DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
October 13, 2006

The Executive Formulary Committee convened on Friday, October 13, 2006 in Room 240 - CO Building 2. The meeting was called to order by Dr. Ward, Interim Chair at 9:30 a.m.

Janet Adams, MSN, RN, CNS	√	Mike Maples	Absent
Rosha Chadwick, R.Ph.	Absent	Michael Woolsey	Absent
Jeanna Heidel, Pharm.D.	√	Jay Norwood, MSN, RN	Absent
J. Brett Hood, M.D.	√	Camille Hemlock, M.D.	√
Lisa Mican, Pharm.D.	√	Nina Muse, M.D.	√
Connie Millhollon, RN,	√	Vacant Medical Director Position	
Victoria B. Morgan, M.D.	Absent	Vacant Center Position	
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Bernardo C. Tarin-Godoy, M.D.	√	Vacant Center Position	
Robert L. Ward, D.O.	√	Vacant State School Position	
Kenny Dudley	Absent	Vacant DADS Nursing Coordinator	
Scott Schalchlin	Absent		

Guest Present: Sharon Tramonte, Pharm.D., San Antonio State School; Rania Kattura, Pharm.D., Resident; Nicole Benson, Pharmacy student; Sylvia Lee, Pharmacy student

Approval of Minutes of June 23, 2006

On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, the minutes of the June 23rd meeting were approved as previously distributed.

Adverse Drug Reaction Reports

The Executive Formulary Committee received four adverse drug reaction reports. In the first case, a 53-year old male patient with HIV was started on a regimen of tipranavir (Aptivus®), emtricitabine (Emtriva®) and ritonavir (Norvir®). The patient also has schizoaffective disorder bipolar type, insulin dependent diabetes, hypertension, GERD and hepatitis C infection. Liver function tests on January 3rd and March 2nd were within normal limits. On April 6th, the patient began to complain of feeling "sick" and "tired." The patient's blood sugars were labile and he was unsteady on his feet. Labs showed a total bilirubin of 11 mg/dl and transaminases were three times the upper limits of normal. The HIV medications were discontinued and the total bilirubin and transaminases improved by April 27th. The only new HIV medication was tipranavir. The patient had received past trials of emtricitabine and ritonavir without significant hepatic decompensation. Tipranavir has a boxed warning regarding hepatic impairment

and toxicity and increased risk in patients with hepatitis.
In the second case, a 15-year old male was prescribed divalproex (Depakote®), oxcarbazepine (Trileptal®), quetiapine (Seroquel®), bupropion (Wellbutrin®) SR, hydroxyzine (Atarax®) and albuterol (Ventolin®) prn. A month after admission, the patient complained of feeling fatigue. Labs showed an increase in transaminases (AST, ALT), platelets of 125 and ANC of 0.9. The divalproex was discontinued and the oxcarbazepine dose was lowered. Labs obtained a couple weeks later showed that the leukopenia, thrombocytopenia and elevated transaminases had resolved.

In the next report, a patient was admitted to the hospital for the treatment of bipolar disorder NOS. The patient did not have a rash or other hypersensitivity reaction. The patient was started on divalproex (Depakote®) ER, lamotrigine (Lamictal®), aripiprazole (Abilify®), levothyroxine (Synthroid®) and amoxicillin (Amoxil®). All of these medications except for the amoxicillin were taken by the patient prior to admission. The amoxicillin was being used for the treatment of strep throat. The patient's compliance prior to admission was unclear. Nursing staff noted a generalized skin redness. The amoxicillin was discontinued. Methylprednisolone dose pack and diphenhydramine were prescribed. Six days later, the nurse noticed that the rash continued to progress even after the discontinuation of the amoxicillin. The rash was maculopapular and covered most of the patient's body including forearms, neck, face, and chest. The patient complained of chest pain and had emesis. Patient was transported to a local hospital for treatment and was prescribed methylprednisolone and was returned to the psychiatric facility. Upon return to the psychiatric facility, the divalproex ER and lamotrigine were placed on hold. The next day, the patient's rash continued and the patient's temperature was 103.5^{O}F and the patient was transported to the local hospital for treatment. The lamotrigine and divalproex ER were discontinued. The patient left the hospital AMA so the patient was lost to follow up. The attending physician reported that the patient's fever had improved but the rash was still present when the patient left the hospital.

In the last report, a 30-year old female patient with a seizure disorder was admitted on lamotrigine (Lamictal®). The day after admission, the AST was 465 IU/L and the ALT was 47 IU/L. The total bilirubin was within normal limits. The lamotrigine was cross tapered to pregabalin (Lyrica®). Four days after admission the lamotrigine level was 7.7 ug/ml and the CPK was 43,754 IU/L. The patient was transferred to a medical facility where it was reported that the patient had rhabdomyolysis, most likely secondary to lamotrigine. The CPK began to normalize following the discontinuation of the lamotrigine.

Psychotropic Audit Criteria

At the previous meeting, it was noted that the Texas Administrative Code title 225, Part 1, Chapter 415, Subchapter A, Rule 415.10, Medication Monitoring, states that for medications known to cause movement disorder, the patient needs to be screened quarterly for abnormal involuntary movements. The current Psychotropic Audit Criteria requires that a tardive dyskinesia evaluation be completed every six months for typical antipsychotics and every 12 months for atypical antipsychotics. This recommendation was based on the Mount Sinai Conference. Dr. Muse was contacted regarding this difference. Dr. Muse noted the following:

- The article (Mount Sinai Conference recommendation) applies only to patients (probably only middle age adults) with schizophrenia while we have a mixed population, diagnosis-wise and age-wise
- Advocates on the committee (that wrote the TAC) were aware that this was a huge issue in the past and part of the RAJ lawsuit, and were not comfortable in loosening this requirement
- Our population is not a representative sample – it is more highly disordered sample with more severe symptoms in the context of poor access to the entire medication history. That is, our population is at much higher risk than the average adult schizophrenic population. Therefore, it makes sense to monitor more closely
- It is known that other neurological conditions predispose to the development of tardive dyskinesia (TD) and our population has a higher rate of these
- The AIMS can pick up other movement disorders besides TD which is common in this population

On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, it was recommended that the Psychotropic Audit Criteria match the TAC requirement. **The screening for abnormal involuntary movements will be changed to every three months for amoxapine (Asendin®) and all the antipsychotics (both typical and atypical).**

The EKG requirement for mesoridazine (Serentil®) and thioridazine (Mellaril®) now match the Formulary requirement.

The Committee discussed the potential problem of myocarditis with clozapine (Clozaril®, Fazaclo®). The Committee recommended that the following be added as a side effect that requires medical attention:

- Symptoms of myocarditis including unexplained fatigue, dyspnea, tachypnea, fever, etc.

The Committee recommended that the following be added to the patient monitoring parameters for clozapine:

- Baseline EKG and as clinically indicated (e.g., myocarditis, unexplained fatigue, tachypnea, etc)
- On the CBC monitoring that the words "or as clinically indicated" be added.

On a motion of Dr. Tarin-Godoy, seconded by Dr. Heidel these recommendations were approved.

