 Antihistamine Agents
 Antiemetics/Antivertigo

Other Issues

The following information was shared with the Committee members:

Reuters reports that Gilead Sciences Inc. announced Thursday that the Food and Drug Administration had approved an expanded indication for the company's hepatitis C drug, Harvoni (ledipasvir and sofosbuvir). According to the company, Harvoni is now approved to treat patients with genotypes 1, 4, 5, and 6 of chronic hepatitis C virus, as well as patients co-infected with HIV. The drug has also been approved to be used in combination with ribavirin for

12 weeks to treat certain patients with hepatitis C and cirrhosis.

MedPage Today reports that in a pilot study, lorazepam (Ativan) “appeared to be a safe and effective treatment for anxiety in patients with alcohol use disorder who were already taking disulfiram (Antabuse)...but adherence to disulfiram was a problem.” The findings were presented in a poster presentation at the American Academy of Addiction Psychiatry meeting. The study was funded by the National Institute on Alcohol Abuse and Alcoholism.

The New York Times reports in a nearly 1,300-word story on the “rapid” rise of cases in which youngsters “age two or younger are prescribed psychiatric medications to address alarmingly violent or withdrawn behavior.” Figures from the prescription data company IMS Health reveal that nearly “20,000 prescriptions for risperidone (commonly known as Risperdal), quetiapine (Seroquel) and other antipsychotic medications were written in 2014 for children two and younger, a 50 percent jump from 13,000 just one year before.” Many physicians are concerned that these medications, which are “designed for adults and only warily accepted for certain school-age youngsters, are being used to treat children still in cribs despite no published research into their effectiveness and potential health risks for children so young.” Some experts attribute the increased use of psychiatric medications in kids of all ages to the “scarcity of child psychiatrists.”

The Los Angeles Times “Science Now” blog reports that after comparing “rates of autism among babies born to women with a history of depression with autism rates among babies born to those who took antidepressants during pregnancy,” the study authors “found that babies whose mothers took an SSRI were still about 75% more likely to get an autism diagnosis than were those whose mothers had a history of depression.”

STAT reports in “Pharmalot” that Johnson & Johnson has lost its fourth trial “in which a young man successfully claimed the company failed to warn that its Risperdal [risperidone] antipsychotic could cause him to grow breasts.” A Pennsylvania state court ordered J&J to pay \$500,000 to the plaintiff in the litigation.

NPR reports in its “Shots” blog and on its “All Things Considered” program that “Medicaid in many states restricts” who can receive the new hepatitis C medication Harvoni (ledipasvir/sofosbuvir), because it “costs about \$95,000” for a full 12-week course. Medicaid “in at least 34 states doesn’t pay for treatment unless a patient already has liver damage, according to a report released in August.” Matt Salo, director of the National Association of Medicaid Directors, said that “it is just not feasible to provide it to everyone,” and that states have to make sure “that those who need it the most get priority treatment.”

Healio reports that the Food and Drug Administration has accepted Minerva Neurosciences’ application for its experimental schizophrenia treatment. The 5-HT_{2A} and sigma 2 antagonist will be studied in a clinical trial of 244 patients to determine its effectiveness at reducing the symptoms of schizophrenia.

The Wall Street Journal reports that Indian drugmaker Dr. Reddy’s Laboratories has changed the color of its generic version of AstraZeneca’s Nexium (esomeprazole magnesium) after a Delaware court held that it infringed on AstraZeneca’s intellectual property. Dr. Reddy’s changed the color from two-tone purple to two-tone blue because AstraZeneca’s marketing of Nexium revolves around its purple color.

The San Diego Business Journal reports that the Food and Drug Administration granted Orphan Drug Designation to Ionis Pharmaceuticals’ experimental drug to treat Huntington’s disease, IONIS-HTTRx. According to Ionis senior VP of research Frank Bennett, the drug is the “first therapy to enter clinical trial development that is designed to treat the underlying cause of this fatal disease.”

Reuters reports that a meta-analysis revealed the use of the antidepressant paroxetine (Paxil, Seroxat) early in pregnancy may be associated with an increased risk of giving birth to babies with congenital malformations. The findings were published online in the British Journal of Clinical Pharmacology.

