

DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
May 16, 2008

The Executive Formulary Committee convened on Friday, May 16, 2008 in Conference Room 240 - CO Building 2. The meeting was called to order by Dr. Matthews, Chair at 9:40 a.m.

Janet Adams, MSN, RN, CNS	Absent	Kenny Dudley (non-voting)	Absent
Emilie A. Becker, M.D.	√	Jill Schalchlin, Acting (non-voting)	Absent
Rosha Chadwick, R.Ph.	Absent	Bob Burnett (non-voting)	Absent
Jeanna Heidel, Pharm.D.	√	Tom Best, Acting (non-voting)	Absent
J. Brett Hood, M.D.	Absent	Eugenia Andrew (non-voting)	Absent
Jeff Matthews, M.D.	√	Jay Norwood, MSN, RN (non-voting)	Absent
Lisa Mican, Pharm.D.	√	Julie McRae, MS, RN, CDDN (non-voting)	Absent
Connie Millhollon, RN,	Absent	Vacant Center Position	
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Bill Race, M.D. (non-voting)	√	Vacant Center Position	
Lilani Muthali, M.D. (non-voting)	Absent	Vacant Center Position	
Nina Muse, M.D. (non-voting)	Absent	Vacant State School Position	

Guest Present: Angela Bird, Pharm.D. Student Volunteer, Austin State Hospital; Steven Nova, Student Volunteer, Austin State Hospital

Approval of Minutes of February 15, 2008

On a motion of Dr. Heidel, seconded by Dr. Mican, the minutes of the February 15th meeting were approved as previously distributed.

Adverse Drug Reaction Reports

The Executive Formulary Committee received one adverse drug reaction report. A 28 year old male was admitted to a State Hospital in September 2007 with a diagnosis of schizoaffective disorder. On January 4th, the patient was started on clozapine (Fazaclon®). On January 15th, the patient began having symptoms of fever, vomiting, tachycardia, and lethargy. On January 24th the patient's amylase was 236 IU/L. The clozapine was discontinued on January 25th. On January 28th, the AST was 253 U/L and lipase was 186 U/L. On February 15th, the AST was 48 U/L, the ALT was 60 U/L and the lipase was 34 U/L. Previously the patient had an AST of 47 U/L and an ALT of 49 U/L on January 2nd. It was decided that the patient had pancreatitis associated with clozapine due to the timing of the initiation and the resolution of the symptoms as compared to the start and withdrawal of clozapine.

New Drug Applications

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

Quetiapine extended release (Seroquel XR™) - discussed by Dr. Mican

Quetiapine extended release (XR) is indicated for acute and maintenance treatment of schizophrenia. The antipsychotic mechanism of action for quetiapine and the active metabolite N-desalkyl quetiapine is thought to be mediated through a combination of dopamine type 2 (D₂) and serotonin type 2 (5HT₂) antagonism. Other actions such as antagonism at histamine (H₁) receptors may explain somnolence and antagonism at adrenergic (α₁) receptors may explain orthostatic hypotension associated with the medication. The peak plasma concentration (T_{max}) is reached 6 hours following administration. Bioavailability is comparable to an equivalent dose of quetiapine immediate release (IR) administered in divided doses twice daily. A high fat meal (800 to 1,000 calories) produces a statistically significant increase in C_{max} (44-52%) and AUC (20-22%). Therefore, it is recommended that quetiapine XR be administered without food or with a light meal. Quetiapine XR should be administered once daily, preferably in the evening. The recommended initial dose is 300 mg. The effective dose range is 400 – 800 mg per day depending on response and tolerance of the individual patient. The tablets should be swallowed whole and not split, chewed, or crushed. For initial dosing in patients with hepatic impairment and geriatric population, use of quetiapine IR is recommended instead of quetiapine XR. The available literature shows similar efficacy and tolerability profiles between quetiapine XR and quetiapine IR, except for the Moller study which found that noninferiority was not shown and the switch was not successful for the MITT population studied in this trial (noninferiority was shown for the per-protocol population). Studies such as BOLDER I and BOLDER II have administered quetiapine IR once daily at bedtime with good tolerability after a short initial titration period (300 mg by day 4). Quetiapine IR offers the advantage of greater dosing flexibility in special patient populations. Currently, quetiapine XR and quetiapine IR are priced the same. Looking at the available peer-reviewed literature, pricing information and potential for generic quetiapine in the future, there does not appear to be a compelling reason to add quetiapine XR to the drug formulary at this time.

Following discussion, on motion of Dr. Heidel, seconded by Dr. Becker, the request to add quetiapine XR (Seroquel XR™) to the formulary was denied.