In addition to these changes, it was recommended that a memo be distributed to the field regarding the action required for a suspected case of clozapine induced myocarditis. Myocarditis should be suspected in clozapine-treated patients with unexplained fatigue, dyspnea, tachypnea, fever, chest pain, palpitations, other signs or symptoms of heart failure, or EKG findings such as ST abnormalities and T wave inversions. If myocarditis is suspected, the clinician should measure the patient's white blood count and troponin serum level. If myocarditis is identified, clozapine should be stopped and the patient should be urgently evaluated by a primary health care provider.

The Committee recommended that "Severe tardive dyskinesia" be added to the Precautions section for amoxapine (Asendin®) and all the antipsychotic guidelines except clozapine. On a motion of Dr. Tarin-Godoy, seconded by Dr. Heidel this recommendation was approved.

Psychotropic Dosing in Children and Adolescents

Dr. Mican presented the medication doses listed in the "Psychotropic Medication Utilization Parameters for Foster Children." She noted that even though this document is listed for foster children, the doses are appropriate for all children. In reviewing the dose recommendations, the Committee agreed that the doses are appropriate for all children. The Committee discussed the definition of a child versus an adolescent. It was decided that an adolescent is a person that ranges in age from 12 years old to less than 18 years old. A child is someone that is less than 12 years old. On a motion of Dr. Tarin-Godoy, seconded by Dr. Mican, it was recommended that these doses for children and adolescents be approved. In addition, it was recommended that these doses be included in the Drug Formulary. Not all of the psychotropic drugs have maximum doses listed in this document; therefore, it was recommended that the other drugs be reviewed in the future.

FDA Alerts

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

> For conjugated estrogens (Premarin®, Premphase®, Pempro®) a boxed warning for cardiovascular and other risks was added. The estrogen-alone sub-study of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with oral conjugated estrogens (0.625 mg) per day relative to placebo. In addition, warnings for cardiovascular disorders, coronary heart disease, venous thromboembolism (VTE), malignant neoplasms and breast cancer were added.
>
> For tizanidine (Zanaflex®), a contraindication for the concomitant use of tizanidine with fluvoxamine (Luvox®) or with ciprofloxacin (Cipro®), potent inhibitors of CYP1A2. Significant alterations of pharmacokinetic parameters of tizanidine including increased AUC, $t_{1/2}$, Cmax, increased oral bioavailability and decreased plasma clearance have been observed with concomitant administration of either fluvoxamine

or ciprofloxacin. This pharmacokinetic interaction can result in potentially serous adverse events. Warnings for hypotension and use in patients with hepatic impairment were also added. Clinically significant hypotension (decrease in both systolic and diastolic pressure) has been reported with concomitant administration of either fluvoxamine or ciprofloxacin and single doses of tizanidine 4 mg. The influence of hepatic impairment on the pharmacokinetics of tizanidine has not been evaluated. Because tizanidine is extensively metabolized in the liver, hepatic impairment would be expected to have significant effects on the pharmacokinetics of tizanidine. Tizanidine should ordinarily be avoided or used with extreme caution with hepatic impairment.

Dexmethylphenidate (Focalin® and Focalin XR®) had the class warning added regarding serious cardiovascular and psychiatric events.

Taking ibuprofen (Motrin®) for pain relief and aspirin at the same time may interfere with the benefits of aspirin taken for the heart. Ibuprofen can interfere with the anti-platelet effect of low dose aspirin (81 mg per day) that may render aspirin less effective when used for cardio-protection and stroke prevention.

For lamotrigine (Lamictal®) the FDA notified healthcare professionals and patients of new preliminary information from the North American Antiepileptic Drug Pregnancy Registry that suggests that babies exposed to lamotrigine during the first three months of pregnancy may have a higher chance of being born with a cleft lip or cleft palate.

The FDA notified healthcare professionals and consumers of new safety information regarding taking medications used to treat migraine headaches (triptans) together with certain types of antidepressant and mood disorder medications [selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs)]. Serotonin syndrome, a life-threatening condition, may occur when triptans are used together with a SSRI or a SNRI. Symptoms of serotonin syndrome may include restlessness, hallucinations, loss of coordination, fast heart beat, rapid changes in blood pressure, increased body temperature, overactive reflexes, nausea, vomiting, and diarrhea.

A Medication Guide is now required with each prescription for warfarin (Coumadin®). The Medication Guide can be found at http://www.fda.gov/cder/Offices/ODS/medication_guides.htm.

Medicare D

Dr. Richards reported that a contract for a third party claims administrator has been executed. The third party claims administrator will assist in billing, claims rejection and posting payments. A problem with billing was recently discovered. For those facilities that fill on a 7-day cycle, a 35 day bill occurs in the months that have 5 days of the week in the month. To resolve this issue, the billing is being completed every 28-days.

Quarterly Non-Formulary Drug Justification Report and Top 10 Non-Formulary Drug Requests

It was noted that the new reporting system for non-formulary drugs has been implemented. Even with this new reporting system, some of the facilities are not submitting their report. In reviewing the Top-10 Non-Formulary Drug Requests it was noted that quetiapine (Seroquel®) 50 mg, 200 mg and 400 mg were the most requested items. These dosage strengths were recently added to the Drug Formulary. Recently, the Committee reviewed requests to add carisoprodol (Soma®), flurazepam (Dalmane®) and bupropion (Wellbutrin®) XL and all have been denied.
Dr. Heidel reported that Rusk uses formaldehyde (Formalyde®) Spray, however, their use will decline as McKesson (wholesaler) will no longer be stocking this product.

The Committee recommended that levetiracetam (Keppra®) 1000 mg be added to the Formulary. On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, this recommendation was approved.

Dr. Heidel reported that she is working with NetSmart to see if the information that is entered into CWS on non-formulary use can be obtained so that Pharmacy can identify the reason for non-formulary use.

New Drug Applications

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

diphtheria, tetanus, acellular pertussis (Tdap) vaccine (Boostrix®, Adacel®) - discussed by Dr. Tramonte

Tdap is a sterile liquid suspension of tetanus and diphtheria toxoids and acellular pertussis components, intended for intramuscular administration. Each antigen is adsorbed onto aluminum phosphate. After shaking, the vaccine is a white, homogenous, cloudy suspension. Like whole-cell pertussis vaccines, acellular pertussis vaccines elicit an active immune response. However, in contrast to killed whole-cell vaccines, acellular pertussis vaccines consist only of specific antigens: inactivated pertussis toxin, filamentous hemagglutinin (FHA) with or without agglutinogens. Protection against disease attributable to C *tetani* and C *diphtheriae* is due to the development of neutralizing antibodies. A serum antitoxin level of at least 0.01 IU/ml, measured by neutralization assay, is considered the minimum protective level. The mechanism of protection from B *pertussis* disease is not well understood. However, the *pertussis* components in Tdap vaccine have been shown to prevent pertussis in infants in clinical trials.
Dr. Tramonte noted that the tip cap and the rubber plunger of the Boostrix® needle-less pre-filled syringes contain dry natural latex rubber that may cause allergic reactions in latex sensitive individuals.

