

DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
October 18, 2013

The Executive Formulary Committee convened on Friday, October 18, 2013 in Room 1077 - ASH Building 631. The meeting was called to order by Dr. Wright, Chair at 9:50 a.m.

Phillip Balfanz, M.D.	√	Jennifer Wright, M.D.	√
James Baker, M.D.	√	Valerie Kipfer, MSN, RN (non-voting)	Absent
Mary Bowers RN, BSN	Absent	Lilani Muthali, M.D. (non-voting)	Absent
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 (via phone)	√	Peggy Perry (non-voting)	Absent
Jeff Matthews, M.D.	√	Joe Vesowate (non-voting)	Absent
Connie Millhollon, RN	√	Mike Maples (non-voting)	Absent
Victoria Morgan, M.D.	√	Kerry Raymond (non-voting)	Absent
Kenda Pittman, Pharm.D.	√	Vacant Medical Director Position	
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Robert L. Ward, D.O.	√	Vacant DADS Physician	

Guests Present: Daniel Dispensa, Pharm.D., Pharmacy Resident, Michelle Blair, Pharm.D., Pharmacy Resident, Lisa Mican, Pharm.D., ASH

Introduction and Other Information

Dr. Baker was introduced as the newest member of the Executive Formulary Committee. Dr. Baker is the new Medical Director, DSHS Hospital Section.

Approval of Minutes of July 12, 2013

On a motion of Dr. Matthews, seconded by Dr. Hall, the minutes of the July 12th meeting were approved as previously distributed.

Conflict of Interest Disclosure Forms

Dr. Baker submitted his conflict of interest disclosure form. Dr. Baker did not report any conflicts of interest. Dr. Heidel reported that she had attended a dinner sponsored by Sunovion. Both Dr. Morgan and Dr. Pittman reported being contacted by Lundbeck's representatives. Lundbeck is the manufacturer of clobazam (Onfi®).

Issues from the Clinical Directors' Meeting

Dr. Baker reported that Formulary-wise, the Clinical Directors are concerned about drugs that lengthen the QT intervals and how to handle this issue in the patient population that is served. Staffing issues in both the recruitment

and retention areas are a concern for the facilities. The Clinical Directors are also concerned about the CMS issues that were raised at Terrell and the impact those issues will have throughout all of the facilities.

Adverse Drug Reaction Reports

The Executive Formulary Committee discussed several adverse drug reaction reports.

In the first case, a routine annual dental exam detected a lesion with exposed bone in a 60 year old male. This individual is edentulous and the lesion was in tooth #8 position. A consult with oral surgeon was completed on August 9th. A biopsy was obtained while under general anesthesia. The biopsy was read on August 20th as dead bone, fibrotic tissue, actinomyces and the diagnosis was made as “a lesion as a result of bisphosphonate therapy.” The bisphosphonate was discontinued on July 19th. Post biopsy, he was treated with penicillin VK 500 mg TID x 10 days and hydrocodone/acetaminophen (Norco®) for pain. A consult to an Infectious Disease Specialist is pending as well as a consult to Endocrinology regarding future treatment of osteoporosis.

A 50 year old male was admitted to a psychiatric hospital with the diagnoses of MDD with psychotic features and alcohol dependence, hepatitis C and scoliosis. Prior to admission, he reported drinking 6 beers daily. Initially, he was placed on chlordiazepoxide (Librium®) detox protocol for the first few days, sertraline (Zoloft®) 50 mg, and hydroxyzine (Atarax®) as needed for anxiety and sleep. He was also given multivitamins, B12, folic acid, thiamine 100 mg (3 IM doses followed by daily oral doses), and ibuprofen (Motrin®) 600 mg every 6 hours as needed for headaches. Over the course of the next month, he was noted to have slight cognitive slowing and confusion. On July 16th, aripiprazole (Abilify®) 10 mg daily was initiated for psychosis. He received his first dose at 11:30 am. At 12:20 pm, he had fallen in the dayroom and reported feeling dizzy. Later that day, he appeared to have a change in mental status including significant cognitive slowing and confusion as well as a report of physical weakness. At that time, aripiprazole was discontinued, and he did not receive a dose the following morning. He was transferred to a local medical hospital that afternoon for a work-up of his new onset altered mental status. He was diagnosed with AMS due to Wernicke’s or a medication side effect. He returned to the psychiatric hospital on July 23rd, and he was restarted on his previous medications and appeared to be back to his baseline. Aripiprazole was restarted at the previous dose of 10 mg on July 25th. He was again transferred back to the medical hospital on July 28th for increased confusion, worsened bilateral leg weakness, and inability to move his legs. The patient also reported that he had an unwitnessed seizure the night before. The Naranjo ADR Probability Scale Score was 8.

A 59 year old male developed lethargy, urinary retention, hypoxia, and leukocytosis on April 16th, shortly after bilateral amputation above the knee on April 8th. He was sent to ER and was diagnosed with UTI and sepsis. He was hospitalized from 16th to the 22nd. The PCP attributed the events to the intrathecal baclofen titration as this reportedly occurred during previous intrathecal baclofen titrations. The intrathecal baclofen is very slowly being tapered by the movement disorder specialists at TIRR. No reported problems have occurred since the taper began.

Of interest, Austin State Supported Living Center and Abilene State Supported Living Center verbally reported similar cases at their facilities. Apparently, this type of adverse effect is a known issue that tends to occur about five years after being on intrathecal baclofen. The Committee expressed some concern about whether the baclofen used was a manufacturer’s product or a compounded product.

A 51 year old female with a stable history of seizure disorder since age 7 and recurrent pneumonias non-aspiration was started on denosumab (Prolia®) on July 9th. She was admitted to the hospital on August 1st for hypoglycemia, hypotension and hypothermia diagnosed as sepsis secondary to *Proteus mirabilis*. She spent time in the ICU on a vasopressor. She was discharged on August 6th with a diagnosis of sepsis due to a UTI caused by *Proteus mirabilis*, dehydration and pneumonitis. Nitrofurantoin prophylaxis was discontinued on return. On August 10th, she developed emesis and was admitted for pneumonia. She was initially treated with piperacillin/tazobactam (Zosyn®) and levofloxacin (Levaquin®) but this was changed to tigecycline (Tygacil®) and the piperacillin/tazobactam was discontinued. She was diagnosed with pneumonia but it was transposed as aspiration pneumonia on return. She was discharged from the medical hospital on August 17th. On August 30th, she was transferred to a medical hospital for altered mental status and hypothermia. At this time, she was diagnosed with severe sepsis and had a rocky course requiring vasopressors to maintain her blood pressure. She returned to the facility on September 8th.

An individual was initiated on a starting dose of clobazam (Onfi®) 30 mg BID on March 26th per epileptologist's

recommendation. In April, it was noted that this individual's aggression and self-injurious behaviors were increasing. A review of the package insert showed aggression was more prevalent at higher doses (14% incidence at 60 mg/day compared to 3% incidence at lower doses). The dose of clobazam was decreased to 40 mg/day and his behaviors improved.

Quetiapine (Seroquel®, Seroquel® XR) Purchases

Dr. Richards reviewed the State Hospital purchases and returns of Seroquel® and Seroquel® XR from July through September. The State Supported Living Centers' purchases were not reviewed since these facilities receive Medicare Part D funding for the majority of their residents. The following is a summary of the State Hospitals' Seroquel® and Seroquel® XR purchases:

Facility	July	August	September	Total	# Patients for Quarter
Austin	\$1,121.88	0	(\$1,121.88)	0	1
Big Spring	0	0	\$1,424.71	\$1,424.71	1
Rio Grande	\$1,121.88	0	\$2,220.46	\$3,342.33	7
Terrell	0	0	\$11,628.60	\$11,628.60	1
Vernon	\$3,383.86	\$1,691.93	\$3,348.72	\$8,424.51	2
Total	\$5,627.62	\$1,691.93	\$17,500.61	\$24,820.16	12

The facilities that did not purchase or return Seroquel® or Seroquel® XR are not included in the table. Currently, there are six patients on Seroquel® XR: Three at Rio Grande State Center - all by the same physician; one at Terrell State Hospital – was on immediate release from 7-23-13 to 8-12-13; and two at the Vernon campus, both have been in a state hospital continuously since 2007.

Dr. Baker inquired about the message the Committee would like to provide to the field regarding the use of Seroquel® XR. The Committee recommended that the hospital medical staff be educated about the differences between extended release product and the immediate release product of quetiapine, including pharmacokinetics, adverse effects and costs. For example, if the six patients currently on the extended release product were switched to immediate release product, there would be a cost savings of about \$74,000 annually. It was noted that due to different cost systems, this same message should not be provided to the community centers.

The Committee recommended to continue to monitor this information.

Drug Deletions

At the last meeting, based on the sectional review it was recommended to delete the following drugs from Formulary:

- Sulfur/resorcinol (Sulforcin®, Rezamid®)
- Dibucaine (Nupercainal®)
- Calcium undecylenate (Caldesene®)
- Zinc undecylenate (Desenex®)
- Methotrexate
- Benzalkonium chloride (Zephiran®)

The field did not provide any feedback regarding this deletion. On a motion of Dr. Ward, seconded by Dr. Matthews, the drugs were deleted.

New Dosage Strengths

The Committee recommended that lurasidone (Latuda®) 60 mg and 120 mg tablets be added to the Formulary. On a motion of Dr. Ward, seconded by Dr. Matthews, these dosage strengths were added to Formulary.

Psychotropic Audit Criteria and Guidelines

The Atypical Antipsychotics Audit Criteria and Guidelines were updated to include Abilify® Long Acting Injection (LAI). The Committee recommended using Maintena™ instead of using “LAI” in the antipsychotic listing. See Attachment A and 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.

Recalls

During the past quarter, two drugs that are prescribed frequently within our facilities had drug recalls. Bzotropine injection manufactured by Nexus Pharmaceuticals was recalled due to visible particulate matter in the vials. There were two specific lot numbers that were recalled. The second recall involved Risperdal® Consta™ 25 mg dose pack. In this case, a stability sample tested positive for *Alternaria alternata*, a mold commonly found in the environment. Again, a specific lot number was recalled. For both recalls, the Pharmacy Directors were notified so that they could take appropriate action for their facility.

New Drug Applications

(Please refer to [Attachment C](#) for the monograph and application that were considered when determining action by the committee.)

Clobazam (Onfi®) - developed by Trushar Patel, Pharm.D. student, reviewed and presented by Dr. Richards

Clobazam is an antiepileptic that is indicated for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years or age or older. The exact mechanism of action is not fully understood but is thought to involve potentiation of the GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABAA receptor. The usual dose is 20 to 30 mg/day given in two doses a day with the maximum dose of 60 mg/day. Patients on high-dose clobazam were more likely to show significant improvements in overall symptoms compared to low-dose clobazam.

Following discussion, on motion of Dr. Matthews, seconded by Dr. Heidel, the request to add clobazam (Onfi®) to the formulary was approved.

meloxicam (Mobic®) – developed and presented by Michelle Blair, Pharm.D. Resident, reviewed by Lisa Mican, Pharm.D.

Meloxicam is a non-steroidal anti-inflammatory (NSAID) drug that has anti-inflammatory, analgesic, and antipyretic activity by reversibly inhibiting cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which result in decreased formation of prostaglandin precursors. Meloxicam may be slightly selective for COX-2, thus gastrointestinal (GI) toxicity may be decreased. Meloxicam is indicated for the treatment of osteoarthritis, rheumatoid arthritis, and juvenile idiopathic arthritis (JIA) in patients 2 years of age and older. Meloxicam carries a black boxed warning that is the same as other NSAIDs regarding an increased risk of adverse cardiovascular thrombotic events, including myocardial infarction (MI) and stroke. For osteoarthritis and rheumatoid arthritis, the initial dose is 7.5 mg once a day, which may be increased to 15 mg/day daily. The maximum dose is 15 mg/day. Currently, meloxicam is used frequently as a non-formulary agent.

Following discussion, on motion of Dr. Matthews, seconded by Dr. Pittman, the request to add meloxicam (Mobic®) to the formulary was approved.

Drug Formulary Sectional Review-

Dermatologicals – Part Two Irrigation Solutions Immunological Agents

Dr. Hall provided the review on the agents in the Dermatologicals (Scabicides to Wound Agents) sections. See Attachment D. After reviewing this section, Dr. Hall did not make any recommended changes.

Dr. Hall provided the review on the agents in the Irrigation section. See Attachment E. Dr. Hall did not make any recommended changes.