Zolpidem extended release (Ambien CR®) - discussed by Dr. Mican

Zolpidem extended release (CR) is a non-benzodiazepine sedative hypnotic agent for the treatment of insomnia characterized by difficulties in sleep onset and/or sleep maintenance. The sedative properties of zolpidem are a result of modulation at the GABA_A receptor chloride channel complex. The primary site of activity is at the alpha subunit, which is also known as the benzodiazepine or omega receptor. Three subtypes of the omega receptor have been identified; however, unlike benzodiazepines which bind non-selectively to all three, zolpidem preferentially binds to the omega-1 subunit. Agonism at this site enhances chloride conduction, leading to a hyperpolarized membrane which has a decreased response to excitatory signals. In the bi-phasic release tablet approximately 60% of the dose is immediate release (delivered within 30 minutes) and the remainder of the tablet is extended release. After administration there is rapid initial absorption from the gastrointestinal tract, then extended plasma concentration last beyond 3 hours after administration. Peak plasma concentrations are reached within 1.5 hours (0.9 hours for Ambien®). The presence of food decreases the mean AUC and C_{max}. The cost of Ambien CR® 12.5 mg is \$3.68 per tablet and the cost of zolpidem 10 mg tablet is \$0.06 per tablet. The efficacy and safety of zolpidem CR for the treatment of insomnia in patients with sleep onset insomnia and sleep maintenance difficulties has been established in controlled trials. Treatment related adverse events and side effects appear to be similar to what has been reported with zolpidem IR. The place in therapy of zolpidem CR compared to the other non-benzodiazepine sedative-hypnotics is less well established. Only one Phase IIIb study is available which compares zolpidem IR and zolpidem CR to placebo; however, the study was not designed to compare the two active treatments. Both zolpidem IR and CR fared better than placebo on all objective PSG primary and secondary outcome measures except for WASO (wake time after sleep onset) for hours 7 to 8 in which neither of the active treatments reached statistical significance vs. placebo. Zolpidem IR 10 mg is available generically at a cost of 61-times less expensive than zolpidem CR 12.5 mg. Based on the available studies to date, it does not appear to be a reasonable strategy to use zolpidem CR without an initial trial of zolpidem IR. Based on the available literature, some patients treated with zolpidem IR may benefit not only from sleep onset insomnia, but possible sleep maintenance insomnia as well. Zolpidem IR is not currently FDA approved for sleep maintenance insomnia.

Following discussion, on motion of Dr. Becker, seconded by Dr. Heidel, the request to add zolpidem extended release (Ambien CR®) to the formulary was denied.

Eszopiclone (Lunesta™) - discussed by Angela Bird, Pharm.D. Student

Eszopiclone is a non-benzodiazepine sedative hypnotic for the treatment of chronic or transient insomnia. The sedative-hypnotic properties of eszopiclone are thought to be a result of modulation at the GABA_A receptor chloride channel complex. The primary site of activity is at the alpha subunit, which is also known as the benzodiazepine or omega receptor. Three subtypes of the omega receptor have been identified; and like benzodiazepines, eszopiclone binds non-selectively to all three. Because of this, eszopiclone provides a sedative effect similar to that of benzodiazepines. The elimination half-life is approximately 6 hours, so one might be concerned about daytime foginess. The initial dose of eszopiclone is 2 mg immediately before bedtime, and may be titrated to a maximum dose of 3 mg. For elderly patients who have difficulty in falling asleep, the initial dose is 1 mg and can be titrated to 2 mg. For elderly patients have that difficulty in staying asleep, the initial dose is 2 mg. For patients with hepatic impairment, the dose is 1 mg. Eszopiclone has been shown to be effective in reducing sleep latency and improving sleep maintenance in both chronic and transient insomnia. Despite the added benefit of approval for long-term use, the cost-effectiveness of eszopiclone remains unclear without head-to-head clinical trials comparing the efficacy of eszopiclone to the other sedative-hypnotic agents available. In addition, other less costly agents, such as zolpidem, have also demonstrated efficacy and tolerability on a long-term basis in clinical trials.

Following discussion, on motion of Dr. Becker, seconded by Dr. Heidel, the request to add eszopiclone (Lunesta®) to the formulary was denied.

Psychotropic Audit Criteria – Comparison to TIMA

Dr. Muse requested that the Committee consider comparing the TIMA Guidelines to the monitoring parameters for consistency between the two documents. The TIMA Procedural Manual for the Schizophrenia Module was last updated in 2003. According to individuals working on this Manual, the Manual is in the final stages of formatting and should be released soon.