Following discussion, on motion of Dr. Tarin-Godoy, seconded by Dr. Hood, the request to add diphtheria, tetanus, acellular pertussis (Tdap) (Boostrix®, Adacel®) to the formulary was approved. The Formulary CheckList was completed. It was recommended that the information regarding the latex in the pre-filled syringes be distributed to the field.

Artificial Tears - discussed by Dr. Tramonte

The ophthalmic lubricants are sterile solutions containing a variety of agents including polyvinyl alcohol, hypromellose (formerly known as hydroxypropylmethylcellulose), carboxymethylcellulose, propylene glycol, dextran 70 or polysorbate 80. Multi-dose containers also contain preservative agents, most commonly benzalkonium. These are generally over-the-counter agents. These products contain balanced amounts of salts to maintain ocular tonicity, buffers to adjust pH, viscosity agents to prolong eye contact time and preservatives for sterility. Artificial Tears are indicated and used as an ophthalmic lubricant for the symptomatic relief of dry eyes or eye irritation.

Following discussion, on motion of Dr. Heidel, seconded by Dr. Mican, the request to add Artificial Tears to the formulary was approved. The Formulary CheckList was completed.

acamprosate (Campral®) - discussed by Sylvia Lee & Nicole Benson (PharmD students) - Dr. Mican

Acamprosate is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at the treatment initiation. Treatment of acamprosate should be part of a comprehensive management program that includes psychosocial support. The mechanism of action is not completely understood. Chronic alcohol exposure is thought to negatively alter the normal balance between neuronal excitation and inhibition. In vitro and in vivo animal studies suggest acamprosate may interact with the glutamate and GABA neurotransmitter systems centrally, and has led to the hypothesis that acamprosate restores this balance. Acamprosate does not undergo metabolism and is excreted renally via the kidneys as acamprosate.

Following discussion, on motion of Dr. Heidel, seconded by Ms. Adams, the request to add acamprosate to the formulary was denied.

aripiprazole (Abilify®) Discmelt - discussed by Dr. Mican

Aripiprazole discmelt is an oral disintegrating tablet (ODT) and is bioequivalent to the aripiprazole tablets. It is recommended that the discmelt be taken without liquid, however, if needed patients can take the tablet with liquid. The discmelt contains phenylalanine, therefore it can be a problem for patients with phenylketonuria. It may be advantageous to use ODT formulation in patients that are suspected of cheeking medication and patients with difficulty in swallowing tablets. Oral aripiprazole solution is available and is lower in cost per mg than the ODT, however, the ODT may be a more convenient dosage form for use.

Following discussion, on motion of Dr. Heidel, seconded by Ms. Millhollon, the request to add aripiprazole discmelt to the formulary was approved. The Formulary CheckList was completed,

The Committee expressed concern over use of novel dosage forms when patients are able to swallow tablets.

aripiprazole (Abilify®) injection - discussed by Dr. Mican

Aripiprazole injection is indicated for the treatment of agitation associated with schizophrenia or bipolar disorder, manic or mixed episode. The dose is 9.75 mg intramuscularly, may repeat every 2 hours, not to exceed 30 mg/day. Doses as low as 5.25 mg may be used when clinical factors warrant. Current studies demonstrate that aripiprazole injection to be superior to placebo, but fail to show separation from haloperidol (Haldol®) or lorazepam (Ativan®). Unlike the olanzapine (Zyprexa®) and ziprasidone (Geodon®) injections, aripiprazole injection does not require reconstitution. This may be advantageous in certain situations. Currently, this product has not been released on the market despite having an "approvable" letter from the FDA.

Following discussion, on motion of Dr. Tarin-Godoy, seconded by Dr. Heidel, the request to add aripiprazole injection to the formulary was approved pending its availability. Price information will be reported at the next meeting.

Proposed Drug Deletion List -

Immunological Agents
Intravenous Solutions and Additives
Nutritional Agents

The Committee did not receive any comments from the field about the proposed deletions for the immunological agents, intravenous solutions and additives and nutritional agents. On a motion of Ms. Millhollon, seconded by Dr. Tarin-Godoy, the motion to delete these agents was approved.

Pharmaceutical Waste

Dr. Tramonte presented some literature on the best way to dispose of medication. Most pharmacies have a contract with a pharmaceutical return/waste company. However, the question arises as to how medication should be destroyed on the units. The Pharmacy Operating Instruction indicates that tablets or capsules can be destroyed by using the waste water system or by placement in the sharps container. Nationally, there have been reports of individuals going through sharps containers to obtain drugs that might have been placed there. Other drug formulations are suppose to be returned to the pharmacy for destruction and if these drugs were exposed to bodily fluids then these drugs must be placed in a resealable container (Ziploc bags). The Committee suggested that further research be completed to determine if there are better options to destroying pharmaceutical waste. Dr. Heidel, Dr. Richards and Dr. Tramonte will complete this task.

Drug Formulary Sectional Review-

Respiratory Agents
Ophthalmic Agents

Dr. Tramonte provided the review of the respiratory agents with her recommendations. Attachment B. The comparative cost index and dosage availability of these agents was reviewed (included in Attachment B).

Dr. Tramonte recommended the addition of levalbuterol (Xopenex®), budesonide (Pulmicort®),

albuterol/ipratropium (Combivent®, Duoneb®) and fluticasone/salmeterol (Advair®).

Levalbuterol is indicated for the treatment or prevention of bronchospasms in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease. It is an inhaled $beta_2$ – adrenergic agonist. Activation of $beta_2$ – adrenergic receptors on airway smooth muscle leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic AMP. The increase in cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation. Levalbuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Levalbuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway.

For a lack of a motion, this product was not added to the Formulary.

Budesonide is used in maintenance treatment of asthma and for patients requiring oral corticosteroid therapy who may be able to reduce or eliminate their requirement for oral corticosteroids. Budesonide is an anti-inflammatory corticosteroid that exhibits potent glucocorticoid activity and weak mineralocorticoid activity. The precise mechanism of corticosteroid actions on inflammation in asthma is not known. Corticosteroids have been shown to have a wide range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic and non-allergic-mediated inflammation. These anti-inflammatory actions of corticosteroids may contribute to their efficacy in asthma.

Following discussion, on motion of Dr. Tarin-Godoy, seconded by Dr. Heidel, the request to add budesonide to the formulary was approved. The Formulary CheckList was completed.

Both albuterol and ipratropium are on the Formulary. The use of the combination product has grown and it is easier for asthmatics to use one inhaler versus two. **Following discussion, on motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, the request to add albuterol/ipratropium (Combivent®) to the formulary was approved.** The Formulary CheckList was completed.

The combination of fluticasone and salmeterol is indicated for the long-term, twice-daily, maintenance treatment of asthma and airflow obstruction in patients with COPD associated with chronic bronchitis. Fluticasone is a synthetic trifluorinated corticosteroid with potent anti-inflammatory activity. Corticosteroids have been shown to inhibit multiple cell types (e.g., mast cells, eosinophils, basophils, lymphocytes, macrophages, and neutrophils) and mediator production or secretion (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in the asthmatic response. These anti-inflammatory actions of corticosteroids contribute to their efficacy in asthma. Salmeterol is a long-acting $beta_2$-adrenergic agonist. The pharmacologic effects of $beta_2$-adrenoceptor agonist drugs is attributable to relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

Following discussion, on motion of Dr. Tarin-Godoy, seconded by Ms. Millhollon, the request to add fluticasone/salmeterol to the formulary was approved. The Formulary CheckList was completed.