In reviewing the immunological Agents, Dr. Hall didn't recommend any changes. See Attachment F.

Drug Formulary Table Review

Drug Formulary Tables were reviewed. The "Psychotropic Medication Utilization Parameters for Children and Youth in Foster Care" was the primary reference used in determining maximum dose in children and adolescents. In some instances, Lexicomp® Online was used as a reference. The following changes were recommended. Unless noted, the reference for the change was the Foster Care Guidelines.

Children and Adolescent Treatment of Behavioral Emergencies Intramuscular short-Acting Agents

- Updated the "Drug Information Handbook" reference to "Lexicomp® Online (accessed 10-8-13)"

Adult Treatment of Behavioral Emergencies Intramuscular Short-Acting Agents

- Update reference 1 to 2013
- Updated reference 3 to "Lexicomp® Online (accessed 10-8-13)"
- Update reference 8 to 2013

Antipsychotics Table

- Add aripiprazole long acting injection (Abilify® Maintena™) with a maximum adult dose of 400 mg
- Chlorpromazine (Lexicomp® Online – accessed 10-8-13)
 - Child dose: 500 (\leq 45.5 kg) (Lit)
 - Adolescent dose: 800 ($>$ 45.5 kg) (Lit)
- Haloperidol
 - Child dose: 0.15 mg/kg (Lit)
 - Adolescent dose: 15 (Lit)
- Lurasidone
 - Child and Adolescent – ID
- Olanzapine
 - Adolescent dose: 20 (Lit)
- Paliperidone
 - Child – ID
 - Adolescent dose: 6 ($<$ 51 kg) and 12 (\geq 51 kg) (Lit)
- Perphenazine
 - Child – ID
 - Adolescent dose: 64 (Lit)
- Quetiapine
 - Child dose: 400 (\leq 9 y/o); 800 (10-12 y/o) (Lit)
 - Adolescent dose: 800 (Lit)
- Ziprasidone
 - Child dose: 80⁶ (\leq 45 kg); 40⁷ (Lit)
 - Adolescent dose: 160⁶ ($>$ 45 kg); 40⁷ (Lit)
 - Add footnotes: ⁶Bipolar Disorder; ⁷Tourettes

It was recommended that boxes under the child and adolescent columns that do not contain any information regarding dosing be shaded to indicate the lack of information.

Antidepressants Table

- Bupropion
 - Child dose: “Lesser of 6 mg/kg⁴ or 300 (Lit)”
 - Adolescent dose: “Lesser 6 mg/kg⁴ or 300 (Lit)”
- Bupropion SR
 - Adolescent dose: 400⁴ (Lit)
- Bupropion XL
 - Adolescent dose: 450⁴ (Lit)
- Duloxetine
 - Adolescent dose: 60 (Lit)
- Escitalopram
 - Adolescent dose: 30 (Lit)
- Imipramine
 - Child dose: “Lesser of 4 mg/kg or 200 (Lit)⁴”
 - Adolescent dose: “Lesser of 4 mg/kg or 200 (Lit)⁴”
- Mirtazapine
 - Delete the child and adolescent dose recommendation
- Nortriptyline
 - Child dose: “Lesser of 2 mg/kg or 100 (Lit)⁴”
 - Adolescent dose: “Lesser of 2 mg/kg or 100 (Lit)⁴”
- Trazodone
 - Child – ID
 - Adolescent dose: 100 (Lit)⁵
- Venlafaxine
 - Child dose: 150 (Lit)
 - Adolescent dose: 375 (Lit)
- Change the footnote for #5 to “sedative hypnotic”

Mood Stabilizers Table

- Lithium
 - Child dose: # (0.6 – 1.2 mEq/L) (Lit)
 - Adolescent dose: # 1,800 (0.6 – 1.2 mEq/L) (Lit)
- Oxcarbazepine
 - Child dose: 60 mg/kg or 1,500 (Lit)
 - Adolescent dose: 60 mg/kg or 2,100 (Lit)
- Valproic acid/valproate/divalproex/divalproex ER
 - Adolescent maximum therapeutic serum concentration – max 125 mcg/ml (Lit)

Stimulants Table

- Methylphenidate sustained release
 - Adolescent dose: Concerta® - 2 mg/kg (not to exceed 108 mg/day) (Lit)

Miscellaneous drugs Used for Psychotropic Purposes Table

- clonidine
 - Child dose: 0.2 (27 - 40.5 kg); 0.3 (40.5 – 45 kg); # (Lit)
 - Adolescent dose: 0.4 (> 45 kg) # (Lit)
- Guanfacine
 - Child dose: 2 (27 - 40.5 kg); 3 (40.5 – 45 kg); # (Lit)
 - Adolescent dose: 4 (> 45 kg) # (Lit)

Anxiolytics Table

- No changes recommended

Sedatives and Hypnotics Table

- Chloral hydrate(Lexicomp® Online – accessed 10-8-13)
 - Child dose: “#Lesser of 100 mg/kg or 2 g”
 - Adolescent dose: “#Lesser of 100 mg/kg or 2 g”

- Hydroxyzine
 - Child dose: 25 (3 – 6 y/o); 50 (6 – 12 y/o) (Lit)
 - Adolescent dose: 100 (>12 y/o) (Lit)
- Temazepam
 - Remove the dosing for both child and adolescent
- Trazodone
 - Child dose: ID
 - Adolescent dose: 100 (Lit)
- Triazolam
 - Remove the dosing for both child and adolescent

Therapeutic Serum Concentrations of Some Anticonvulsants Table

- Only recommended change was to update the reference to “Lexicomp® Online (accessed 10-8-13)”

On a motion of Dr. Morgan, seconded by Dr. Ward, the recommended changes to the Formulary Tables were approved.

Reserve Drugs Review

In reviewing the Reserve Drugs in the Drug Formulary, Dr. Richards did not recommend any changes. On a motion of Dr. Matthews, seconded by Dr. Heidel, the Reserve Drugs were approved.

DSHS/DADS 2014 Drug Formulary

The 2014 Drug Formulary was presented to the Committee. It was recommended that the changes made in the meeting be included in the 2014 version. On a motion of Dr. Matthews, seconded by Dr. Heidel, the 2014 Drug Formulary was approved.

Dr. Richards will facilitate the updating of the Formulary and will arrange for posting on our website.

FDA Drug Safety Communications

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

The FDA notified healthcare professionals and patients that acetaminophen (Tylenol®) has been associated with a risk of rare but serious skin reactions. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels. Health care professionals should be aware of this rare risk and consider acetaminophen, along with other drugs already known to have such an association, when assessing patients with potentially drug-induced skin reactions. Any patient who develops a skin rash or reaction while using acetaminophen or any other pain reliever/fever reducer should stop the drug and seek medical attention right away. Anyone who has experienced a serious skin reaction with acetaminophen should not take the drug again and should contact their health care professional to discuss alternative pain relievers/fever reducers. The FDA will require that a warning be added to the labels of prescription drug products containing acetaminophen to address the risk of serious skin reactions. In addition, the FDA will also request that manufacturers add a warning about serious skin reactions to the product labels of OTC acetaminophen drug products marketed under a new drug application and will encourage manufacturers of drug products marketed under the OTC monograph do the same.

As previously discussed, Nexus Pharmaceuticals Inc. is recalling two lots of benzotropine mesylate injection 2 mg/2 mL (1mg/mL) in 2 mL single dose vials due to the presence of visible particulate matter in the vials.

The product is manufactured by Allergy Laboratories, Inc. and was distributed by Nexus Pharmaceuticals Inc. Affected product includes Lot Numbers 030712, 112911. The administration of particulate, if present in a parenteral drug, poses a safety risk to patients. Sequelae of thromboembolism, some life-threatening (such as pulmonary emboli), may occur. There is also risk for particulates causing phlebitis, mechanical block of the capillaries or arterioles, activation of platelets, subsequent generation of microthrombi, and emboli. Patients with preexisting condition of trauma or other medical condition that adversely affects the microvascular blood supply are at an increased risk. Administration of a particulate can also lead to formation of granulomas, which represent a protective local inflammatory response to the foreign material and are typically non-serious. Nexus Pharmaceuticals is notifying its distributors and is arranging for return of all recalled products.

The FDA is requiring color changes to the writing on fentanyl (Duragesic®) pain patches so they can be seen more easily. The FDA continues to learn of deaths from accidental exposure to fentanyl patches. Patients and health care professionals are reminded that fentanyl patches are dangerous even after they've been used because they still contain high amounts of strong narcotic pain medicine. Accidental exposure to these patches can cause serious harm and death in children, pets, and others. In an effort to minimize the risk of accidental exposure to fentanyl patches, the FDA is requiring all manufacturers of fentanyl patches to print the name and strength of the drug on the patch in long-lasting ink, in a color that is clearly visible to patients and caregivers. The current ink color varies by strength and is not always easy to see. This change is intended to enable patients and caregivers to more easily find patches on patients' bodies and see patches that have fallen off, which children or pets could accidentally touch or ingest. Patients should be aware that patches that are not stuck to the skin tightly enough may accidentally fall off a patient and stick to someone in close contact, such as a child.

Quarterly Non-Formulary Drug Justification Report

For the fourth quarter of fiscal year 2013, all facilities reported use of non-formulary agents. The DADS facilities submitted 662 non-formulary requests and the DSHS facilities had 492 requests. The following were the top non-formulary agents that were prescribed:

- Meloxicam (Mobic®)
- Guanfacine ER (Intuniv® ER)
- Quetiapine extended release (Seroquel® XR)
- Lansoprazole (Prevacid®) Solutab

Meloxicam (Mobic®) was added to the Formulary earlier in the meeting.

Sectional Review for Next Meeting

The following sections will be reviewed at the next meeting:

- Blood Modifying Agents
- Antidotes/Deterrents/Poison Control Agents
- Antidiabetic Agents
- Intravenous Solutions & Additives

Other Issues

The following information was shared with the Committee members:

The US Food and Drug Administration announced approval of the use of NEBA Health's Neuropsychiatric EEG-Based Assessment Aid System as the "first brain wave test to help diagnose attention deficit hyperactivity disorder in children." The approval was based in part on data that the Augusta, Georgia-based medical device manufacturer submitted to the FDA "from a study of 275 children and adolescents, ages 6 to 17, with attention or hyperactivity problems." In the study, clinicians used the

NEBA System in “combination with traditional testing methods, like listing the criteria in the Diagnostic and Statistical Manual of Mental Disorders, behavioral questionnaires and I.Q. testing.”

According to research presented at the Alzheimer’s Association International Conference, “an investigational drug targeting a key enzyme involved in beta-amyloid protein release dramatically reduced production of the protein in a small, early-stage trial.” During a one-week trial that included 30 individuals “with mild to moderate Alzheimer’s disease, daily doses of 12 to 60 mg/day of a BACE1 inhibitor called MK-8931 led to reductions in cerebrospinal fluid (CSF) levels of both major types of beta-amyloid protein of up to 84%, whereas those given placebo showed slight increases, said Mark Forman, MD, PhD, of Merck Research Laboratories.”

Valby, Denmark-based H. Lundbeck A/S and Tokyo-based Otsuka Pharmaceutical Company announced Tuesday that their investigational Alzheimer’s treatment, Lu AE58054, improved cognitive performance in patients with a moderate form of the disease. During the six-month, Phase II clinical trial, the study participants who were treated with Lu AE58054 as adjunctive therapy to donepezil had a statistically significant improvement in cognitive symptoms compared to the group that was treated with donepezil only, Lundbeck and Otsuka said. They are planning to launch a 3,000-patient, Phase III clinical trial to test the novel therapy within the next few months.

Transition Therapeutics Inc. announced that the US Food and Drug Administration has granted its investigational Alzheimer’s disease treatment, ELND005, fast track status. The Toronto-based biopharmaceutical company is testing ELND005 as a treatment for AD-related neuropsychiatric symptoms (NPS). Additionally, Transition’s licensing and marketing partner, Dublin-based Elan Corporation, is testing ELND005 for several other neuropsychiatric indications.

According to a study published in the journal *Neuropharmacology*, the synthetic chemical 3,4-methylenedioxypyrovalerone (MDPV), which is “found in illicit drugs known as ‘bath salts’ may be more addictive than methamphetamine.” The researchers at the Scripps Research Institute in La Jolla, California, conducted a series of tests, which showed that after exposing a group of rats to MDPV, the rodents “went on to press a lever for a single intravenous infusion of MDPV” for an average of 600 times compared to an average of 60 presses for meth “across a wide range of doses.”