FDA Alerts

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

Rosiglitazone (Avandia®) has a new Medication Guide. The FDA requires a Medication Guide to be provided with each prescription dispensed for products that FDA determines pose a serious and significant public health concern. The Medication Guide can be found at:
http://www.fda.gov/cder/offices/ods/medication_guides.htm

A “Dear Healthcare Professional” letter was distributed regarding exenatide (Byetta®). The FDA has reviewed 30 postmarketing reports of acute pancreatitis in patients taking exenatide, a drug used to treat adults with type 2 diabetes. An association between exenatide and acute pancreatitis is suspected in some of the cases. Healthcare professionals should be alert to the signs and symptoms of acute pancreatitis and instruct patients taking exenatide to seek prompt medical care if they experience unexplained, persistent, severe abdominal pain which may or may not be accompanied by vomiting. If pancreatitis is suspected, exenatide should be discontinued. If pancreatitis is confirmed, exenatide should not be restarted unless an alternative etiology is identified.

The FDA notified healthcare professionals and patients of the Agency’s investigation of the possible association between the use of montelukast (Singulair®) and behavior/mood changes, suicidality (suicidal thinking and behavior) and suicide. Montelukast is a leukotriene receptor antagonist used to treat asthma and the symptoms of allergic rhinitis, and to prevent exercise-induced asthma. Patients should not stop taking montelukast before talking to their doctor if they have questions about the new information. Healthcare professionals and caregivers should monitor patients taking montelukast for suicidality (suicide thinking and behavior) and changes in behavior and mood.

The FDA informed healthcare professionals and consumers of the correct way to use tiotropium inhalation powder capsules (Spiriva®) and formoterol inhalation powder (Foradil®). The FDA and the American Association of Poison Control Center's National Poison Data System have received many reports of patients swallowing tiotropium and formoterol inhalation capsules rather than placing the capsules in the inhalation devices.

Carbamazepine Medication Audit Criteria and Guidelines

At the last meeting, the Committee discussed the need for patients with Asian descent to have a genetic test for HLA-B*1502 prior to the initiation of carbamazepine. As a result, the carbamazepine medication audit criteria and guidelines were changed as follows (See Attachment B):

- “Positive HLA-B*1502 –benefit must outweigh risk of serious skin reactions” was added to the Relative Contraindications
- “For patients with Asian Descent, genetic test for HLA-B*1502 at baseline (prior to the initiation of carbamazepine). May use results of previously completed testing.” was added to the Patient Monitoring Parameters.

On a motion of Dr. Heidel, seconded by Dr. Mican, the revised carbamazepine medication audit criteria and guidelines were approved.

Injectable Antipsychotic Dose Guidelines

Dr. Mican presented the “Treatment of Behavioral Emergencies Intramuscular Short-Acting Agents.” See Attachment C. The doses presented were for the adult population and did not address the child or adolescent population. It was noted that the literature does not make recommendations for dosage guidelines in the child or adolescent population, thus one can not develop evidence based dosing guidelines for injectable medications in the treatment of behavioral emergencies in this population. However, based on actual use of these medications for this population within our system, one can develop guidelines that are based on this use. On a motion of Dr. Becker, seconded by Dr. Heidel, the “Treatment of Behavioral Emergencies Intramuscular Short-Acting Agent” was approved. It was recommended that these guidelines be placed in the Drug Formulary. In addition, the guidelines will be distributed to the field. Dr. Richards will follow up with a survey to the facilities that treat the child and adolescent population in our facilities.

Injectable Syringe Compatibility

Dr. Mican presented the “Psychotropic Injectable Compatibility Chart” for review. See Attachment D. This chart reports the compatibility of commonly used injectable medication in the same syringe. On a motion of Dr. Becker, seconded by Dr. Heidel, the “Psychotropic Injectable Compatibility Chart” was approved. The Chart will be distributed to the field for their use.

Omega-3 Review

At the last meeting, omega-3-acid ethyl esters (Lovaza®) was reviewed for addition to the Drug Formulary. At that time, the Committee chose to table the request until further information could be obtained on the availability of products that meet the USP standards. Dr. Mican reported the following:

The USP verification process for dietary supplements began in 2003. The USP Verified Dietary Supplement Mark is awarded to dietary supplements that pass USP's comprehensive verification processes. Manufacturers can display the mark on the label of USP Verified products. The mark represents the USP has rigorously tested and verified the supplement to assure the following:

1. What's on the label is in fact in the bottle – all the listed ingredients in the declared amount.

2. The supplement does not contain harmful levels of contaminants.
3. The supplement will break down and release ingredients in the body.
4. The supplement has been made under good manufacturing practices.