Dr. Tramonte made the following recommendations:

- Add Vospire® ER as a trade name for albuterol
- Remove Vanceril® as a trade name for beclomethasone
- Add the following dosage forms/strengths of agents already on Formulary
    - Aminophylline tablet: 200 mg
    - Beclomethasone (QVAR®) spray, nasal: 40 mcg/actuation

- Brompheniramine/pseudoephedrine tablet, SR: 6 mg/120 mg
- Brompheniramine/pseudoephedrine liquid, oral: 15 mg/ 1 mg per 5 ml, 12 mg/1 mg per 5 ml
- Guaifenesin/dextromethorphan tablet, SR: 600 mg/30 mg
- Guaifenesin/dextromethorphan liquid, oral: 100 mg/15 mg per 5 ml, 66.7 mg/6.7 mg per 5 ml
- Loratadine liquid, oral: 5 mg/5 ml
- Montelukast tablet, chewable: 5 mg
- Theophylline tablet, timed release tablet SR (12 hour): 100 mg, 200 mg, 300 mg

On a motion of Dr. Tarin-Godoy, seconded by Dr. Heidel, the request to make these changes to the Formulary was approved.

Dr. Tramonte did not make any recommendations regarding the deletion of any products.

Dr. Tramonte provided the review of the ophthalmic agents with her recommendations. Attachment C. The comparative cost index and dosage availability of these agents was reviewed (included in Attachment C).

Dr. Tramonte recommended the addition of an ophthalmic irrigation solution (BSS®, Eye Stream®, AK-Rinse®) and prednisolone ophthalmic.

Ophthalmic irrigating solutions are sterile isotonic solutions used to irrigate the eyes. There is no systemic absorption.

Following discussion, on motion of Ms. Adams, seconded by Dr. Tarin-Godoy, the request to add an ophthalmic irrigating solution to the formulary was approved. The Formulary CheckList was completed.

Prednisolone ophthalmic is indicated for the treatment of steroid-responsive inflammation of the conjunctiva, cornea and anterior segment of the globe. Corticosteroids diffuse across cell membranes and complex with specific cytoplasmic receptors. These complexes then enter the cell nucleus, bind to DNA, and stimulate transcription of mRNA and subsequent protein synthesis of enzymes ultimately responsible for anti-inflammatory effects of topical application of corticosteroids to the eye. In high concentrations, which may be achieved after topical applications, corticosteroids may exert direct membrane effects. Corticosteroids decrease cellular and fibrinous exudation and tissue infiltration, inhibit fibroblastic and collagen-forming activity, retard epithelial regeneration, diminish post-inflammatory neovascularization, and reduce toward normal levels the excessive permeability of inflamed capillaries.

Following discussion, on motion of Ms. Adams, seconded by Dr. Tarin-Godoy, the request to add prednisolone ophthalmic to the formulary was approved. However, it was recommended that since it is a steroid that it be placed in the reserve category with the requirement of needing an ophthalmologist consultation prior to initiation. The Formulary CheckList was completed.

In addition, Dr. Tramonte recommended adding cromolyn to the decongestant/anti-allergy section.

2007 Drug Formulary

Dr. Tramonte presented the 2007 Drug Formulary Book and Dr. Mican discussed the psychotropic dosage tables. For the psychotropic dosage tables the following were recommended:

- For the stimulant table, include in the title reference to Medication for Attention Disorders
- For divalproex extended release (Depakote® ER) change the plasma concentrations to reflect the concentrations needed for the treatment of bipolar disorder
- Delete verapamil from the mood stabilizer table

- Add ziprasidone (Geodon®) intramuscular and olanzapine (Zyprexa®) intramuscular to the table using the maximum dose listed in the package insert

The 2007 Drug Formulary would include those drugs that were added at the meeting today. On a motion of Dr. Tarin-Godoy, seconded by Dr. Heidel, the 2007 Drug Formulary was approved.

Wound Care

Ms. Millhollon presented an issue regarding wound care at Terrell State Hospital. The Committee reviewed the issue and decided that it was a local issue that needed to be addressed by the hospital.

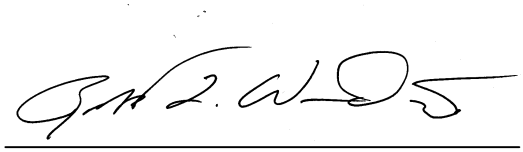
Next Meeting Date

The next meeting was scheduled for January 12, 2007.

Adjourn

There being no further business, the meeting was adjourned at 2:35 p.m.

Approved:



Robert Ward, D.O.
Interim Chair

Attachments

Attachment A – New Drug Applications
Attachment B – Respiratory Agents Class Review & Cost Review and Alphabetical Listing
Attachment C – Ophthalmic Agents Class Review & Cost Review and Alphabetical Listing

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

Diphtheria, Tetanus, Acellular Pertussis Vaccine (Tdap)
(Boostrix®, Adacel®)

Classification: Immunologic agents; Toxiods

Description: Tdap is a sterile liquid suspension of tetanus and diphtheria toxoids and acellular pertussis components, intended for intramuscular administration. Each antigen is adsorbed onto aluminum phosphate. After shaking, the vaccine is a white, homogenous, cloudy suspension.

Like whole-cell pertussis vaccines, acellular pertussis vaccines elicit an active immune response. However, in contrast to killed whole-cell vaccines, acellular pertussis vaccines consist only of specific antigens: inactivated pertussis toxin, filamentous hemagglutinin (FHA) with or without agglutinogens.

Adacel® and Boostrix® are not interchangeable as they contain different amounts of the different toxins. Adacel® is manufactured with reduced quantities of Diphtheria toxoid and Pertussin toxin.

Component	Adacel®	Boostrix®
Tetanus toxoid (T)	5 Lf	5 Lf
Diphtheria toxoid (d)	2 Lf	2.5 Lf
Pertussin toxin (PT)	2.5 µg	8 mcg
Hemagglutinin (FHA)	5 µg	8 mcg
Pertactin (PRN)	3 µg	2.5 mcg
Fimbriae types 2 & 3 (FIM)	5 µg	-

Pharmacology: Protection against disease attributable to C tetani and C *diphtheriae* is due to the development of neutralizing antibodies. A serum antitoxin level of at least 0.01 IU/mL, measured by neutralization assay, is considered the minimum protective level. The mechanism of protection from B *pertussis* disease is not well understood. However, the *pertussis* components in Tdap vaccine have been shown to prevent pertussis in infants in clinical trials.

Pharmacokinetics:

Onset: Immunity at 1 month (80%-90% demonstrate at least a fourfold increase in antibody titers; these antibody levels are at least 20-fold higher than the minimally protective level).