The FDA has taken more interest in the impact that sleep aids like zolpidem have on users the next day, particularly their role in automobile accidents. The agency rejected Merck’s application for suvorexant last month because of testing showing an impact on the next day’s driving. Warnings have also been given by the FDA about the drowsiness impacts of allergy medications like diphenhydramine. It has also ordered halving the dosages of zolpidem for women. Overall, the FDA is asking pharmaceutical companies to conduct more extensive driving tests for new sleep medications, and asserted it now will take a longer look at any medication that causes extended drowsiness.

According to a study published online Aug. 14 in *JAMA Psychiatry*, brain gyrification patterns, that is, cortical folding, may serve as a biomarker as to whether people with psychosis will respond to antipsychotic medications. After using magnetic resonance imaging to scan the brains of 46 mentally healthy controls and 80 patients who had experienced their first episode of psychosis both at study start and again 12 weeks later after the patients had started taking antipsychotics, researchers discovered that patients with psychosis who did not respond to treatment with medication appeared to have less brain gyrification, particularly in the frontal and temporal lobes.

According to a study published online Aug. 13 in the journal *Bipolar Disorders*, youngsters “at high risk for developing bipolar disorder [BD] are likely to react badly to antidepressant treatment.” The study involved “21 exposed children were drawn from a cohort of 118 youths, aged between 9 and 20 years, who had at least one parent with bipolar I disorder.” Researchers found that “more than half of exposed children in the study had to discontinue treatment,” due to increases in aggression, irritability or impulsivity, psychosis, insomnia, suicidal ideation, or increased hyperactivity.

Haloperidol, commonly used to prevent delirium in critical care, showed no such effect in a double-blind study reported in the *Lancet Respiratory Medicine*. Researchers randomized 140 adult patients requiring mechanical ventilation in an intensive care unit to either 2.5 mg of haloperidol every 8 hours for up to 14 days, or saline placebo. Patients with agitation received limited doses of rescue antipsychotics, most often haloperidol. The two groups spent about the same amount of time free of delirium and coma. The haloperidol group had less need for rescue antipsychotics. The authors conclude: “Haloperidol did not modify the prevalence or duration of delirium or coma.” A commentator agrees that the study “constitutes evidence of no benefit.” She asks whether delirium requires drug therapy, saying that “the challenge lies in the distress delirium symptoms cause in caregivers.” Her final question: “Are we treating the patients or our own discomfort?”

According to a study published online Aug. 21 in *JAMA Psychiatry*, the use of antipsychotic medications may increase the risk of type 2 diabetes (T2D) in youngsters as well as in adults. What’s more, children taking antipsychotics appear to have an even greater risk for developing T2D than adults do.

According to a study published online Aug. 21 in the *BMJ*, “antidepressant use by pregnant women around the time of delivery is linked to an increased risk for postpartum hemorrhage.” The study of 106,000 pregnant women of childbearing age diagnosed with either anxiety or a mood disorder revealed “a 1.5-fold increased risk for postpartum hemorrhage associated with all classes of antidepressants and not just selective serotonin reuptake inhibitors.” An accompanying editorial called the increased risk a “cause for concern.”

According to a study published online Aug. 28 in the *American Journal of Psychiatry*, “a single intravenous dose of ketamine, a glutamate N-methyl-D-aspartate (NMDA) receptor antagonist, improved depression in 64% of patients within 24 hours of administration vs. 28% of patients who received the anesthetic midazolam.” The study involved “73 participants with treatment-resistant major depression” who were randomized “in a 2:1 ratio to receive IV ketamine (n = 47) or midazolam (n = 25).”

According to a study published online Aug. 28 in *JAMA Psychiatry*, “suspicions that psychiatric medications increase the mortality risk associated with mental illness were not borne out in a review of clinical trial data.” In the majority of cases, “death rates among more than 90,000 adult participants in trials of drugs for depression, schizophrenia, bipolar disorder, anxiety, and attention-deficit/hyperactivity disorder (AD/HD) were, for the most part, the same or lower in those assigned to active” medications versus placebo, with the sole exception of “heterocyclic antidepressants, a class of old-line agents such as imipramine and amitriptyline.”

A new study from the Centers for Disease Control and Prevention’s National Center for Health Statistics found that sleeping medication use increases with a person’s age and level of education. The study found that around four percent of adults aged 20 and older had taken sleep medication, with three percent of people without high school diplomas reporting use of “sleep aids, compared with 4.4 percent of those with high school degrees or higher education.”

Research published online in the Journal of Clinical Endocrinology and Metabolism suggests that “the use of selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants among women in midlife didn’t lead to a greater rate of bone loss.” Researchers found that, “among women enrolled in the longitudinal Study of Women’s Health Across the Nation, yearly decrease in bone mineral density (BMD) at the lumbar spine averaged 0.63% in new users of SSRIs compared with 0.68% in those not taking antidepressants (P=0.37).” The study also indicated that “among those taking the tricyclic antidepressants, the annual lumbar spine BMD decrease was 0.40% (P=0.16 compared with nonusers).”

The Food and Drug Administration approved vortioxetine (Brintellix), a novel SSRI variant. Announcing its decision, the FDA noted the drug was shown to be “‘effective in treating depression’ in six clinical trials that compared outcomes in subjects taking the drug against those of subjects who received a placebo.” The medication “will carry a boxed warning alerting patients and physicians that with children, adolescents and young adults between 18 and 24, antidepressants can increase the risk of suicidal thoughts and behavior.” According to the FDA’s acting director of the Center for Drug Evaluation and Research’s division of psychiatry, Dr. Mitchell Mathis, “Since medications affect everyone differently, it is important to have a variety of treatment options available for patients who suffer from depression.”

Next Meeting Date

The next meeting was scheduled for January 31, 2014.

Adjourn

There being no further business, the meeting was adjourned at 1:26 p.m.

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

Attachments

- Attachment A – Atypical Antipsychotics Guidelines
- Attachment B – Atypical Antipsychotics Drug Audit Checklist
- Attachment C – New Drug Application
- Attachment D – Dermatologicals Part Two Sectional Review
- Attachment E – Irrigation Sectional Review
- Attachment F – Immunological Sectional Review

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

ANTIPSYCHOTICS

chlorpromazine (Thorazine®), fluphenazine (Prolixin®), haloperidol (Haldol®), loxapine (Loxitane®), perphenazine (Trilafon®), thiothixene (Navane®), trifluoperazine (Stelazine®)

INDICATIONS

- 1) Disorders with psychotic symptoms (schizophrenia, schizoaffective disorder, manic disorders, depression with psychotic features, drug-induced psychosis, psychosis associated with other organic conditions)
- 2) Tourette's disorder (haloperidol only)
- 3) Personality disorders – schizotypal, paranoid and borderline
- 4) Acute and/or short term use for management of aggressive or violent behavior
- 5) Stereotypies

PRECAUTIONS TO CONSIDERContraindications*Absolute:*

- 1) History of anaphylactic reaction and similarly severe significant hypersensitivity to medication prescribed or structurally related medication
- 2) Severe CNS depression

Relative:

- 1) Pregnancy/nursing mothers
- 2) History of drug-induced agranulocytosis or leukopenia
- 3) Breast cancer
- 4) History of neuroleptic malignant syndrome
- 5) Narrow angle glaucoma (for chlorpromazine)
- 6) Impaired hepatic function
- 7) Prostatic hypertrophy (for chlorpromazine)
- 8) Parkinson's disease
- 9) Severe cardiovascular diseases, including certain conduction disturbances

Precautions

Alcoholism (active), recent or current blood dyscrasias, angina, hypotension, congestive heart failure, arrhythmias, glaucoma, poorly controlled seizure disorder, urinary retention, patients at risk for paralytic ileus, severe tardive dyskinesia, dementia-related psychosis.

Pregnancy and Breast-Feeding

See relative contraindications. Most antipsychotics are FDA Pregnancy Category C.

ANTIPSYCHOTICS - (continued)

chlorpromazine (Thorazine®), fluphenazine (Prolixin®), haloperidol (Haldol®), loxapine (Loxitane®), perphenazine (Trilafon®), thiothixene (Navane®), trifluoperazine (Stelazine®)

PRECAUTIONS TO CONSIDER (continued)

Drug Interactions of Major Significance

- 1) Concomitant use of CNS depressants
- 2) Antithyroid agents
- 3) Concomitant use of agents that cause EPS (including droperidol, prochlorperazine, promethazine, metoclopramide, amoxapine, metyrosine, pimozide, reserpine)
- 4) Concomitant use of hypotension producing agents
- 5) Levodopa
- 6) Concomitant anticholinergic drugs (for chlorpromazine)
- 7) Strong inhibitors or inducers of Cytochrome P450
- 8) The following are the major metabolic pathways for the typical antipsychotics:
Chlorpromazine: major substrate CYP 2D6, major inhibitor CYP 2D6
Fluphenazine: major substrate CYP 2D6
Haloperidol: major substrate CYP 2D6 and 3A4, moderate inhibitor CYP2D6 and 3A4
Loxapine: unknown
Perphenazine: major substrate CYP 2D6
Thiothixene: major substrate CYP 1A2
Trifluoperazine: major substrate CYP 1A2

SEE TABLE A: **Cytochrome P450 Drug Metabolism/Inhibition**

Age-Specific Considerations

- 1) Conservative dosing and careful monitoring are advised in children and the elderly

Side Effects Which Require Medical Attention

- 1) Anticholinergic effects
- 2) Visual changes
- 3) Extrapyramidal side effects (dystonia, pseudo-Parkinsonism)
- 4) Akathisia
- 5) Tardive dyskinesia
- 6) Hypotension
- 7) Rashes, photosensitivity and altered pigmentation
- 8) Early symptoms of agranulocytosis effects (fever, sore throat, weakness)
- 9) Galactorrhea
- 10) Amenorrhea
- 11) Gynecomastia
- 12) Poikilothermia
- 13) Fluctuating vital signs
- 14) Altered consciousness
- 15) Signs and symptoms of neuroleptic malignant syndrome

ANTIPSYCHOTICS - (continued)

chlorpromazine (Thorazine®), fluphenazine (Prolixin®), haloperidol (Haldol®), loxapine (Loxitane®), perphenazine (Trilafon®), thiothixene (Navane®), trifluoperazine (Stelazine®)

PATIENT MONITORING

Patient Monitoring Parameters

- 1) Pregnancy test – as clinically indicated
- 2) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated, and quarterly when the antipsychotic dose is stable.
- 3) Fasting plasma glucose level or hemoglobin A_{1c} – before initiating a new antipsychotic, then yearly.

If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly.

- 4) Lipid screening [total cholesterol, low- and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl

If no lipid screening has been done within the last 2 years, then a lipid profile should be obtained within 30 days of initiation of the drug.

- 5) Sexual function inquiry – inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbance yearly.

If a patient is receiving an antipsychotic known to be associated with prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly.

- 6) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory yearly.
- 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase
- 8) Tardive dyskinesia evaluation – every 3 months and as clinically indicated
- 9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly
- 10) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients.

Dosing

See DSHS/DADS Drug Formulary for dosage guidelines.

Exceptions to maximum dosage must be justified as per medication rule.

ANTIPSYCHOTICS

thioridazine (Mellaril®)

INDICATIONS

- 1) Schizophrenia, refractory (failed other classes of antipsychotics)

PRECAUTIONS TO CONSIDERContraindications*Absolute:*

- 1) History of anaphylactic reaction and similarly severe significant hypersensitivity to medication prescribed or structurally related medication
- 2) Severe CNS depression
- 3) QTc > 450 msec
- 4) Concomitant use of other drugs known to prolong QTc interval
- 5) Congenital long QT syndrome
- 6) Personal history of syncope
- 7) Family history of sudden death at an early age (under age of 40 years)
- 8) Known heart disease
- 9) Hypomagnesemia
- 10) Hypokalemia
- 11) Retinitis Pigmentosa
- 12) Known poor CYP2D6 metabolizer
- 13) Concomitant use with drugs that inhibit thioridazine metabolism (fluvoxamine, propranolol, pindolol)
- 14) Concomitant use with drugs that inhibit CYP2D6 (fluoxetine, paroxetine)

Relative:

- 1) Pregnancy/nursing mothers
- 2) History of drug induced agranulocytosis or leukopenia
- 3) Breast cancer
- 4) History of neuroleptic malignant syndrome
- 5) Narrow angle glaucoma
- 6) Impaired hepatic function
- 7) Prostatic hypertrophy
- 8) Parkinson's disease

Precautions

Alcoholism (active), recent or current blood dyscrasias, angina, hypotension, congestive heart failure, arrhythmias, glaucoma, poorly controlled seizure disorder, urinary retention, patients at risk for paralytic ileus, severe tardive dyskinesia, dementia-related psychosis.