MedPage Today reports that a meta-analysis published in JAMA Psychiatry indicated “younger patients on antipsychotic medications faced far higher risks of developing type 2 diabetes than did healthy controls.” Investigators looked at data from “13 studies and found that youth (age 2 to 24) who had taken antipsychotic medications had an odds ratio of 2.58 for getting type 2 diabetes (95% CI, 1.56-4.24; P<0.0001) and an incidence rate ratio (IRR) of 3.02 (95% CI, 1.71-5.35) compared with healthy controls.” Altogether, “youth who had taken antipsychotics had a cumulative type 2 diabetes risk of 5.72 per 1,000 patients...and an incidence rate of 3.09 per 1,000 patient-years.”

MedPage Today reports that moving hydrocodone combination products “from schedule III to the more restrictive schedule II on the federal controlled substances list was associated with 1.1 billion fewer tablets and 26.3 million fewer prescriptions for the drugs in the first year following the change,” a research letter published online Jan 25 in JAMA Internal Medicine indicates. Christopher Jones, PharmD, now of the Department of Health and Human Services and formerly of the FDA, “published the report with FDA colleagues Peter Lurie, MD, MPH, and Douglas Throckmorton, MD.”

US News & World Report reports Adapt Pharma announced at the Clinton Health Matters Initiative on Monday that it was offering its emergency opioid overdose drug naloxone free of charge at American high schools. US News & World Report points out that the Department of Health and Human Services “has made opioid overdoses a national public health priority.”

Reuters reports that the Food and Drug Administration has approved Neos Therapeutics Inc.’s Adzenys XR-ODT (amphetamine) for the treatment of attention-deficit/hyperactivity disorder (AD/HD) for patients six years and older. Adzenys XR-ODT is a longer-acting form of amphetamine in the form of an orally disintegrating tablet.

HealthDay reports, “Antidepressants appear to be much more dangerous for children and teens than reported in medical journals, because initial published results from clinical trials did not accurately note instances of suicide and aggression,” a review published Jan. 27 in the BMJ suggests. Researchers arrived at that conclusion after analyzing data from “68 clinical study reports from 70 drug trials that involved more than 18,500 patients.” The clinical studies “involved five specific antidepressants: duloxetine (Cymbalta), fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft) and venlafaxine (Effexor).”

From CredibleMeds®

We have also reviewed the available evidence for **asenapine** (Saphris®, Sycrest®), an antipsychotic drug, and found convincing evidence that it can prolong the QT interval. Furthermore, the extended release forms of the opiate pain reliever **hydrocodone** (Hysingla ER and Zohydro ER) have been found to produce QT prolongation.

Therefore, **asenapine** and the sustained release form of **hydrocodone** have been added to the list of drugs with **Possible Risk of TdP**. We are not aware of any relevant studies of the immediate release form of hydrocodone but we suggest caution as we continue to monitor the evidence. At this time, our listing for hydrocodone specifies only the extended release formulation.

Next Meeting Date

The next meeting was scheduled for April 29, 2016.

Adjourn

There being no further business, the meeting was adjourned at 1:55 p.m.

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

Attachments

- Attachment A – Psychotropic Consent List
- Attachment B – New Drug Applications
- Attachment C–DADS/DSHS Medication Use Evaluation; Hydroxyzine

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

Classes of Medications Frequently Used for Psychiatric Indications

Consent is required for any medication that is used in the treatment of a psychiatric diagnosis or symptom, whether or not the medication is included in this list. Refer to physician order for determination of indication for use.

The classification of psychotropic medication is fairly standard but medications can be used for treatment of illnesses that would be considered listed under a different classification. For example, some medications listed under antipsychotics may be used as a mood stabilizer.

The Executive Formulary Committee does not endorse the use of nonformulary drugs

Antidepressants

amitriptyline (Elavil)
amoxapine (Asendin)
bupropion (Wellbutrin, Wellbutrin SR)
bupropion (Wellbutrin XL)
citalopram (Celexa)
desipramine (Norpramin)
desvenlafaxine (Pristiq, Khedezla) *nonformulary*
doxepin (Sinequan)
duloxetine (Cymbalta)
escitalopram (Lexapro)
fluoxetine (Prozac)
imipramine (Tofranil)
levomilnacipran (Fetzima) *nonformulary*
maprotiline (Ludiomil)
mirtazapine (Remeron, Remeron SolTab)
nefazodone (Serzone) *nonformulary*
nortriptyline (Pamelor, Aventyl)
paroxetine (Paxil, Paxil CR)
protriptyline (Vivactil)
sertraline (Zoloft)
trazodone (Desyrel)
trimipramine (Surmontil)
venlafaxine (Effexor, Effexor XR)
vilazodone (Viibryd) *nonformulary*
vortioxetine (Brintellix) *non-formulary*