Duration: at least 16 months (antibodies to pertussis toxin (antitoxin) are measurable at least 16 months after administration of 2 to 3 doses at monthly intervals. Following adequate immunization, protection against diphtheria and tetanus is thought to persist for 10 years.

Indications: Indicated for booster vaccination against diphtheria, tetanus and pertussis.

Dosage: booster dose, 0.5 mL IM x 1 dose

- **SHAKE WELL** to distribute the suspension uniformly.
- The preferred site is into the deltoid muscle.

- Five years should have elapsed since the recipient's last dose of tetanus toxoid, diphtheria toxoid and/or pertussis containing vaccine.

Contraindications and Precautions:

- Pregnancy category C
- Contraindicated in:
  a) History of encephalopathy within 7 days of previous DTaP or DTwP vaccination
  b) Outbreak of poliomyelitis; defer vaccination
  c) History of hypersensitivity or serious allergic reaction (e.g. anaphylaxis) to any vaccine component
  e) Progressive neurologic disorder (e.g. infantile spasm, uncontrolled epilepsy, progressive encephalopathy); defer vaccination until neurologic status is clarified and stabilized
- Use with caution in:
  a) acute infection or moderate/severe febrile illness; defer vaccination
  b) central nervous system disorders
  c) coagulation disorders, including thrombocytopenia, hemophilia, or concomitant anticoagulant therapy; risk of hemorrhage
  d) collapse or shock-like state (hypotonic-hypo responsive episode) within 48 hours of receipt of whole-cell or acellular DTP vaccine
  e) convulsions with or without fever occurring within 3 days of receipt of whole-cell or acellular DTP vaccine
  f) history of Guillain-Barre syndrome within 6 weeks of previous tetanus toxoid-containing vaccination; carefully consider the benefits and possible risks
- Impaired immune responsiveness; immune responses to vaccine may be suboptimal
- special care should be taken to prevent injection into a blood vessel
- temperature of 40.5 degrees C (105 degrees F) or greater within 48 hours of receipt of whole-cell or acellular DTP vaccine not due to another identifiable cause
- ***The tip cap and the rubber plunger of the Boostrix needle less profiled syringes contain dry natural latex rubber that may cause allergic reactions in latex sensitive individuals.***

Interactions: Immunosuppressive therapies, including corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines.

Adverse Reactions:

- Dermatologic reactions include erythema, induration, swelling and tenderness at the injection site.
- Infrequent adverse reactions include: fever (3%-8%), fussiness, anorexia, vomiting and drowsiness.
- Serious Adverse Effects include: Anaphylaxis, persistent crying (≥3 hours), fever (≥104 degrees F), and seizure.

Costs and Monitoring:

Boostrix: $ 34.81 for both the profiled syringe and the multi-dose vial
Adacel: $ 30.52

Product Identification:

Injection

Conclusions:

Acellular pertussis vaccines were developed in an attempt to reduce the incidence of adverse effects associated with the whole-cell preparation. As compared to diphtheria/tetanus (DT) vaccines, diphtheria/tetanus/pertussis (DTwP) vaccines cause more local and systemic reactions such as anorexia, erythema and induration, fever, fretfulness, hypotonia, pain, swelling, and vomiting. In addition, serious neurotoxic reactions, such as seizures and other encephalopathic syndromes with permanent neurologic sequelae, have been observed with DTP vaccines containing whole-cell Bordetella pertussis.

The tetanus toxoid, reduced diphtheria, and acellular pertussis vaccine (Tdap) has primarily replaced the tetanus and diphtheria toxoids vaccine (Td) as routine booster immunization for both adults (19 to 64 years of age) and adolescents (11 to 18 years of age).

<u>Recommendations from the Advisory Committee on Immunization Practices</u>

The Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices (ACIP) recommends that adults from 19 to 64 years of age be vaccinated with tetanus toxoid, reduced diphtheria, and acellular pertussis (Tdap) vaccine in place of the tetanus and diphtheria toxoids (Td) vaccine. Adults should be vaccinated if they have not had a Td vaccine in at least 10 years. In addition, adults who will have close contact with an infant less than 12 months of age should be vaccinated with Tdap. If possible, vaccination should occur at least 1 month before the beginning of close contact with infants. Intervals shorter than 10 years since the last Td vaccination may be necessary but a minimum interval of 2 years is recommended to minimize the risk of reactions following vaccination

Recommendation: add to formulary

References:

Tdap monograph. MICROMEDEX(R) Healthcare Series Vol. 129 (2006)

Prepared by:
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11 October 2006

Artificial Tears

Classification: Ophthalmics; Lubricants

Description: The ophthalmic lubricants are sterile solutions containing a variety of agents including polyvinyl alcohol, hypromellose (formerly known as hydroxypropylmethylcellulose), carboxymethylcellulose, propylene glycol, dextran 70 or polysorbate 80. Multi-dose containers also contain preservative agents, most commonly Benzalkonium. These are generally all over-the-counter agents.

Pharmacology: These products contain balanced amounts of salts to maintain ocular tonicity, buffers to adjust pH, viscosity agents to prolong eye contact time and preservatives for sterility.

Pharmacokinetics: Topical agent with no systemic absorption demonstrated.

Indications: Indicated and used as an ophthalmic lubricant for the symptomatic relief of dry eyes or eye irritation.

Dosage: Instill 1-2 drops in affected eye(s) up to four times daily.

Contraindications and Precautions:

- Care must be taken to ensure the multi-dose container does not become contaminated
- Contact lens should be removed for 15 minutes prior to the installation of the drops.

Interactions: none known

Adverse Reactions: Adverse reactions are typically transient and local in nature and include burning, stinging or blurred vision in up to 10% of patients.

Costs and Monitoring:

Costs range from $ 0.87 to $ 14.99 for product sizes ranging from 15 mL to 30 mL.

Product Identification:

Solution, ophthalmic

Conclusions:

For decades, it was believed that dry spots or physical drying on the surface of the cornea caused dry eye. As a result of this long-held belief, most artificial tears were designed and formulated to solely cover the cornea effectively. Recent research has now demonstrated that the pathology of dry eye is significantly more complicated than the eye merely drying out. Although not fully elucidated, the pathology of dry eye lies in decreased tear secretion secondary to lacrimal gland disease or decreased corneal sensation or increased tear evaporation secondary to increased palpebral fissure or meibomian gland dysfunction. Both these mechanisms result in increased tear osmolarity. Therefore the goal of therapy must address lowering the increased tear osmolarity and the accompanying inflammation. Artificial tears address none of the underlying mechanisms of dry eye.

Just as important as not treating the underlying cause of dry eye is the exposure of the patient to the adverse effects of the preservatives contained in multi-dose containers. Preservatives are needed to preserve the sterility of ophthalmic formulations after multi-dose containers are opened. Without preservatives, the contents of multi-dose containers used twice daily usually become contaminated within one to two weeks even when meticulous administration practices are observed. However, long-term use of topical medications containing preservatives may induce changes in the ocular surface and damage conjunctival and corneal epithelial cells.