Pregnancy and Breast-Feeding

See relative contraindications. Most antipsychotics are FDA Pregnancy Category C.

ANTIPSYCHOTICS - continued

thioridazine (Mellaril®)

PRECAUTIONS TO CONSIDER (continued)

Drug Interactions of Major Significance

- 1) Concomitant use of CNS depressants
- 2) Antithyroid agents
- 3) Concomitant use of agents that cause EPS (including droperidol metoclopramide, amoxapine, metyrosine, pimozide, reserpine)
- 4) Concomitant use of hypotension producing agents
- 5) Levodopa
- 6) Concomitant anticholinergic drugs
- 7) Concomitant use with drugs that inhibit thioridazine metabolism (fluvoxamine, propranolol, pindolol)
- 8) Concomitant use with drugs that inhibit CYP2D6 (fluoxetine, paroxetine)
- 9) Concomitant use of CYP2D6 inducers

SEE TABLE A: Cytochrome P450 Drug Metabolism/Inhibition

Age-Specific Considerations

- 1) Conservative dosing and careful monitoring are advised in children and the elderly

Side Effects Which Require Medical Attention

- 1) Anticholinergic effects
- 2) Visual changes
- 3) Extrapyramidal side effects (akathisia, dystonia, pseudo-Parkinsonism)
- 4) Tardive dyskinesia
- 5) Hypotension
- 6) Rashes, photosensitivity and altered pigmentation
- 7) Early symptoms of agranulocytosis (fever, sore throat, weakness)
- 8) Galactorrhea
- 9) Amenorrhea
- 10) Gynecomastia
- 11) Fluctuating vital signs
- 12) Altered consciousness

PATIENT MONITORING

Patient Monitoring Parameters

- 1) Pregnancy test – as clinically indicated
- 2) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated and quarterly when the antipsychotic dose is stable.

ANTIPSYCHOTICS - continued

thioridazine (Mellaril®)

PATIENT MONITORING (continued)

- 3) Fasting plasma glucose level or hemoglobin A_{1c} – before initiating a new antipsychotic, then yearly.

If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly.

- 4) Lipid screening [total cholesterol, low- and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl

If no lipid screening has been done within the last 2 years, then a lipid profile should be obtained within 30 days of initiation of the drug.

- 5) Sexual function inquiry – inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbance yearly.

If a patient is receiving an antipsychotic known to be associated with prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly

- 6) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory yearly.
- 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase
- 8) Tardive dyskinesia evaluation – every 3 months and as clinically indicated.
- 9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly
- 10) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients
- 11) Serum potassium level – baseline, every six months and as clinically indicated
- 12) Serum magnesium level – baseline and as clinically indicated (especially if potassium level is low)
- 13) EKG prior to initiating therapy; 7-14 days after dose change; 7-14 days after other medication changes that could significantly alter the cardiac effects of thioridazine; every six months; and as clinically indicated.

Dosing

See DSHS/DADS Drug Formulary for dosage guidelines.

Exceptions to maximum dosage must be justified as per medication rule.

Medication Audit Criteria and Guidelines
Drug Audit Checklist 23

Reviewer:	Date:
Class:	
Drug: risperidone (Risperdal®, Risperdal Consta®), olanzapine (Zyprexa®, Zyprexa ®Relprevv™), paliperidone (Invega®, Invega Sustenna®), quetiapine (Seroquel®) ziprasidone (Geodon®), aripiprazole (Abilify®, Abilify® Maintena™), asenapine (Saphris®), iloperidone (Fanapt®), lurasidone (Latuda®)	

Audit#	Comments	Requires Phys. Review	
		Yes	No
Patient#			
Ordering Physician			

INDICATIONS	1) Disorders with psychotic symptoms (schizophrenia, schizoaffective disorder, manic disorders, depression with psychotic features, drug-induced psychosis, psychosis associated with other medical conditions)			
	2) Schizophrenia adolescents – risperidone (13 to 17 years old), olanzapine (13 to 17 years old), paliperidone (12 to 17 years old), quetiapine (13 to 17 years old), aripiprazole (13 to 17 years old)			
	3) Severe aggression secondary to a psychiatric disorder			
	4) Self Injurious Behavior secondary to a psychiatric disorder			
	5) Bipolar disorder (not paliperidone, iloperidone, or lurasidone)			
	6) Bipolar disorder, adolescents – risperidone (10 to 17 years old, monotherapy), quetiapine (10 to 17 years old, adjunct & monotherapy), olanzapine (13 to 17 years old, acute & maintenance), aripiprazole (10 to 17 years old, adjunct & monotherapy)			
	7) Irritability associated with autistic disorders in children and adolescent – risperidone (5 to 16 years old) and aripiprazole (6 to 17 years old)			
	8) Adjunct for patients on antidepressants for major depressive disorder (aripiprazole, quetiapine)			

**Medication Audit Criteria and Guidelines
Drug Audit Checklist 23**

Reviewer:	Date:
Class:	
Drug: <i>risperidone (Risperdal®, Risperdal Consta®), olanzapine (Zyprexa®, Zyprexa ®Relprevv™), paliperidone (Invega®, Invega Sustenna®), quetiapine (Seroquel®) ziprasidone (Geodon®), aripiprazole (Abilify®, Abilify® Maintena™), asenapine (Saphris®), loperidone (Fanapt®), lurasidone (Latuda®)</i>	

Contraindications	<i>Absolute</i>	1) History of anaphylactic reaction and similarly severe significant hypersensitivity to medication prescribed			
		2) For ziprasidone - Recent myocardial infarction, uncompensated congestive heart failure or when other drugs are being used that also prolong the QT interval such as (not complete list) quinidine, dofetilide, pimoziide, sotalol, thioridazine, moxifloxacin, and sparfloxacin			
		3) For lurasidone – use of ketoconazole (3A4 inhibitor) or rifampin (3A4 inducer)			
	<i>Relative</i>	1) Pregnancy/nursing mothers			
		2) History of drug induced agranulocytosis or leukopenia			
		3) Breast cancer			
		4) History of neuroleptic malignant syndrome			
		5) Impaired hepatic function			
		6) Parkinson’s disease			
		7) Severe cardiovascular diseases			
		8) Known clinically significant QTc prolongation			

Drug audit Checklist 23 (Continued)

Drug: <i>risperidone (Risperdal®, Risperdal Consta®), olanzapine (Zyprexa®, Zyprexa ®Relprevv™), paliperidone (Invega®, Invega Sustenna®), quetiapine (Seroquel®) ziprasidone (Geodon®), aripiprazole (Abilify®, Abilify® Maintena™), asenapine (Saphris®), iloperidone (Fanapt®), lurasidone (Latuda®)</i>		Page 3.
Patient#	Comments	Requires Phys. Review
Ordering Physician		Yes No

PATIENT MONITORING	Patient Monitoring Parameters	1) Pregnancy test – as clinically indicated			
		2) BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated, and quarterly when the antipsychotic dose is stable			
		3) Fasting plasma glucose level or hemoglobin A _{1c} – before initiating a new antipsychotic, then yearly. If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly.			
		4) Lipid screening [total cholesterol, low- and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl If no lipid screening has been done within the last 2 years, then a lipid profile should be obtained within 30 days of initiation of the drug.			
		5) EKG (for patients on ziprasidone)– For 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), or congenital long QT syndrome, then a baseline EKG before treatment is initiated. A subsequent EKG is indicated if the patient presents with symptoms associated with a prolonged QT interval (e.g., syncope).			
		6) EKG (for patients on iloperidone) – at baseline			

Drug audit Checklist 23 (Continued)

Drug: *risperidone (Risperdal®), Risperdal Consta®), olanzapine (Zyprexa®, Zyprexa ®Relprevv™), paliperidone (Invega®, Invega Sustenna®), quetiapine (Seroquel®) ziprasidone (Geodon®), aripiprazole (Abilify®, Abilify® Mainena™), asenapine (Saphris®), iloperidone (Fanapt®), lurasidone (Latuda®)*

Patient#	Comments	Requires Phys. Review	
		Yes	No
Ordering Physician			

PATIENT MONITORING (continued)	Patient Monitoring Parameters (continued)	7) Serum potassium and magnesium level baseline and periodic for patients on iloperidone who are at risk for significant electrolyte disturbances				
		8) Sexual function inquiry – inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbance yearly If a patient is receiving an antipsychotic known to be associated with prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly.				
		9) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory yearly.				
		10) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase				
		11) Tardive dyskinesia evaluation – every 3 months and as clinically indicated.				
		12) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly				
		13) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients				
		14) After each olanzapine pamoate injection continuously observe patient for at least 3 hours for symptoms consistent with olanzapine overdose, including sedation (ranging from mild in severity to coma) and/or delirium (including confusion, disorientation, agitation, anxiety, and other cognitive impairment) (Post-Injection Delirium /Sedation Syndrome)				
		Dosing	See DSHS/DADS Drug Formulary for dosage guidelines.			
			Exceptions to maximum dosage must be justified as per medication rule.			

Drug audit Checklist 23 (Continued)

Drug: <i>risperidone (Risperdal®), Risperdal Consta®, olanzapine (Zyprexa®, Zyprexa ®Relprevv™), paliperidone (Invega®, Invega Sustenna®), quetiapine (Seroquel®) ziprasidone (Geodon®), aripiprazole (Abilify®, Abilify® Maintena™), asenapine (Saphris®), iloperidone (Fanapt®), lurasidone (Latuda®)</i>		Page 5
Patient#	Comments	Requires Phys. Review
		Yes No
Ordering Physician		

Date Referred	Date Reviewed	Comments	Physician's Signature

Additional Comments:

APPENDIX 1: NEW DRUG APPLICATION FORM

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: 6/4/13

Name of practitioner submitting the application: Robin Blankenburg, RN

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

Information regarding new drug:

Therapeutic Classification	Anticonvulsant / Benzodiazepine
Generic Name	Clobazam
Trade Name(s)	Onfi
Manufacturer(s)	Lundbeck
Dosage Form(s)	5mg, 10mg, 20mg

Explain the pharmacological action or use of this drug: *Onfi is indicated as adjunct treatment of seizures associated with Lennox-Gastaut syndrome by potentiation of GABA neurotransmission.*

Explain the advantages of this drug over those listed in the formulary: *Better side effect profile; fewer cognitive deficits vs the older anticonvulsants*

State which drugs this new drug would replace or supplement:

Older Anticonvulsants, such as; Pheno barbitol, Mysoline Dilantin

application is approved

signature of chairman of facility pharmacy and therapeutics committee

OR

application is appropriate and complete

signature of clinical/medical director or designee

Clobazam (Onfi®)

Classification:

Antiepileptic (Long acting benzodiazepines)

Pharmacology:

The exact mechanism of action of clobazam is not fully understood but is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABA_A receptor.

Pharmacokinetics:

Absorption: Clobazam is rapidly and extensively absorbed after oral administration. Clobazam oral tablet is 100% bioavailable compared to its liquid (suspension) formulation. Though, both formulations were shown to have similar bioavailability under fasted condition.

Distribution: it is lipophilic and distributes rapidly throughout the body. At steady state, apparent volume of distribution is 100 L.

Metabolism: it is extensively metabolized in the liver via N-demethylation by CYP3A4 (lesser extent, CYP2C19 and CYP2B6) to the active metabolite N-desmethylclobazam. The capacity for N-demethylation of clobazam declines with age in men; however, age has minimal effect on the clearance of the drug in women. There are data to suggest that clobazam is metabolized more extensively in children than in adult. The active metabolite is also metabolized by CYP2C19 enzyme.

Excretion: Clobazam is 82% renally excreted. It has elimination half-life of 36-42 hours. Clobazam metabolite (N-desmethylclobazam) has 71-82 hours of half-life.

Indication:

Clobazam is indicated for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older.

Dosage and Administration:

- Pediatrics: safety and efficacy not established in patients less than 2 years of age.
- Adults: 20-30 mg/day by mouth divided into daily or twice a day dosing.
- Elderly patients can be start on 10 mg/day. The maximum recommended dose is 60 mg/day.
- Each dose (based on body weight) in following table has been shown to be effective, although effectiveness increases with increasing dose. Dose is based on patient's body weight. The total daily dose should be divided and given twice daily. A total daily dose of 5 mg (2 mL) can be given once daily.