Anxiolytics/Sedatives/Hypnotics

alprazolam (Xanax, Xanax XR)
buspirone (BuSpar)
chlordiazepoxide (Librium)
clonazepam (Klonopin)
clorazepate (Tranxene)
diazepam (Valium)
diphenhydramine (Benadryl)
eszopiclone (Lunesta) *nonformulary*
flurazepam (Dalmane) *nonformulary*
hydroxyzine (Atarax, Vistaril)
lorazepam (Ativan)
oxazepam (Serax)

pentobarbital (Nembutal) *nonformulary*

ramelteon (Rozerem) *nonformulary*
suvorexant (Belsomra) *nonformulary*
temazepam (Restoril)
triazolam (Halcion)
zaleplon (Sonata)
zolpidem (Ambien)
zolpidem (Ambien CR) *nonformulary*

Antipsychotics

aripiprazole (Abilify, Abilify Discmelt)
aripiprazole (Abilify Maintena)
Aripiprazole lauroxil (Aristada) *nonformulary*
asenapine (Saphris)
brexpiprazole (Rexulti®)
chlorpromazine (Thorazine)
clozapine (Clozaril, Fazaclor, Versacloz) Reserve
droperidol (Inapsine) *nonformulary*
fluphenazine (Prolixin)
fluphenazine decanoate (Prolixin D)
haloperidol (Haldol)
haloperidol decanoate (Haldol D)
iloperidone (Fanapt) Reserve
loxapine (Loxitane)
loxapine inhalant (Adasuve) *nonformulary*
lurasidone (Latuda)
molindone *nonformulary*
olanzapine (Zyprexa, Zyprexa Zydis)
olanzapine pamoate (Zyprexa Relprevv) Reserve
paliperidone (Invega)
paliperidone palmitate (Invega Sustenna)
paliperidone palmitate (Invega Trinza) *nonformulary*
perphenazine (Trilafon)
pimozide (Orap) *nonformulary*
quetiapine (Seroquel)
quetiapine (Seroquel XR) *nonformulary*
risperidone (Risperdal, Risperdal M-Tab)
risperidone (Risperdal Consta)
thioridazine (Mellaril)
thiothixene (Navane)
trifluoperazine (Stelazine)
ziprasidone (Geodon)

Chemical Dependency Adjuncts

acamprosate (Campral)
disulfiram (Antabuse)
naltrexone (ReVia, Vivitrol)
topiramate (Topamax)

Monoamine Oxidase Inhibitors

isocarboxazid (Marplan) *nonformulary*
phenelzine (Nardil)
selegiline (Emsam) *nonformulary*
tranylcypromine (Parnate)

Miscellaneous Drugs

atomoxetine (Strattera)
atenolol (Tenormin)
clomipramine (Anafranil)
clonidine (Catapres)
clonidine ER (Kapvay) *nonformulary*
fluvoxamine (Luvox)
gabapentin (Neurontin)
guanfacine (Tenex)

guanfacine ER (Intuniv) nonformulary

metoprolol (Lopressor)
nadolol (Corgard)
propranolol (Inderal)
reserpine (Serpasil) *nonformulary*
naltrexone (ReVia)
olanzapine/fluoxetine (Symbyax) *nonformulary*
pindolol (Visken) *nonformulary*
prazosin (Minipress)

Other

This category must be approved prior to inclusion in this Instrument

Mood Stabilizers

carbamazepine (Tegretol, Tegretol XR, Carbatrol, Equetro)
divalproex sodium (Depakote, Depakote ER, Depakote Sprinkles)
lithium (Eskalith, Eskalith CR, Lithobid)
valproic acid (Depakene)
oxcarbazepine (Trileptal)
lamotrigine (Lamictal)

Stimulants

amphetamine/dextroamphetamine mixture (Adderall, Adderall XR)
dexmethylphenidate (Focalin, Focalin XR) *nonformulary*
dextroamphetamine (Dexedrine, Dexedrine ER-)
lisdexamfetamine (Vyvanse)
methamphetamine (Desoxyn) *nonformulary*
methylphenidate (Ritalin, Ritalin SR, Concerta, Metadate, Metadate CD)
methylphenidate patch (Daytrana) *nonformulary*
methylphenidate soln (Quillivant XR)

APPENDIX 1: NEW DRUG APPLICATION FORM

DSHS/DADS

(Formerly: Texas Department of Mental Health and Mental Retardation)

NEW DRUG APPLICATION

(for inclusion in the *DSHS/DADS Drug Formulary*)