Benzalkonium chloride is the most commonly used preservative in ophthalmic preparations and is used at an average concentration of 0.01% (range 0.004% - 0.02%). Benzalkonium is a quaternary ammonium compound that is a highly effective antimicrobial agent that acts by denaturing proteins and disrupting cytoplasmic membranes. It can accumulate and remain in ocular tissue for relatively lengthy periods and may induce cell death in a dose-dependent manner. Benzalkonium has been demonstrated to adversely affect both the cornea and conjunctiva. For these reasons, most ophthalmologists recommend that non-preserved ophthalmic preparations be used whenever possible.

Recommendation: Do not add to formulary.

References:

1. Gilbard JP. The scientific context and basis of the pharmacologic management of dry eyes. Ophthal Clinics N Am 2005; 18: 475-484.
2. Smith RE. The tear film complex: pathogenesis and emerging therapies for dry eyes. Cornea 2005; 24: 1-7.
3. Chung SH, Lee SK, Cristol SM, Lee ES, Lee DW, Seo KY, et. al. Impact of short-term exposure of commercial eyedrops preserved with Benzalkonium chloride on precorneal mucin. Molecular Vision 2006; 12: 415-21.
4. Noecker RJ, Herrygers LA, Anwaruddin R. Corneal and conjunctival changes caused by commonly used glaucoma medications. Cornea 2004; 23: 490-496.

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8 October 2006

Acamprosate Calcium Delayed-Release Tablets
(Campral@, Forsest Pharmaceuticals, Inc.)

Classification:
Deterrent for Alcohol Dependency

Pharmacology:
The mechanism of action is not completely understood. Chronic alcohol exposure is thought to negatively alter the normal balance between neuronal excitation and inhibition In vitro and in vivo animal studies suggest acamprosate may interact with the glutamate and GABA neurotransmitter systems centrally, and has led to the hypothesis that acarnprosate restores this balance.

Pharmacokinetics:

Absorption:	Peak plasma concentrations occur 3-8 hours post dose. Coadministration with food decreases bioavailability, but the effect on absorption is not clinically significant; no dosage adjustment is necessary.
Distribution:	Volume of distribution is 72-l09liters (approximately lUkg). Plasma protein binding is negligible.
Metabolism:	Acamprosate does not undergo metabolism.
Elimination:	Terminal half-life is from 20-33 hours. Acamprosate is excreted renally via the kidneys as acamprosate.

Indications:
Acamprosate is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment of acamprosate should be part of a comprehensive management program that includes psychosocial support.

The efficacy of acamprosate in promoting abstinence has not been demonstrated in subjects who have not undergone detoxification and not achieved alcohol abstinence prior to beginning acamprosate. The efficacy of acamprosate in promoting abstinence from alcohol in polysubstance abusers has not been adequately assessed.

Dosage:
The recommended dose of acamprosate is two 333 mg tablets taken three times daily. For patients with moderate renal impairment (CrCI 30-50 m1/min), the recommended dose is one 333 mg tablet three times daily. Although dosing may be done without regard to meals, dosing with meals was employed during clinical trials and is suggested as an aid to compliance in those patients who regularly eat three meals daily.

Treatment should be initiated as soon as possible after the period of alcohol withdrawal when the patient has achieved abstinence, and should be maintained if the patient relapses.

Contraindications:
- Hypersensitivity to acamprosate or any of its components .
- Severe renal impairment (CrCl ~ 30 *mUmin)*

Precautions:

- Use of acamprosate does not eliminate withdrawal symptoms .Pregnancy Category C
- Lactation: Use with caution. It is unknown whether acamprosate is excreted in human breastmilk.
- Renal impairment: Patients with moderate renal impairment (CrCl 30 to 50 mUrnin) require a dose reduction.
- Elderly: Use caution in selecting acamprosate dose and monitor renal function. .Suicidality: Monitor patients for emergent symptoms of suicidality or depression.

Interactions:

- Acamprosate has not been reported to have any clinically significant CYP inhibition nor induction of CYP lA2 and 3A4 enzymes.
- Naltrexone: Combination of acamprosate and naltrexone may increase AUC and Cmax of acamprosate; however, no dosage adjustment is recommended in such patients.

Adverse Reactions

Diarrhea (10% to17%), insomnia (6 to 9%), anxiety (5% to 8%), depression (4% to 8%), nausea (3% to 4%)

Costs

Campral 333mg UD tab, $0.60 each. $3.60/day (2 tabs, three times daily

Price Comparison:
Naltrexone 50mg tab, $1.39 each. $1.39/day (1 tab daily).
Antabuse (disulfiram) 250mg tab, $1.20 each. $2.40/day (2 tabs daily

Monitoring

- Obtain baseline Scr to estimate CrCl.
- Monitor for suicidal ideation and depression

Product Identification

333 mg tablets enteric-coated tablets

Efficacy

The efficacy of acamprosate in the maintenance of abstinence as an adjunct to psychosocial therapy was supported by 3 double-blind, placebo-controlled trials with treatment duration ranging from 3 to 12 months. Studies involved a total of 998 alcohol dependent patients who had undergone patient detoxification and were abstinent from alcohol on the day of randomization. Continuous abstinence rates of acamprosate were statistically significant compared to placebo. In a 13-week study, 41% of acamprosate- treated patients maintained complete abstinence versus 15% for placebo-treated patients. In a 48-week trial, 39% of patients taking acamprosate maintained complete abstinence versus 17% of those taking placebo. In a third, 52-week study, 19.1% of acamprosate- treated patients remained abstinent throughout the year, versus 11.3% on placebo. Clinical trials have shown that acamprosate significantly helps maintain complete abstinence in 2-3 times more alcohol-dependent patients and reduces the risk of relapse compared to placebo when used in combination with psychosocial support.

In the COMBINE study, 8 groups of patients received 16 weeks of acamprosate or naltrexone, both, and/or both placebos with or without combined behavioral intervention (CBI). A ninth group received CBI only (no medication). The study included 1,383 patients. Patients were evaluated for

up to one year after treatment. There were no statistically significant differences in patients receiving acamprosate (with or without CBI; with or without naltrexone) compared to placebo. The authors were surprised by the lack of acamprosate efficacy given the positive results of previous trials. A possible explanation of the negative results is that the study design only required 4 days of abstinence prior to treatment; other acamprosate studied required longer pre-treatment abstinence periods.

Conclusions

Acamprosate has several advantages and disadvantages. Acamprosate has long-term efficacy data that supports the maintenance of complete abstinence. It is not contraindicated in patients with hepatic impairment, is well tolerated, and there are no known clinically significant drug interactions. Unlike naltrexone, acamprosate can be administered to patients receiving opioid medication. On the other hand, acamprosate has a high pill burden (2 pills, three time daily), and can be costly to the patient ($110/month). Additionally, acamprosate costs more than naltrexone ($3.60 daily vs. $1.39 daily, respectively).

Recommendation

Addition of acamprosate to the formulary is recommended. Consider adding acamprosate to the reserved drug use list. Since acamprosate is more costly than naltrexone, consider using the medication only when patient meets certain requirements.