Daily dose	≤30 kg body weight		>30 kg body weight	
	Tablets	Oral suspension	Tablets	Oral suspension
Starting dose (low)	5 mg	2 mL	10 mg	4 mL
Starting dose (medium)	10 mg	4 mL	20 mg	8 mL
Starting dose (high)	20 mg	8 mL	40 mg	16 mL

- Clobazam tablets can be administered as whole, broken in half along the score, or crushed and mixed in applesauce.
- Clobazam suspension can be taken with or without food and should be shaken well before each administration. Patient should only use the oral dosing syringes provided with each carton. Two

syringes are provided and the second one should be reserved as replacement in case the first syringe is damaged or lost.

Dosage adjustment:

- Renal impairment (mild to moderate) – no dosage adjustment required
- Hepatic impairment (Child-Pugh score 5 to 9): initial 5 mg orally once daily, titrated no faster than every 7 days to 10 to 20 mg/day in 2 divided doses depending on weight. Maximum dose is 20 to 40 mg/day if tolerated, starting on day 21.
- Concurrent use of CYP2C19 inhibitors (e.g. fluconazole, fluvoxamine, ticlopidine, omeprazole) may require clobazam dose reduction as it increases drug concentration (up to five fold).
- Geriatric: initially 5mg orally once daily, titrated no faster than every 7 days to 10 to 20 mg/day in 2 divided doses depending on weight; if tolerated may titrate to max dose of 20 to 40 mg/day depending on weight starting on day 21.

Adverse Reactions:

- Neurologic: Ataxia (2% to 10%), Insomnia (2% to 7%), Dysarthria (2% to 5%), Somnolence (16% to 25%), Sedation (2% to 9%), lethargy (5% to 10)
- Gastrointestinal: Drooling (3% to 14%), Constipation (2% to 10%), Vomiting (5% to 9%)
- Renal: Urinary tract infection (2% to 5%)
- Psychiatric: Aggressive behavior (3% to 14%),
- Respiratory: Cough (3% to 7%), Upper respiratory tract infection (10% to 14%)
- Others: Fever (10% to 17%),

Contraindications: None

Interactions:

- Concurrent use of clobazam and thioridazine may result in increased thioridazine plasma concentrations which may lead to potential life-threatening, pro-arrhythmic effects such as torsade de pointes.
- Hormonal Contraceptives: Clobazam is a weak CYP3A4 inducer. As some hormonal contraceptives are metabolized by CYP3A4, their effectiveness may be diminished when given with clobazam. Additional non-hormonal forms of contraception are recommended when using clobazam.
- Drugs Metabolized by CYP2D6: Clobazam inhibits CYP2D6. Dose adjustment of drugs metabolized by CYP2D6 may be necessary.
- Strong and moderate inhibitors of CYP2C19: Strong and moderate inhibitors of CYP2C19 may result in increased exposure to N-desmethylclobazam, the active metabolite of clobazam. This may increase the risk of dose-related adverse reactions. Dosage adjustment of clobazam may be necessary when co-administered with strong CYP2C19 inhibitors (e.g., fluconazole, fluvoxamine, ticlopidine) or moderate CYP2C19 inhibitors (e.g., omeprazole).
- CNS Depressants and Alcohol: Concomitant use of clobazam with other CNS depressant (including alcohol) may increase risk of sedation and somnolence.

Precautions:

- Pregnancy category - C
- Avoid abrupt discontinuation of this drug as it may cause precipitate or exacerbate seizures or result in withdrawal syndrome (taper dose gradually to discontinue)
- hepatic impairment; dose adjustment recommended
- physical or psychological dependence may occur
- somnolence and sedation have been reported, particularly with concomitant use with other CNS depressants; monitoring recommended
- suicidal behavior and ideation may occur; monitoring recommended.
- Use cautiously in the elderly as it may accumulate and lead to psychomotor impairment

Cost:

Drug Name	Strength	Package Size	AWP Price
Clobazam (Onfi) tablet	10 mg	100 tablets	\$886.96
Clobazam (Onfi) tablet	20 mg	100 tablets	\$1773.90
Clobazam (Onfi) suspension	2.5 mg/mL	120 mL	\$579.60

Monitoring Parameters:

- Decreased frequency or resolution of seizures is indicative of clinical efficacy
- Signs and symptoms of CNS depression
- worsening depression, suicidal thoughts or behaviors, and unusual changes in mood or behavior

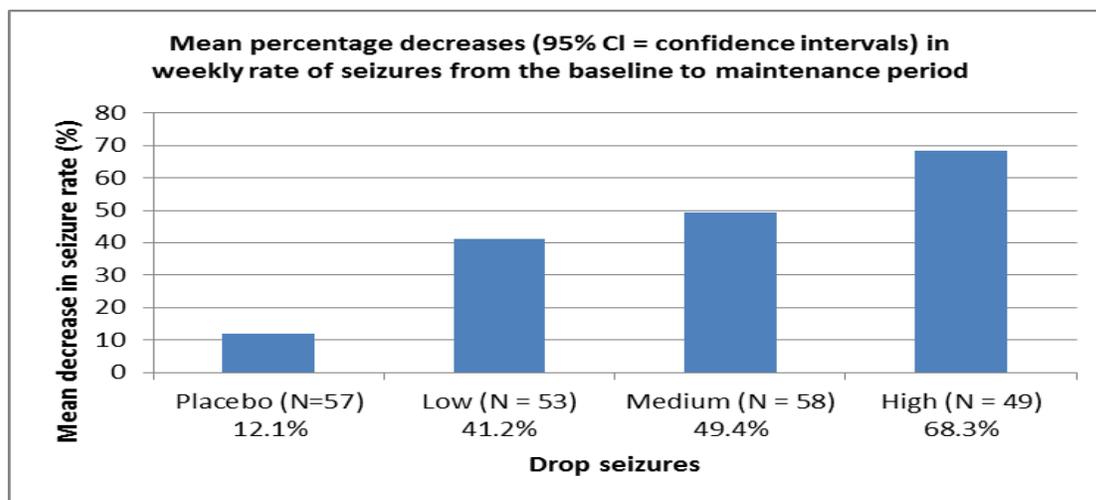
Product Identification:

Clobazam is schedule-IV controlled substance as it can be abused or lead to dependence.

Dose	Manufacturer	Color	Shape	Imprint
10 mg tablet	Catalent Pharma U.S.A.	White	Oval	"1" and "0"
20 mg tablet	Catalent Pharma U.S.A.	White	Oval	"2" and "0"
2.5 mg/mL suspension	Rosemont Pharmaceuticals Ltd. U.K.	Off-white liquid	N/A	N/A

Efficacy:

A randomized, multicenter, double-blind, placebo controlled study (N=238) was performed to assess effectiveness of clobazam. Patients age 2-54 years weighing ≥ 12.5 kg and who had onset of LGS before 11 years ago were randomly selected to receive placebo or one of three difference maintenance doses of clobazam. Primary efficacy was measured based on the percent reduction in the weekly frequency of drop seizures (atonic, tonic, or myoclonic), from the 4-week baseline period followed by a 3-week titration period and 12-week maintenance period. Different clobazam doses low (0.25 mg/kg/day), medium (0.5 mg/kg/day), and high (1.0 mg/kg/day) were statistically superior ($p \leq 0.05$) to the placebo group. There was no evidence that tolerance to the therapeutic effect of clobazam developed during 3-months maintenance period. Efficacy was dosage dependent, with decrease in drop seizure frequency in low, medium, and high dosage groups were 41.2% ($p = 0.0120$), 49.4% ($p = 0.0015$), and 68.3% ($p < 0.0001$) respectively which is also presented Figure A. In both medium and high dosage groups, more patients had decreases in weekly drop seizures $>50\%$ relative to those in placebo groups. Clobazam exhibited similar efficacy for older patients as well as younger patients and response to treatment was both persistent and early. [Reference 4]



A phase II, multicenter, randomized, double-blind, dosage-ranging study (N=68) was designed to evaluate safety and efficacy of clobazam. The patients (age 2-26 years) populations were selected from the following criteria for the study : (1) diagnosed with LGS, (2) have greater than one type of generalized seizure, (3) be less than 11 years of age at the onset of LGS, (4) weigh a minimum of 12.5 kg, (5) be on 1-3 antiepileptic drugs and on a stable dose for at least 4 weeks before screening and (6) have at least two drop seizures per week. The study comprised a 4 week baseline, 3 weeks titration and 4 week maintenance period of clobazam low dose (0.25 mg/kg/day) and high dose (1.0 mg/kg/day). The primary efficacy analysis was the percent reduction in drop seizure rates (average per week) from the 4-week baseline period compared to the 4-week maintenance period within each treatment group. Significantly more patients in the high-dose group (N=36) compared to the low dose group (N=32) has a reduction in weekly drop seizure rates of $\geq 25\%$ ($p=0.0025$), $\geq 50\%$ ($p=0.0001$), $\geq 75\%$ ($p=0.0006$) from baseline to maintenance. All patients in the high-dose group showed a $\geq 40\%$ improvement in drop seizure rates from baseline to maintenance. This study concluded that the reduction in drop seizure rates were significantly greater in the high-dose group compared with the low-dose group ($p=0.0001$). [Reference 3]

Additionally, a group of 56 patients (age 6-59 years) were studied for finding out efficacy of clobazam in following categories: the eradication of seizures, a reduction of seizures by more than 50%, no effects and seizures made worse. The maintenance dose of clobazam varied from 10 to 30 mg per day and it had to be taken for 1 month to 8 years. The results were excellent. In 14 patients, seizures were completely eradicated. In 27 patients, there was reduction in seizures more than 50%. Overall 75% of patient benefited from clobazam use. Ten patients did not see beneficial effects with clobazam. Among the participants, three patients took clobazam throughout a pregnancy. A 30 year old woman with primary generalized epilepsy whose seizures had been eradicated for 8 years after commencing clobazam 10mg twice a day along with carbamazepine, had a normal infant. [Reference 8]

Conclusions:

Clobazam is well-tolerated and is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in patients 2 years of age or older. Patients on high-dose clobazam were more likely to show significant improvements in overall symptoms compared to low-dose clobazam. In most patients, mild and transient side effects were reported with withdrawal of clobazam therapy but are lower in comparison to other benzodiazepines compounds. Clobazam has proven to be a promising agent for treatment of seizures in Lennox-Gastaut Syndrome patients

Recommendation: Add to formulary

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3. Conry J, Yu-Tze N, Stolle J, et al. Clobazam in the treatment of Lennox-Gastaut syndrome. *Epilepsia (series 4)*. May 2009;50(5):1128-1166. Available from: Academic Search Complete, Ipswich, MA. Accessed August 19, 2013.
4. Ng Y, Conry J, Drummond R, Stolle J, Weinberg M. Randomized, Phase III study results of clobazam in Lennox-Gastaut syndrome. *Neurology*. October 11, 2011;77(15): 1473-1481. Available from: MEDLINE, Ipswich, MA. Accessed September 16, 2013
5. Wheless J, Phelps S. Clobazam: a newly approved but well-established drug for the treatment of intractable epilepsy syndromes. *Journal of child Neurology*. February 2013;28(2):219-229. Available from: MEDLINE, Ipswich, MA, Accessed August 19, 2013

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8. Buchanan N. Clobazam in the treatment of epilepsy: prospective follow-up to 8 years. *Journal of The Royal Society Of Medicine*. July 1993;86(7):378-380. Available from: MEDLINE, Ipswich, MA. Accessed August 23, 2013.

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Disclosures: No conflicts of interest to disclose

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September 18, 2013

**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*)

Date: September 26, 2013

Name of practitioner submitting the application: Ann L. Richards, Pharm.D. (For EFC)

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)):

Executive Formulary Committee – based on non-formulary use

Information regarding new drug:

Therapeutic Classification	Non-steroidal anti-inflammatory (NSAID)
Generic Name	Meloxicam
Trade Name(s)	Mobic
Manufacturer(s)	Various
Dosage Form(s)	Tablets 7.5 mg, 15 mg, Suspension 7.5 mg/5 ml (not requesting)

Explain the pharmacological action or use of this drug

NSAID with anti-inflammatory, analgesic & antipyretic activity. Reversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which decreases formation of prostaglandin precursors

Explain the advantages of this drug over those listed in the formulary:

Generic. Commonly being used in the community

State which drugs this new drug would replace or supplement:

Supplement

application is approved

Ann L. Richards, Pharm.D.
signature of chairman of facility pharmacy and therapeutics committee

OR

application is appropriate and complete

signature of clinical/medical director or designee

Meloxicam (Mobic®)

Classification:

Non-steroidal anti-inflammatory (NSAID)

Pharmacology:^{1,2,3}

Meloxicam is a NSAID drug that has anti-inflammatory, analgesic, and antipyretic activity by reversibly inhibiting cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which result in decreased formation of prostaglandin precursors. Meloxicam may be slightly selective for COX-2, thus gastrointestinal (GI) toxicity may be decreased.