**** (THE NEW DRUG APPLICATION PROCESS IS DESCRIBED ON THE BACK OF THIS FORM.) ****

Date: 1/29/16

Name of practitioner submitting the application: Executive Formulary Committee (Ann Richards)

Name of entity with which the practitioner is associated by employment or contract (i.e., state hospital, state supported living center, state center, or local authority (state-operated community services (SOCS) or community MHMR center)):

Information regarding new drug:

Therapeutic Classification	Antipsychotics - Atypical
Generic Name	brexpiprazole
Trade Name(s)	Rexulti
Manufacturer(s)	Otsuka
Dosage Form(s)	Tablet

Explain the pharmacological action or use of this drug:
used to treat schizophrenia

Explain the advantages of this drug over those listed in the formulary:
Another option for treatment

State which drugs this new drug would replace or supplement:
supplement antipsychotics

application is approved

[Signature]
signature of chairman of facility pharmacy and therapeutics committee

OR

application is appropriate and complete

signature of clinical/medical director or designee

**DADS/DSHS Medication Use Evaluation
Hydroxyzine**

Background:

At the April 2015 meeting, the Executive Formulary Committee (EFC) discussed the February 13, 2015 recommendations by the European Medicine Agency Pharmacovigilance Risk Assessment Committee (PRAC). These recommendations included new measures to minimize cardiac risk of hydroxyzine. The PRAC concluded that hydroxyzine has a small but definite risk of QT prolongation and Torsade de Pointes. Hydroxyzine is commonly prescribed for anxiety and insomnia at the State Hospitals and State Supported Living Centers.

The PRAC recommended a maximum daily dose of 2 mg/kg body weight in children up to 40 kg (18.2 lb) weight, 100 mg in adults, and 50 mg in elderly if use cannot be avoided. Hydroxyzine should be used at the lowest effective dose for as short as possible. It should be avoided in patients at risk for arrhythmia or taking other medications with risk of prolonging QT interval.

The DADS/DSHS Drug Formulary currently lists the following dosing information regarding hydroxyzine:

- Hypnotic
 - Under 65 years old – 400 mg/day
 - 65 years old and older – 300 mg/day
 - Child 3-6 years old – 25 mg/day (based on literature)
 - Child 6-12 years old – 50 mg/day (based on literature)
 - Adolescent > 12 years old but less than 18 years old – 100 mg (based on literature)

At the April EFC meeting, the Austin State Hospital (ASH) presented the results of their hydroxyzine MUE that was completed based on this PRAC release. This MUE included a sample of 42 patients prescribed hydroxyzine during a 2-month period between 12/23/14 and 2/23/15. Forty-five percent of the patients had an EKG after hydroxyzine was prescribed. No incidents of QTc > 450 msec for males or >460 msec for females were identified. Seven patients had EKG readings before and after the initiation of hydroxyzine, and the mean QTc change was 9.14 msec. There was a 10 msec difference in the mean QTc between the patients prescribed with hydroxyzine ≤ 100 mg (419 msec; n=15) and those prescribed with hydroxyzine > 100 mg (429 msec; n=4.)

As a result of the PRAC recommendations and the ASH MUE, the EFC recommended conducting a hydroxyzine MUE on a statewide level.

Method of Evaluation

As part of this MUE review, each facility was requested to audit the routine (scheduled use) of hydroxyzine for a concurrent two-month time period or until 30 eligible patients had been reviewed, whichever occurred first. Each facility was asked to identify their own two-month time between 1-1-15 and 7-31-15.

Results:

- Patients evaluated = 220 patients from 17 facilities
- Ages ranged from 10 to 70 years
 - Mean = 39.2 ± 14.0
- A hundred and sixteen patients had a baseline EKG
 - Thirty-seven had a follow-up EKG
 - Thirty had a hydroxyzine dose reported at the time of the follow-up EKG

Table 1. Demographics

Age group	N (%)
Children (<12 y/o)	1 (0.5%)
Adolescents (12-17 y/o)	9 (4.1%)
Adults (18-64 y/o)	202 (91.8%)
Elderly (≥65 y/o)	8 (3.6%)
Gender	
Female	75 (34.1%)
Male	145 (65.9%)