Recommended requirements:

- Reserve this medication for patients with hepatic impairment.
- Ensure medication will be able to be continued on an outpatient basis. .
- Patients must be enrolled in a substance abuse program.

References:

1. Campral @ Package Insert. Forest Pharmaceuticals, Inc. St. Louis MO, 2005.
2. Pelc I, Verbanck, Le Bon 0, et al. Efficacy and safety of acamprosate in the treatment of detoxified alcohol-dependent patients. A 90-day placebo-controoled dose-finding study. *BrJPsychiatry* 1997;171:73-77.
3. Sass H, Soyka M, Mann K, et al. Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. *Arch Gen Psychiatry* 1996;53:673-80.
4. Paille PM, Guelfi, ill, Perkins AC, et al. Double-blind Randomized Multicentre trial of Acamprosate in Maintaining Abstinence from Alcohol. *Alcohol Alcohol* 1995;30(2):239-47.
5. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence. The COMBINE Study: A Randomized Controlled Trial. *JAMA* 2006;295(17):2003-17.
6. Scott U, Figgitt DP, Keam SJ, et al. Acamprosate: A Review of its Use in the Maintenance of Abstinence in Patients with Alcohol Dependence. *CNS Drugs* 2005; 19(5):445-64.

Prepared by:

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October 13, 2006

Aripiprazole Orally Disintegrating Tablets (ODT)
(Ability@ DISCMEL TTM, Bristol-Myers Squibb)

Classification: Antipsychotic agent, atypical

Pharmacology:
The exact mechanism of action of aripiprazole for the treatment of schizophrenia, bipolar disorder is not known. However its primary mechanism of action is thought to involve partial agonistic activity at the O2 and S-HT 1A receptor sites and antagonistic activity at the SHT 2A receptor site.

Pharmacokinetics:
Aripiprazole ODT are bioequivalent to aripiprazole tablets

Absorption:	Absolute oral bioavailability is 87%; aripiprazole can be administered with or without food
Distribution:	Approximately 99% protein bound (primarily to albumin) and high steady state volume of distribution (4.9Ukg)
Metabolism:	Hepatic via GYP 2D6 and 3A4
Elimination:	Half-life of aripiprazole and dehydroaripiprazole is 75 and 94 hours respectively

Indications: Treatment of schizophrenia, acute manic or mixed episodes of bipolar disorder and maintenance treatment following response in acute manic or mixed episodes

Dosage: Aripiprazole ODT are available in 10 mg and 15 mg strengths (Dosage range in Schizophrenia and Bipolar Disorder 10-30 mg per day)

Administration: Do not open blister until ready to administer. To administer, peel back the foil to reveal the tablet, do not push tablet through the foil. With dry hands remove the tablet and place on tongue. It is recommended that the ODT be taken without liquid; however, if needed, patient's can take the tablet with liquid.

Contraindications:
- Patients with hypersensitivity to aripiprazole or other ingredients in the product

Warnings:
- Boxed Warning: increased mortality in elderly patients with dementia related psychosis
  Neuroleptic Malignant Syndrome (NMS)
- Tardive Dyskinesia .
- Hyperglycemia

Precautions:
- Patients with phenylketonuria- product contains phenylalanine (10 mg ODT 1.12 mg phenylalanine, 15 mg ODT 1.68 mg phenylalanine)
- Patients who have known cardiovascular disease, cerebrovascular disease or conditions that would predispose them to hypotension
- Patients with a history of seizures or other conditions that lower seizure threshold
  Pregnancy Category C

Interactions:

- GYP 3A4 inducers such as carbamazepine could increase clearance of aripiprazole thus leading to lower blood levels. GYP 3A4 inhibitors such as ketoconazole decrease aripiprazole elimination leading to increased blood levels.
- GYP 206 inhibitors such as quinidine, fluoxetine, and paroxetine decrease aripiprazole elimination leading to increased blood levels

Adverse Reactions:
Most common treatment emergent adverse events include akathisia (7%), vomiting (5%), insomnia (5%), somnolence (4%), nausea (4%), and constipation (4%)* *% reported as active drug -placebo incidence

Costs and Monitoring:

10 mg and 15 mg aripiprazole orally disintegrating tablets $11.83 each (10 mg and 15 mg aripiprazole tablets $9.94; aripiprazole oral solution 1 mg/ml $61.60 per 150 ml bottle so 10 mg $4.11 and 15 mg $6.16)

Product Identification:
10 mg is pink with scattered specks; tablet markings "A" and "640" "10"; blister pack 15mg is yellow with scattered specks; tablet markings "A" and "641" "15"; blister pack

Storage:

Store at room temperature (25°C) in blister packaging

Efficacy:

Approval based on aripiprazole oral tablet efficacy studies. Bioavailability of aripiprazole **ODT** is bioequivalent to aripiprazole oral tablets.

Conclusions:
Currently there are no studies suggesting advantages regarding efficacy or side effects with the ODT over oral aripiprazole tablets. It may be advantageous to use the ODT formulation in patient's suspected of cheeking medication and patient's with difficulty swallowing tablets. Oral aripiprazole solution is available and is lower in cost per mg than the ODT; however, the ODT may be a more convenient dosage form for use.

Recommendation:
Recommeded *for* addition to the formulary.

References:
1. Ability Package Insert. Bristol Myers Squibb. Princteton, NJ. Sept. 2006

Prepared by:
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October 13. 2006

Memorandum

To: Executive Formulary Committee

From: Sharon M. Tramonte, Pharm.D.

Through: Ann L. Richards, Pharm.D.

Subject: Class Review

Date: 12 October 2006

Upon review, the following is a synopsis of recommended changes to the DSHS/DADS Formulary.

Recommended for addition:

- Levalbuterol (Xopenex)
- Budesonide (Pulmicort)
- Albuterol/Ipratropium (Combivent, Duoneb)
- Fluticasone/Salmeterol (Advair)

Other Recommendations:

- Add Vospire ER as trade name for Albuterol
- Remove Vanceril as trade name for Beclomethasone
- Add dosage forms/strengths of agents already on formulary
  - Aminophylline tablet: 200 mg
  - Beclomethasone (QVAR) spray, nasal: 40 mcg/actuation
  - Brompheniramine/Pseudoephedrine tablet, SR: 6 mg/120 mg
  - Brompheniramine/Pseudoephedrine liquid, oral: 15 mg/1 mg per 5 mL, 12 mg/1 mg per 5 mL
  - Guaifenesin/Dextromethorphan tablet, SR: 600 mg/30 mg
  - Guaifenesin/Dextromethorphan liquid, oral: 100 mg/15 mg per 5 mL, 66.7 mg/6.7 mg per 5 mL
  - Loratadine liquid, oral: 5 mg/5 mL
  - Montelukast tablet, chewable: 5 mg
  - Theophylline tablet, timed release: Tablet SR (12 hour): 100 mg, 200 mg, 300 mg

RESPIRATORY AGENTS

BRONCHODILATORS

Albuterol (Proventil, Ventolin)	$ - $$$
Aminophylline	$$ - $$
Metaproterenol (Alupent)	$ - $$$$$
Salmeterol (Serevent)	$$$$$$
Terbutaline (Brethine)	$ - $$$$$
Theophylline (Elixophyllin)	$ - $$