Other proposed mechanisms possibly contributing in the anti-inflammatory effect include inhibiting chemotaxis, altering lymphocyte activity, inhibiting neutrophil aggregation/activation, and decreasing proinflammatory cytokine levels.

Pharmacokinetics:^{1,2,3}

Absorption: Absolute bioavailability is 89%. Food has no effect.
 Distribution: Approximately 99% protein bound; primarily bound to albumin.
 Metabolism: Hepatic via CYP2C9 (major) and CYP3A4 (minor); forms 4 inactive metabolites.
 Excretion: Fecal (1.6% unchanged) and renal (0.2% unchanged). Not dialyzable.

Indication:¹

Meloxicam is indicated for the treatment of osteoarthritis, rheumatoid arthritis, and juvenile idiopathic arthritis (JIA) in patients 2 years of age and older.

Dosage and Administration:^{1,2,3}

Indication	Dose
Osteoarthritis & Rheumatoid Arthritis	<ul style="list-style-type: none"> • Initial: 7.5 mg PO once daily; may increase dose to 15 mg PO once daily • Maximum daily dose: 15 mg/day
Juvenile Idiopathic Arthritis	<ul style="list-style-type: none"> • Children ≥2 years: 0.125 mg/kg/day • Maximum daily dose: 7.5 mg/day
Renal Impairment	Severe (CrCl < 20 mL/min): use not recommended
Hemodialysis	Maximum daily dose: 7.5 mg/day

Food and Drug Administration (FDA) Black Boxed Warning:^{1,2,3}

- Cardiovascular events: NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including myocardial infarction (MI) and stroke
- Coronary artery bypass graft surgery: Use is contraindicated for treatment of perioperative pain in the setting of CABG surgery
- GI events: NSAIDs may increase risk of GI irritation, inflammation, ulceration, bleeding, and perforation

Contraindications:^{1,2,3}

- Known hypersensitivity to meloxicam or any excipient of the product. There is a potential for cross sensitivity to acetylsalicylic acid and other NSAIDs.
- Perioperative pain in setting of coronary artery bypass graft (CABG) surgery

Warnings and Precautions:^{1,2,3}

- Anemia may occur; monitoring recommended with long-term use of NSAIDs
- Aspirin triad (rhinitis with or without nasal polyps or severe potentially fatal bronchospasm after taking aspirin or NSAID); risk of anaphylactoid reaction; meloxicam use should be avoided
- Cardiovascular disease, known or risk factors for; increasing risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke
- Coagulation disorder or anticoagulant use; monitoring recommended
- Concomitant use with aspirin and sodium polystyrene sulfonate (Kayexalate®) is not recommended
- Corticosteroid treatment; do not use meloxicam as corticosteroid substitute or for corticosteroid insufficiency
- Delayed ovulation (reversible) has been reported; female patients with difficulty conceiving or undergoing infertility investigation; use not recommended
- GI adverse events including ulceration, bleeding, perforation of stomach or intestines, may occur with long term use and can be fatal; may occur without warning; use caution in elderly
- Hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis, and hepatic failure have been reported
- Hypertension; risk of new or worsening symptoms
- Increased risk of severe bronchospasm in preexisting asthma
- Increased risk of renal injury with chronic use; considerable dehydration can occur
- Intestinal necrosis, possibly fatal, has occurred with concomitant use of sorbitol and sodium polystyrene sulfonate (Kayexalate®); oral suspension contains sorbitol
- Pregnancy category C; may cause premature closure of the ductus arteriosus; avoid in third trimester
- Skin reactions; potentially fatal adverse events including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis may occur
- Smoking or alcohol use; increased risk of potentially fatal GI bleeding, ulceration, or perforation that may occur without warning
- Use with caution in patients with heart failure; edema and fluid retention have been reported
- Use with caution in patients with a history of liver dysfunction; increased risk of renal toxicity and liver injury
- Use with caution in patients with renal impairment; increased risk of renal toxicity; monitoring recommended; use not recommended in severe renal disease

Interactions:^{1,2,3}

- ACE Inhibitors: May enhance the adverse/toxic effect of NSAIDs; specifically the combination may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE Inhibitors.
- Agents with Antiplatelet properties [e.g., P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor), NSAIDs, SSRIs, etc.]: NSAIDs may enhance the adverse/toxic effect of agents with antiplatelet properties. An increased risk of bleeding may occur. NSAIDs may diminish the cardioprotective effect of agents with antiplatelet properties.
- Aliskiren: NSAIDs may diminish the antihypertensive effect and may enhance the nephrotoxic effect of Aliskiren. Management: Monitor renal function periodically in patients receiving aliskiren and any NSAID.
- Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides in premature infants.
- Angiotensin II Receptor Blockers (ARBs): May enhance the adverse/toxic effect of NSAIDs; specifically the combination may result in a significant decrease in renal function. NSAIDs may diminish the therapeutic effect of ARBs. The combination of these two agents may also significantly decrease glomerular filtration and renal function.
- Anticoagulants: NSAIDs may enhance the effect of anticoagulants.
- Antidepressants (Tricyclic, Tertiary Amine): May enhance the antiplatelet effect of NSAIDs
- Beta-Blockers: NSAIDs may diminish the antihypertensive effect of Beta-Blockers. **Exceptions:** Levobunolol; Metipranolol.

- Bile Acid Sequestrants: May decrease the absorption of NSAIDs.
- Bisphosphonate Derivatives: NSAIDs may enhance the adverse/toxic effect of Bisphosphonate Derivatives. Both an increased risk of GI ulceration and nephrotoxicity are of concern.
- Calcium Polystyrene Sulfonate: Meloxicam may enhance the adverse/toxic effect of Calcium Polystyrene Sulfonate; more specifically, concomitant use of meloxicam oral suspension (which contains sorbitol) may increase the risk for intestinal necrosis.
- Collagenase (Systemic): Agents with antiplatelet properties may enhance the adverse/toxic effect of systemic collagenase; the risk of injection site bruising and/or bleeding may increase.
- Corticosteroids (Systemic): May enhance the adverse/toxic effect of nonselective NSAIDs.
- Cyclosporine (Systemic): NSAIDs may enhance the nephrotoxic effect and increase serum concentrations of systemic cyclosporine. Systemic cyclosporine may increase the serum concentration of NSAIDs. Management: Consider alternatives to NSAIDs. Monitor for evidence of nephrotoxicity, as well as increased serum cyclosporine concentrations and systemic effects (e.g., hypertension) during concomitant therapy with NSAIDs.
- Dasatinib: May enhance the anticoagulant effect of agents with antiplatelet properties.
- Deferasirox: NSAIDs may enhance the adverse/toxic effect of deferasirox; specifically, the risk for GI ulceration/irritation or GI bleeding may be increased.
- Desmopressin: NSAIDs may enhance the adverse/toxic effect of desmopressin.
- Digoxin: NSAIDs may increase the serum concentration of digoxin.
- Drotrecogin Alfa (Activated): Agents with antiplatelet properties may enhance the adverse/toxic effect of drotrecogin alfa (activated). Bleeding may occur. Management: When possible, avoid use of drotrecogin within 7 days of use of any IIb/IIIa antagonists, higher dose aspirin (more than 650 mg/day), or use of other antiplatelet agents.
- Eplerenone: NSAIDs may diminish the antihypertensive effect of eplerenone. NSAIDs may enhance the hyperkalemic effect of Eplerenone.
- Ethanol: Avoid ethanol; may enhance gastric mucosal irritation.
- Floctafenine: May enhance the adverse/toxic effect of NSAIDs.
- Haloperidol: NSAIDs may enhance the adverse/toxic effect of haloperidol. Specifically including drowsiness and confusion.
- Herbs (Anticoagulant/Antiplatelet properties) (eg, Alfalfa, Anise, Bilberry): May enhance the adverse/toxic effect of NSAIDs and agents with antiplatelet properties. Bleeding may occur. Management: Concomitant treatment with these agents should generally be avoided. If used concomitantly, increased diligence in monitoring for adverse effects (eg, bleeding, bruising, and altered mental status due to CNS bleeds) must be employed.
- Herb/Nutraceutical: Avoid alfalfa, anise, bilberry, bladderwrack, bromelain, cat's claw, celery, chamomile, coleus, cordyceps, dong quai, evening primrose, fenugreek, feverfew, garlic, ginger, ginkgo biloba, ginseng (American, Panax, Siberian), glucosamine, grapeseed, green tea, guggul, horse chestnut seed, horseradish, licorice, prickly ash, red clover, reishi, SAME (S-adenosylmethionine), sweet clover, turmeric, white willow (all have additional antiplatelet activity).
- Hydralazine: NSAIDs may diminish the antihypertensive effect of hydralazine.
- Ibritumomab: Agents with antiplatelet properties may enhance the adverse/toxic effect of Ibritumomab. Both agents may contribute to impaired platelet function and an increased risk of bleeding.
- Ketorolac (Nasal & Systemic): May enhance the adverse/toxic effect of NSAIDs.
- Lithium: NSAIDs may increase the serum concentration of Lithium.
- Loop Diuretics: NSAIDs may diminish the diuretic effect of Loop Diuretics. Management: Monitor for decreased therapeutic effects of loop diuretics with concurrent use of an NSAID. Consider avoiding concomitant use of these agents in CHF or cirrhosis with ascites.
- Methotrexate: NSAIDs may increase the serum concentration of methotrexate.
- Multivitamins/Fluoride (with ADE): May enhance the antiplatelet effect of agents with antiplatelet properties.
- NSAIDs: May enhance the adverse/toxic effect of other NSAIDs and COX-2 Inhibitors.
- Omacetaxine: NSAIDs may enhance the adverse/toxic effect of omacetaxine. Specifically, the risk for bleeding-related events may be increased. Management: Avoid concurrent use of NSAIDs with omacetaxine in patients with a platelet count of less than 50,000/uL.

- Omega-3 Fatty Acids: May enhance the antiplatelet effect of agents with antiplatelet properties.
- Pemetrexed: Nonselective NSAIDs may increase the serum concentration of pemetrexed. Management: Patients with mild-to-moderate renal insufficiency (estimated CrCl 45-79 mL/min) should avoid NSAIDs for 2-5 days prior to, the day of, and 2 days after pemetrexed.
- Pentosan Polysulfate Sodium: May enhance the adverse/toxic effect of agents with antiplatelet properties. Specifically, the risk of bleeding may be increased by concurrent use of these agents.
- Pentoxifylline: May enhance the antiplatelet effect of agents with antiplatelet properties.
- Porfimer: Photosensitizing agents may enhance the photosensitizing effect of Porfimer.
- Potassium-Sparing Diuretics: NSAIDs may diminish the antihypertensive effect of potassium-sparing diuretics. NSAIDs may enhance the hyperkalemic effect of potassium-sparing diuretics.
- Pralatrexate: NSAIDs may increase the serum concentration of pralatrexate. More specifically, NSAIDs may decrease the renal excretion of pralatrexate. Management: Closely monitor for increased pralatrexate serum levels and/or toxicity if used concomitantly with an NSAID. Monitor for decreased pralatrexate serum levels with NSAID discontinuation.
- Probenecid: May increase the serum concentration of NSAIDs.
- Prostacyclin Analogues: May enhance the antiplatelet effect of agents with antiplatelet properties.
- Prostaglandins (Ophthalmic): NSAIDs may enhance or diminish the therapeutic effects of ophthalmic prostaglandins.
- Quinolone Antibiotics: NSAIDs may increase the serum concentration and enhance the neuroexcitatory and/or seizure-potentiating effect of quinolone antibiotics.
- Rivaroxaban: Agents with antiplatelet properties may enhance the anticoagulant effect of rivaroxaban. Management: Avoid concurrent use of rivaroxaban with other antiplatelet agents whenever possible.
- Salicylates: Nonselective NSAIDs may enhance the adverse/toxic effect of salicylates. An increased risk of bleeding may be associated with use of this combination. Nonselective NSAIDs may diminish the cardioprotective effect of salicylates. Salicylates may decrease the serum concentration of nonselective NSAIDs. **Exceptions:** Choline Magnesium Trisalicylate.
- Selective Serotonin Reuptake Inhibitors (SSRIs): May enhance the antiplatelet effect of NSAIDs. NSAIDs may diminish the therapeutic effect of SSRIs. Management: Consider using alternative analgesics, when appropriate, and/or addition of a gastroprotective agent. Monitor patients closely for signs/symptoms of bleeding, and for evidence of diminished SSRI effectiveness with concurrent use.
- Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs): May enhance the antiplatelet effect of NSAIDs.
- Sodium Phosphates: May enhance the nephrotoxic effect of NSAIDs; specifically, the risk of acute phosphate nephropathy may be enhanced. Management: Consider avoiding this combination by temporarily suspending treatment with NSAIDs, or seeking alternatives to oral sodium phosphate bowel preparation. If the combination cannot be avoided, maintain adequate hydration and monitor renal function closely.
- Sodium Polystyrene Sulfonate: Meloxicam may enhance the adverse/toxic effect of sodium polystyrene sulfonate; more specifically, concomitant use of meloxicam oral suspension (which contains sorbitol) may increase the risk for intestinal necrosis.
- Thiazide Diuretics: NSAIDs may diminish the therapeutic effect of thiazide diuretics.
- Thrombolytic Agents: NSAIDs may enhance the adverse/toxic effect of thrombolytic agents. An increased risk of bleeding may occur.
- Tipranavir: May enhance the antiplatelet effect of agents with antiplatelet properties.
- Tositumomab and Iodine I 131 Tositumomab: Agents with antiplatelet properties may enhance the adverse/toxic effect of tositumomab and iodine I 131 tositumomab. Risk of bleeding-related adverse events may be increased.
- Treprostinil: May enhance the adverse/toxic effect of NSAIDs. Bleeding may occur.
- Vancomycin: NSAIDs may increase the serum concentration of vancomycin.
- Vitamin K Antagonists (eg, warfarin): NSAIDs may enhance the anticoagulant effect of vitamin K antagonists.