USP is an independent, not-for-profit organization. No other organization in the U.S. that tests supplements is recognized in federal law as the nation's official standard-setting body for medicines and supplements. USP standards are enforceable by the FDA.

The USP (www.usp.org) lists the following products as being USP Verified omega-3 fish oil supplements:

- Berkley & Jensen brand supplements: Fish oil – 1,000 mg with Omega 3 Fatty Acid
- Equaline brand supplements: Fish oil – 1,000 mg with Omega 3 Fatty Acids
- Kirkland Signature brand supplements: Fish oil concentrate – 1,000 mg
- Nutri Plus brand supplements: Fish oil 1,000 mg
- Nature Made brand supplements: Fish Oil – Extra Strength

Only the Nature Made brand is available through our wholesaler. The cost for 2 grams of EPA for the Nature Made brand is \$0.54. For Lovaza® the cost of 2 grams of EPA is \$4.26.

The Committee discussed the fact that supplements are not drugs and that in the past this Committee has not added any supplements to the Drug Formulary. Supplements are not regulated by the FDA and the quality of product can not be guaranteed from batch to batch unless the product is USP Verified. The Committee noted that melatonin has been routinely listed in the non-formulary purchases. The Committee discussed the possibility of adding a Supplement Section to the Drug Formulary. As part of this discussion, the Committee suggested that if a Supplement Section is added, then the product should be USP Verified and have therapeutic support for its indication. In addition, it was suggested that the process for adding supplements to the Formulary be the same as adding drugs to the Formulary. On a motion of Dr. Becker, seconded by Dr. Heidel, it was recommended that a "Supplement Section" be added to the Formulary, that products added to the Supplement Section be USP Verified and that there be literature to support its use.

As a result of the previous action, the Committee discussed the addition of Nature Made Fish Oil 1,200 mg capsules to the Formulary. On a motion of Dr. Becker, seconded by Dr. Mican, the recommendation to add Nature Made Fish Oil 1,200 mg USP Verified to the "Supplement Section" was approved.

The Committee will review melatonin for possible inclusion in the "Supplement Section" of the Drug Formulary.

Quarterly Non-Formulary Drug Justification Report

In reviewing the second quarter's non-formulary drug purchases, it was noted that different forms of multivitamins were listed as non-formulary. WORx™ will need to be adjusted to indicate that these products are Formulary.

Drug Formulary Sectional Review-

Cardiovascular Agents

Dr. Tramonte was not available to provide the Cardiovascular Agent Review.

Sectional Review for Next Meeting

The cardiovascular agents will be reviewed at the next meeting.

Miscellaneous Items

The Committee reviewed "Principles of Antipsychotic Prescribing for Policy Makers, Circa 2008. Translating Knowledge to Promote Individualized Treatment" which includes the National Association of State Mental Health Program Directors Medical Directors' Statement on Comparative Effectiveness of Antipsychotic Medications and

Individualized Treatment. Basically this document recommends appropriate access, efficient utilization, promotion of best practice use of antipsychotic medications, timely availability and dissemination of necessary clinical trial information. Currently, all antipsychotics are available in the Drug Formulary and any dosage form not included can

be obtained through the non-formulary process. The Agency utilizes TIMA and the Psychotropic Medication Audit Criteria and Guidelines for medication use.

At the last meeting, generic fenofibrate was added to the Formulary. In reviewing the availability of the products and their costs, it was noted that fenofibrate nanocrystallized is available as the name brand Tricor NFE®. Fenofibrate micronized is available in both tablets and capsules in name brand (Antara®, Lofibra®) and generically. Plain fenofibrate is available in multiple trade names (Fenoglide®, Triglide®, Lipofen®) in tablets and capsules. The Committee decided that the generic version of fenofibrate micronized will be added to the Drug Formulary.

Next Meeting Date

The next meeting was scheduled for August 22, 2008.

Adjourn

There being no further business, the meeting was adjourned at 12:50 p.m.

APPROVED:



A handwritten signature in black ink, appearing to read "Jeff R. Matthews", is written over a horizontal line. The signature is cursive and includes a small flourish at the end.

Jeff R. Matthews, M.D., Chairman

Attachments

- Attachment A – New Drug Applications
- Attachment B – Carbamazepine (Tegretol®) Guidelines
- Attachment C – Treatment of Behavioral Emergencies Intramuscular Short-Acting Agents.
- Attachment D – Psychotropic Injectable Compatibility Chart

Minutes Prepared by:

Ann L. Richards, Pharm.D., BCPP