Table 2. Hydroxyzine order information

Order information	N (%)
Indications	
Aggression & agitation	5 (2.3%)
Anxiety	102 (46.4%)
EPS	10 (4.5%)
Insomnia	61 (27.7%)
Other ¹	42 (19.1%)
Absolute Contraindications	
Anticholinergic intoxication	0 (0%)
Delirium	0 (0%)
None or not reported	220 (100%)
Relative Contraindications²	
Elderly or debilitated	9 (4.1%)
Hepatic Impairment	8 (3.6%)
Increased risk of anticholinergic activity	17 (7.7%)
Lower respiratory tract symptom (eg. Asthma)	7 (3.2%)
Renal impairment	8 (3.6%)
None or not reported	178 (80.9%)
Precautions	
Photosensitivity	5 (2.7%)
Respiratory impairment	12 (5.5%)
None or not reported	203 (92.3%)

¹Approximately 76% (32/42) of Other Indication were for allergy or skin conditions

²Can report more than one item

Table 3. Adverse events

Adverse events	N (%)
Disinhibition	2 (0.9%)
Dizziness or lightheadedness	2 (0.9%)
Headache	7 (3.2%)
Nausea	3 (1.4%)
Somnolence	2 (0.9%)
Worsening confusion or agitation	10 (4.5%)
Other	11 (5.0%)
Constipation	9 (4.1%)
None or not reported	163 (74.1%)

Table 4. Major drug interactions

Drug interaction	N (%)
MAOI	0 (0%)
Antipsychotics	159 (72.3%)
Antidepressant	90 (40.9%)
Lithium	17 (7.7%)
Diphenhydramine	22 (10%)
Promethazine	2 (0.9%)
None or not reported	29 (13.2%)
Number of concurrent QTc prolonging drug	
0	29 (13.2%)
1	70 (31.8%)
2	83 (37.7%)
3	29 (13.2%)
4 or more	6 (2.7%)
Not reported	3 (1.4%)

Table 5. EKG Monitoring

Had a baseline EKG?	N	QTc Interval (ms) ± SD
Yes	116	417 ± 21
Had 1 or more follow-up EKG?		
Yes ^{1,2}	37	423 ± 20 (1 st follow-up EKG)

¹Mean QTc change = 4.3 ± 21.4 ms (ranging from -42 to 54 ms); estimated effect size ~0.2

²Baseline QTc and 1st follow-up QTC were not statistically different (t=-1.2, df=36, p=0.229)

Table 6. Interpretation of QTc according to age and gender

	Age 1 to 15 yrs	Men	Women
Normal	<440 ms	<430 ms	<450 ms
Borderline	440-460 ms	430-450 ms	450-470 ms
Prolonged (upper 1%)	>460 ms	>450 ms	>470 ms

Moss AJ. Am J Cardiol. 1993;72(6):23B-25B.

Table 7. Interpretation of baseline QTc

	N (%)
Normal	95 (81.9%)
Borderline^{1,2}	17 (14.7%)
Prolonged³	4 (3.4%)
Total	116 (100%)

¹Age 16 to 58 years; one patient <18 yrs weighed more than 40 kg; two patients had doses >100 mg

²Six had at least 1 follow-up EKG, and two had an increased QTc on the subsequent EKG; both had doses <100 mg and were follow-up with 2nd and 3rd EKGs

³Age 34 to 51 years; No follow-up EKG was reported; No hydroxyzine dose was reported

Discussion

1. There was no statistically difference between change in QTc and hydroxyzine; the effect size of hydroxyzine on QTc change is estimated to be small
2. There was no correlation between hydroxyzine dose and QTc change (p=0.812)
3. Hydroxyzine dose was only collected when there was a follow-up EKG (whether there is a baseline EKG)
 - a. Seventy-eight patients had a hydroxyzine dose reported
 - b. Daily hydroxyzine doses ranged from 10 mg to 400 mg
 - c. DSHS guidelines compliance rate was 98.7% (one pediatric patient <12 y/o received 200 mg/day)
 - d. EMA PRAC recommendation compliance rate was 24.4% (19/78)
 - e. About half of the patients who received hydroxyzine doses > EMA PRAC recommendations had both a baseline and at least one follow-up EKG (10/19)
4. There is no change yet in prescribing information available on FDA's website regarding to risk of QTc prolongation or arrhythmia
5. Most cases had other risk factors according to the statement of EMA PRAC

Recommendations

- Keep current DSHS guidelines on maximum hydroxyzine doses
- Add additional monitoring requirements for hydroxyzine; a baseline EKG should be initiated in
 - Patients with known heart disease, a personal history of syncope, a family history of sudden death at an early age (under age 40 years, especially if both parents had sudden death), congenital long QT syndrome, significant electrolyte imbalance, or significant bradycardia
 - Patients with concomitant use of other QT prolonging agent
 - A subsequent EKG is indicated if the patient presents with symptoms associated with prolonged QT interval