- Voriconazole: May increase the serum concentration of meloxicam.

Adverse Reactions:^{1,2,3}

Common adverse effects (2% to 10%) include:

- Cardiovascular: Edema (≤5%)
- Central nervous system: Headache (2% to 8%), dizziness (≤4%), insomnia (≤4%)
- Dermatologic: Pruritus (≤2%), rash (≤3%)
- GI: Dyspepsia (4% to 10%), diarrhea (2% to 8%), nausea (2% to 7%), abdominal pain (2% to 5%), constipation (≤3%), flatulence (≤3%), vomiting (≤3%)
- Genitourinary: Urinary tract infection (≤7%), micturition (≤2%)
- Hematologic: Anemia (≤4%)
- Neuromuscular & skeletal: Arthralgia (≤5%), back pain (≤3%)
- Respiratory: Upper respiratory infection (≤8%), cough (≤2%), pharyngitis (≤3%)
- Miscellaneous: Flu-like syndrome (2% to 6%), falls (≤3%)

Relative Cost Index* Comparison of NSAIDs:⁴

Generic	Brand	Strength (mg)	Price Per Dose
Ibuprofen	Motrin®	200	0.03 ud
		400, 600	0.04 ud
		800	0.05 ud
Meloxicam	Mobic®	7.5	0.11 ud
		15	0.14 ud
Nabumetone	Relafen® (Reserve Use)	500	1.15 ud
		750	1.35 ud
		220, 250, 375	0.06 bulk
		275	0.23 ud / 0.05 bulk
Naproxen	Naprosyn®	500	0.27 ud / 0.05 bulk
		550	0.26 ud / 0.07 bulk
		550 CR	0.11 bulk
		150	0.12 bulk
Sulindac	Clinoril®	200	0.34 ud / 0.18 bulk

*DSHS Drug Formulary 2013; CR = controlled release; ud = unit dose

Monitoring Parameters:^{1,2,3}

- Blood pressure, complete blood cell count (CBC), complete metabolic panel (CMP), liver function tests (LFTs), serum creatinine (Scr), blood urea nitrogen (BUN), stool guaiac
- Improved range of motion, decreased morning stiffness and painful/swollen joints
- Signs/symptoms of GI ulcers/ bleeding, cardiovascular adverse events, serious skin reactions, and anaphylactoid reactions

Product Identification:

Dose	Formulation	Color	Shape	Imprint	Package Size	NDC
Meloxicam 7.5 mg	Oral tablet	Light yellow	Round	M 66	100 count	51079-0457-01
Meloxicam 15 mg	Oral tablet	Light yellow	Round	M 89	100 count	51079-0459-20

Efficacy:⁵

Meloxicam, a partially selective NSAID, was associated with similar pain reduction relative to nonselective NSAIDs. In multiple double-blinded studies comparing meloxicam 7.5 mg and 15 mg to other NSAIDs, there were generally no differences in efficacy.

A multicenter, double-blind, randomized trial by Hosie et al. compared the efficacy and safety of meloxicam with diclofenac for the treatment of osteoarthritis of the hip and knee.⁶ Three hundred and thirty-six patients were treated with meloxicam 7.5 mg or diclofenac 100 mg daily for 6 months. Results showed no significant differences between the treatment groups with respect to overall pain, pain on movement, and global efficacy or quality of life at the end of treatment. The median dose of concomitant paracetamol use was significantly lower in the meloxicam group than the diclofenac group (185 vs. 245 mg/day; $p < 0.0123$). Both drugs were well tolerated, and severe adverse events, treatment withdrawal and clinically significant laboratory abnormalities were more common with diclofenac than with meloxicam.⁶

A double-blind, randomized trial conducted by Goei Thè et al. compared meloxicam 15 mg with diclofenac 100 mg in the treatment of osteoarthritis of the knee.⁷ Two hundred and fifty-eight patients were included in the trial. Efficacy results showed a trend in favor of meloxicam regarding pain and movement, global efficacy and paracetamol consumption, although differences were not statistically significant. GI adverse effects occurred in both groups, however, there was a higher incidence (26 vs. 16%) of GI adverse events in the diclofenac group compared to meloxicam group.⁷

Wojtulewski et al. conducted a six-month double-blind parallel-group trial comparing the efficacy and safety of meloxicam 7.5 mg and naproxen 750 mg daily in patients with rheumatoid arthritis.⁸ Results indicated there was no significant difference between treatment groups regarding global efficacy assessed by the patient and investigator and number of painful/tender joints. Meloxicam was better tolerated in the GI tract, with fewer GI adverse effects in the meloxicam group (30.3%) than in the naproxen group (44.7%). Two patients developed ulcers while taking naproxen, while meloxicam patients had no ulcers develop. Significantly more patients discontinued naproxen due to GI adverse events compared to meloxicam. There was a significant decrease in hemoglobin, and increase in serum creatinine and urea in patients taking naproxen versus meloxicam.⁸

Valat et al. compared the efficacy and tolerability of meloxicam and diclofenac in the treatment of patients with osteoarthritis of the lumbar spine in 229 patients.⁹ Meloxicam 7.5 mg daily and diclofenac 100 mg daily were assessed for efficacy and tolerability after 3, 7, and 14 days of treatment. Results showed both drugs had equal short-term efficacy, with pain on motion significantly decreased at day 3. ($p < 0.05$) Meloxicam was better tolerated compared to diclofenac, as assessed by the investigators ($p = 0.0079$) and the patients ($p = 0.049$).⁹

Safety:⁵

Meloxicam was not associated with any clear safety advantages relative to nonselective NSAIDs.

Gastrointestinal Side Effects

The majority of meloxicam safety studies are short-term RCTs that focused on rates of perforation, symptomatic ulcer, or bleeding. Results did not generally suggest that meloxicam was associated with lower rates of ulcer complications than other nonselective NSAIDs.

One meta-analysis looked at RCT or controlled trials comparing time dependent risk of GI complications induced by NSAIDs.¹⁰ Meloxicam at doses of 3.75, 7.5, 15, and 22.5 mg were not associated with lower rates or time to onset of GI complications compared to other nonselective NSAIDs, with maximum risk at 50 days. Meloxicam was associated with lower rates of GI complications compared to indomethacin, which had a maximum relative risk for complication at 14 days.¹⁰

Hepatotoxicity Effects

A systemic review of sixty-seven RCT looked at the incidence of NSAID induced hepatic toxicity.¹¹ Meloxicam was not associated with an increased risk of hepatotoxicity relative to placebo. Diclofenac (3.55%; CI 3.12-4.03) and rofecoxib (1.80%; CI 0.17-0.51) had higher rates of aminotransferase >3 x upper limit of normal than placebo and the other NSAIDs including meloxicam (all $\leq 0.43\%$).¹¹

Cardiovascular Effects

In a population-based, retrospective cohort study assessed the influence of various NSAIDs, including meloxicam, on the risk for a first myocardial infarction (MI).¹² Limited evidence from two observational studies suggests that meloxicam was not associated with increased risk of MI relative to nonuse after 2.4 years.

FDA Black Boxed Warning^{13,14}

In April 2005, the FDA asked the manufacturers of all marked prescription NSAIDs (nonselective and COX-2 selective), to revise the labeling for all products to include a black boxed warning. The black box warning states that NSAIDs may cause an increased risk of potentially fatal cardiovascular thrombotic events, myocardial infarction, and stroke. All NSAIDs may have a similar risk, which increases with longer duration of use. Patients with cardiovascular disease or cardiovascular risk factors may be at greater risk. All NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of CABG surgery. NSAIDs cause an increased risk of potentially fatal bleeding, ulceration, and perforation of the stomach or intestines, occurring at any time during use and without warning. Elderly patients are at greater risk for serious GI events.

Short-term use of meloxicam is generally safe in patients who are well hydrated; who have good renal function; and who do not have heart failure, hypertension or diabetes. Long-term use and high daily doses of meloxicam should be avoided if possible. Patients at high risk of NSAID-induced kidney disease should receive SCr measurements every 2 to 4 weeks for several weeks after initiation of therapy because renal insufficiency may occur early in the course of therapy.

Conclusions:

Meloxicam has been shown to be effective at reducing pain in rheumatoid and osteoarthritis in both short-term and long-term settings, with comparable efficacy to the other NSAIDs available. Meloxicam has comparable incidence of GI adverse events; however, was not associated with increased hepatotoxicity or cardiovascular risks compared to other NSAIDs. Finally, meloxicam is cost-effective compared to the NSAIDs currently on formulary.

Recommendation:

Consider adding meloxicam 7.5 mg and 15 mg tablets to formulary.

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September 24, 2013

MEMORANDUM

To: Executive Formulary Committee
From: Catherine S. Hall, Pharm.D., BCPP
Through: Ann L. Richards, Pharm.D., BCPP
Subject: Class Review, Dermatologicals, part 2
Date: October 18, 2013

Recommendation: No recommended changes

Dermatologicals

Burn Agents

Bacitracin (Baciguent)	\$
Silver Sulfadiazine (Silvadene)	\$\$ - \$\$\$\$\$\$

Corticosteroids

Ultra High Potency

Betamethasone dipropionate, augmented (Diprolene A/F) - RESERVE USE	\$\$\$\$\$\$\$
Clobetasol (Clobex, Cormax, Temovate) - RESERVE USE	\$\$ - \$\$\$\$\$\$

High Potency

Betamethasone dipropionate (Diprolene)	\$\$ - \$\$\$\$\$\$
Fluocinonide (Lidex)	\$ - \$\$\$

Medium Potency

Betamethasone Valerate (Valisone)	\$\$ - \$\$\$\$
Fluocinolone (Capex, Derma Smooth FS, Synalar)	\$\$\$\$ - \$\$\$\$\$\$
Triamcinolone (Aristocort, Kenacort)	\$ - \$\$\$\$\$

Low Potency

Desonide (Desowen, Lokara, Tridesilon)	\$\$ - \$\$\$\$\$\$
Hydrocortisone (Lanacort, Corticaine)	\$ - \$\$

Diaper Rash Agents

Diaper Rash Ointment (Desitin, Vitamin A&D Topical, Diaperene)	\$ - \$\$
Diaper Rash Powder (Mexsana)	\$\$
Zinc Oxide	\$\$\$ - \$\$\$\$\$\$

Emollients

Emollient Gel (Clinac O.C.)	\$\$\$\$
Emollient Lotion/Cream (Lubriderm, Allercrème, Keri Lotion, Cetaphil, Lac-Hydrin, Eucerin, Nutraderm)	\$\$ - \$\$\$\$
Emollient Ointment (Lanolin, Aquaphor)	\$ - \$\$\$

Keratolytics

Podophyllum Resin (Podocon-25)	\$\$\$\$\$\$\$
Salicylic Acid(Compound W, DuoFilm, Mediplast, Salex, Neutrogena)	\$\$ - \$\$\$\$\$\$
Urea	\$\$\$\$ - \$\$\$\$\$\$

Ointment & Lotion Bases

Petrolatum, White (Vaseline)	\$ - \$\$
Oxybenzone/PDO/Pet Hy-Phl (Vaseline Lip Therapy)	\$

Rubs and Liniments

Menthol	\$\$ - \$\$\$\$
Menthol/Methyl Salicylate (Ben-Gay)	\$\$ - \$\$\$\$

Skin Cleansers

Abrasive Cleanser (Brasivol, Pernox, Salac, Seba-nil)	\$\$\$\$
Non-Soap Cleanser (Cetaphil)	\$\$\$ - \$\$\$\$
Salicylic Acid/Sulfur	\$-\$\$\$\$

Scabicides & Pediculicides

Permethrin 1% Liquid (NIX)	\$\$\$
Permethrin 5% Cream (Actinin, Elimite)	\$\$\$ - \$\$\$\$\$
Pyrethins/Piperonyl Butoxide (Pronto, RID)	

Skin Protectants

Benzoin, Compound Tincture	\$\$
Silver Sulfadiazine (Silvadene)	\$\$ - \$\$\$\$\$\$
Zinc Oxide	\$\$\$ - \$\$\$\$\$\$

Sunscreens

Cream/Lotion: contains a minimum SPF of 15	\$\$\$\$
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Tar-Containing Agents

Coal Tar (Ionil-T, Tegrin, Pentrax, Polytar)	\$\$\$ - \$\$\$\$\$\$
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Wound Agents

Collagenase (Santyl)	\$\$\$\$\$\$
Papin/Urea (Accuzyme, Kovia, Ethezyme)	\$\$\$\$\$ - \$\$\$\$\$\$\$
Papin/Urea/Chlorophyllin (Gladase, Panafil)	\$\$\$\$\$ - \$\$\$\$\$\$\$
Trypsin/Balsam Peru/Castor Oil (Granulex, GranuloDerm, Revina, TBC, Vasolex, Xenaderm)	\$\$\$\$\$\$
Wound Cleanser (Wound Wash, CarraKlenz)	\$\$\$\$-\$\$\$\$\$

Miscellaneous Dermatologicals

Aluminum Chloride Hexahydrate (Drysol)	\$\$\$\$
Camphor-Phenol (Campho-Phenique)	\$\$
Hydrogen Peroxide	\$
Pimecrolimus (Elidel)	\$\$\$\$\$\$
Silver Nitrate	\$\$
Tacrolimus (Protopic)	\$\$\$\$\$\$
Trypsin/Balsam Peru/Castor Oil (Granulex)	\$\$\$\$ - \$\$\$\$\$

Bacitracin (Baciguent)

Ointment, topical: 500 units/g

Silver Sulfadiazine (Silvadene)

Cream, topical: 1%

Betamethasone dipropionate, augmented (Diprolene A/F) RESERVE USE

Cream: 0.05%

Gel: 0.05%

Lotion: 0.05%

Ointment: 0.05%

Clobetasol (Temovate, Cormax, Clobex) - RESERVE USE

Cream, topical: 0.05%

Cream, topical, in emollient base: 0.05%

Gel, topical: 0.05%

Lotion, topical: 0.05%

Ointment, topical: 0.05%

Solution, topical scalp application: 0.05%

Betamethasone dipropionate (Diprolene)

Cream: 0.05%

Gel: 0.05%

Lotion: 0.05%

Ointment 0.05%

Fluocinonide (Lidex)

Cream, topical: 0.05%

Gel, topical: 0.05%

Ointment, topical: 0.05%

Solution, topical: 0.05%

Betamethasone Valerate (Valisone)

Cream, topical: 0.01%, 0.1%

Lotion: 0.1%

Ointment, topical: 0.1%

Fluocinolone (Capex, Derma-Smooth/FS, Synalar)

Cream, topical: 0.01%, 0.025%

Oil: 0.01%

Ointment, topical: 0.025%

Shampoo: 0.01%

Solution, topical: 0.01%

Triamcinolone (Aristocort, Kenacort, Azmacort, Nasacort)

Aerosol, topical: 0.2 mg/2 second spray

Cream, topical: 0.025%, 0.1%, 0.5%

Lotion, topical: 0.025%, 0.1%

Ointment, topical: 0.025%, 0.1%, 0.5%

Desonide (Desowen, Lokara, Tridesilon)

Cream: 0.05%
Lotion: 0.05%
Ointment: 0.05%

Hydrocortisone, topical (Lanacort, Corticaine)

Cream, topical: 0.5%, 1%, 2.5%
Lotion, topical: 0.5%, 1%, 2%, 2.5%
Ointment, topical: 0.5%, 1%, 2.5%

Diaper Rash Ointment (Desitin, Diaperene, Vitamin A&D)

Cod Liver Oil/Zinc Oxide/Talc (Desitin)

Ointment, topical: 40% Zinc Oxide [with Cod Liver Oil, Talc, Petrolatum, Lanolin, and Methylparaben]

Vitamin A&D Topical

Cream
Ointment

Zinc Oxide/Petrolatum/Imidazolidinyl Urea (Diaperene) Ointment, topical

Diaper Rash Powder (Mexsana)

Powder: contains kaolin, eucalyptus oil, camphor, corn starch, lemon oil, zinc oxide

Zinc Oxide

Ointment, topical: 20% in white ointment
Paste, topical: 25% in white petrolatum

Emollient Lotion/Cream (Lubriderm, Allercrème, Keri Lotion, Cetaphil, Lac-Hydrin, Eucerin, Nutraderm, Cliniac O.C.)

Cream, topical
Gel, topical
Lotion, topical

Emollient Ointment (Lanolin, Aquaphor)

Ointment, topical

Podophyllum Resin (Podocon-25)

Liquid, topical: 25% in benzoin

Salicylic Acid (Compound W, DuoFilm, Mediplast, Saalex, Neutrogena)

Cleaning Pads
Cleanser
Gel, topical: 6%, 17%
Liquid, topical: 17%
Lotion: 3%
Plaster: 40%
Shampoo
Soap: 2%
Wash

Urea

Cream: 10%, 20, 40%
Lotion: 10%, 40%
Shampoo: 10%

Petrolatum, White (Vaseline)

Ointment, topical: 430 g

Oxybenzone/PDO/Pet Hy-Phl (Vaseline Lip Therapy)

Ointment

Menthol

Cream
Liquid
Ointment
Patch
Spray

Menthol/Methyl Salicylate (Ben-Gay)

Cream, topical: 30%

Abrasive Cleanser (Brasivol, Pernox, Salac, Seba-Nil)

Cleanser:
Lotion:

Non-Soap Cleanser (Cetaphil)

Bar
Lotion

Permethrin (Acticin, Elimite, NIX)

Cream, topical: 5%
Lotion: 1%
Shampoo: 1%

Pyrethins 0.33%/Piperonyl Butoxide 4% (Pronto, RID)

Liquid, topical: 0.18%, 0.3%
Shampoo: 0.3%, 0.33%

Benzoin, Compound Tincture

Tincture, topical (also contains aloe, storax, tolu balsam, 74% to 80% alcohol): 30 mL, 60 mL,

120 mL, 480 mL, 4000 mL

Silver Sulfadiazine (Silvadene)

Cream, topical: 1%

Zinc Oxide

Ointment, topical: 20% in white ointment

Paste, topical: 25% in white petrolatum

Sunscreen/block

Cream/Lotion: contains a minimum SPF of 15

Coal Tar (Ionil-T, Tegrin, Pentrax, Polytar)

Cream, topical: 2%

Liquid, topical: 30%

Shampoo: 1%, 2%, 2.5%, 5%

Solution, topical: 120 mL, 480 mL

Collagenase (Santyl)

Ointment, topical: 0.03%, 0.1%

Papin/Urea (Accuzyme, Ethezyme, Kevia)

Ointment

Papin/Urea/Chlorophyllin (Gladase-C, Panafil)

Ointment

Trypsin/Balsam Peru/Castor Oil (Granulex GranuloDerm, Revina, TBC, Xenoderm, Vasolex)

Aerosol: Trypsin 0.1 mg/Balsam Peru 72.5 mg/Castor Oil 650 mg per 0.82 mL

Ointment: Trypsin 90 units/Balsam Peru 87 mg/Castor Oil 788 mg per gram

Wound Cleanser (CarraKlenz)

Topical, spray

Pimecrolimus (Elidel)

Cream: 1%

Silver Nitrate

Applicator sticks

Tacrolimus (Protopic)

Ointment: 0.03%, 0.1%

Trypsin/Balsam Peru/Castor Oil (Granulex GranuloDerm, Revina, TBC, Xenoderm, Vasolex)

Aerosol: Trypsin 0.1 mg/Balsam Peru 72.5 mg/Castor Oil 650 mg per 0.82 mL

Ointment: Trypsin 90 units/Balsam Peru 87 mg/Castor Oil 788 mg per gram

MEMORANDUM

To: Executive Formulary Committee
From: Catherine S. Hall, Pharm.D., BCPP
Through: Ann L. Richards, Pharm.D., BCPP
Subject: Class Review, Irrigation Solutions
Date: October 18, 2013

Recommendation: No recommended changes

Irrigation Solutions

Sodium Chloride	\$\$\$
Water for Injection	\$\$ - \$\$\$\$

Sodium Chloride

Solution, irrigation: 0.45%, 0.9%

Water for Injection

Infusion

Water for Irrigation

Solution, irrigation

MEMORANDUM

To: Executive Formulary Committee
From: Catherine S. Hall, Pharm.D., BCPP
Through: Ann L. Richards, Pharm.D., BCPP
Subject: Class Review, Immunological Agents
Date: October 18, 2013

Recommendation: No recommended changes

Immunological Agents

Immune Serums

Hepatitis B Immune Globulin (HBIG)	\$\$\$\$\$\$\$
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Bacterial Vaccines

Pneumococcal Vaccine, Polyvalent (Pneumovax)	\$\$\$\$\$
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Viral Vaccines

Hepatitis A Vaccine (Vaqta) Havrix)	\$\$\$\$\$\$\$
Hepatitis A/Hepatitis B Vaccine (Twinrix)	\$\$\$\$\$\$\$
Hepatitis B Virus Vaccine, Recombinant (Recombivax HB, Engerix-B)	\$\$\$\$\$\$\$
Influenza Virus Vaccine (Fluzone, Fluviron)	\$\$
Measles, Mumps and Rubella Virus Vaccine, Live (MMR II)	\$\$\$\$\$\$\$
Varicella Virus Vaccine, Live (Varivax)	\$\$\$\$\$\$\$

Toxoids

Diphtheria & Tetanus Toxoids Adsorbed (DT)	\$\$\$\$
Diphtheria & Tetanus Toxoids Adsorbed for Adult Use (Td)	\$\$\$
Diphtheria, Tetanus, & Acellular Pertussis (Tdap) (Boostrix, Adacel)	\$\$\$\$\$\$\$

In-Vivo Diagnostic Biologicals

Tuberculin, Purified Protein Derivative (P.P.D.)	\$\$ - \$\$\$\$\$\$
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Hepatitis B Immune Globulin (HBIG)

Injection, single dose

Pneumococcal Vaccine, Polyvalent (Pneumovax)

Injection, single dose

Hepatitis A Vaccine (Vaqta, Havrix)

Injection, single dose

Hepatitis A/Hepatitis B Vaccine (Twinrix)

Injection, single dose

Hepatitis B Virus Vaccine, Recombinant (Recombivax HB, Engerix-B)

Injection: 5 mcg/mL, 10 mcg/mL, 20 mcg/mL

Influenza Virus Vaccine (Fluzone, Fluviron)

Injection, single dose

Measles, Mumps and Rubella Virus Vaccine, Live (MMR II)

Injection, single dose

Varicella Virus Vaccine, Live (Varivax)

Injection, single dose

Diphtheria & Tetanus Toxoids Adsorbed (DT)

Injection, single dose

Diphtheria & Tetanus Toxoids Adsorbed for Adult Use (Td)

Injection, single dose

Diphtheria, Tetanus, & Acellular Pertussis (Tdap) (Boostrix, Adacel)

Injection, single dose

Tuberculin, Purified Protein Derivative (P.P.D.)

Intermediate test strength: 5 TU/0.1 mL