DECONGESTANTS

Pseudoephedrine (Sudafed)	$ - $$

STEROIDS

Beclomethasone (Vanceril, Beconase)	$$$$$$
Fluticasone (Flonase, Flovent)	$$$$$$
Mometasone (Nasonex)	$$$$$$
Triamcinolone (Azmacort, Nasacort)	$$$$$$

ANTITUSSIVES

Dextromethorphan	$ - $$

EXPECTORANTS

Guaifenesin (Robitussin)	$ - $$
Potassium Iodide (SSKI)	$ - $

COUGH AND COLD PREPARATIONS

Brompheniramine/Pseudoephedrine (Bromfed)	$$
Chlorpheniramine (Chlor-Trimeton, Teldrin)	$ - $$
diphenhydrAMINE (Benadryl)	$
Fexofenadine (Allegra)	$$
Fexofenadine/Pseudoephedrine (Allegra-D)	$$
Guaifenesin/Dextromethorphan (Robitussin DM)	$ - $$
Guaifenesin/Pseudoephedrine (Entex PSE)	$
Hydrocodone/Guaifenesin (Hycotuss, Kwelcof)	$$
Loratadine (Claritin)	$$
Triprolidine/Pseudoephedrine (Actifed	$

MISCELLANEOUS RESPIRATORY DRUGS

Acetylcysteine (Mucomyst)	$$$$ - $$$$$$
Cromolyn (Intal)	$$$$$$$
Ipratropium (Atrovent Inhaler)	$$$$$$$
Montelukast (Singulair)	$$
Sodium Chloride	$ - $
Zafirlukast (Accolate)	$$

Acetylcysteine (Mucomyst)
Solution, inhalation: 10% [100 mg/mL], 20% [200 mg/mL]

Albuterol (Proventil, Ventolin)
Aerosol, inhalation, chlorofluorocarbon free: 90 mcg/dose (17g) [200 doses]
Solution, inhalation: 0.083% [83 mg/mL], 0.5% [50 mg/mL]
Syrup: 2 mg/5 mL
Tablet: 2 mg, 4 mg
Tablet, extended release: 4 mg, 8 mg

Aminophylline (79% Theophylline)
Injection: 25 mg/mL
Suppository, rectal: 250 mg

Beclomethasone (Vanceril, Beconase)
Spray, nasal: 0.084% (19 g) [120 metered doses]
Spray, nasal, aqueous: 42 mcg/inhalation (25 g) [≥200 metered doses], 84 mcg/inhalation (25 g) [≥200 metered doses]

Brompheniramine/Pseudoephedrine (Bromfed)
Capsule: 12 mg Brompheniramine/120 mg Pseudoephedrine
Elixir: 4 mg Brompheniramine/30 mg Pseudoephedrine
Syrup: 2 mg Brompheniramine/30 mg Pseudoephedrine
Tablet: 4 mg Brompheniramine/60 mg Pseudoephedrine

Chlorpheniramine (Chlor-Trimeton, Teldrin)
Capsule: 12 mg
Syrup: 2 mg/5 mL
Tablet: 4 mg, 8 mg, 12 mg
Tablet, chewable: 2 mg
Tablet, timed release: 8 mg, 12 mg

Cromolyn (Intal)
Inhalation, oral: 800 mcg/spray
Solution, nebulizing: 10 mg/mL
Solution, nasal: 40 mg/mL
Solution, ophthalmic: 4%

Dextromethorphan
Capsule: 30 mg
Liquid, oral: 3.5 mg/5 mL, 7.5 mg/5 mL, 10 mg/15 mL, 15 mg/5 mL
Liquid, oral, sustained release: 30 mg/5 mL
Lozenges: 2.5 mg, 5 mg, 7.5 mg

diphenhydrAMINE (Benadryl)
Capsule: 25 mg, 50 mg
Cream, topical: 2%
Injection: 50 mg/mL
Liquid, oral: 12.5 mg/5 mL
Lotion: 1%
Tablet: 25 mg, 50 mg

Fexofenadine (Allegra)
Tablet: 30 mg, 60 mg, 180 mg

Fexofenadine/Pseudoephedrine (Allegra-D)
Tablet, extended release: 60 mg Fexofenadine/120 mg Pseudoephedrine

Fluticasone (Flonase, Flovent)
Aerosol, inhalation, oral: 44 mcg/actuation, 110 mcg/actuation, 220 mcg/actuation
Inhalation, nasal: 50 mcg/actuation

Guaifenesin (Robitussin)
Caplet, sustained release: 600 mg
Liquid, oral: 100 mg/5 mL, 200 mg/5 mL
Tablet: 100 mg, 200 mg
Tablet, sustained release: 600 mg

Guaifenesin/Dextromethorphan (Robitussin DM)
Liquid, oral: Guaifenesin 100 mg/Dextromethorphan 10 mg per 5 mL

Guaifenesin/Pseudoephedrine (Entex PSE)
Tablet: Guaifenesin 600 mg/Pseudoephedrine 120 mg

Hydrocodone/Guaifenesin (Hycotuss, Kwelcof)
Liquid, oral: Hydrocodone 5 mg/Guaifenesin 100 mg per 5 mL

Ipratropium (Atrovent)
Inhalation: 18 mcg/actuation
Solution, nasal: 0.03%, 0.06%
Solution, nebulizing: 0.02%

Loratadine (Claritin)
Tablet: 10 mg

Metaproterenol (Alupent)
Aerosol, oral: 0.65 mg/metered dose
Solution for inhalation: 0.4%, 0.6%, 5%

Montelukast (Singulair)
Tablet, chewable: 4 mg
Tablet: 10 mg

Mometasone (Nasonex)
Inhalation, nasal: 50 mcg/actuation

Potassium Iodide (SSKI)
Solution, oral: 100 mg/mL,1 g/mL

Pseudoephedrine (Sudafed)
Liquid, oral: 15 mg/5 mL, 30 mg/mL
Tablet, immediate release: 30 mg, 60 mg
Tablet, timed release: 120 mg
Tablet, extended release: 120 mg, 240 mg

Salmeterol (Serevent)
Aerosol, inhalation: 25 mcg/dose
Powder, inhalation: 50 mcg

Sodium Chloride
Drops, nasal: 0.9%
Infusion: 0.2%, 0.45%, 0.9%, 3%, 5%, 20%, 23.4%
Injection, bacteriostatic: 0.9%
Injection, for admixtures: 50 mEq, 100 mEq, 635 mEq
Ointment, ophthalmic: 5%
Solution, irrigation: 0.45%, 0.9%
Solution, nasal: 0.4%, 0.6%, 0.65%
Solution, nebulizing: 0.9%
Solution, ophthalmic: 2%, 5%
Tablet: 650 mg, 1 g
Tablet, enteric coated: 1 g
Tablet, slow release: 600 mg

Terbutaline (Brethine)
Aerosol, oral: 0.2 mg/actuation
Injection: 1 mg/mL
Tablet: 2.5 mg, 5 mg

Triprolidine/Pseudoephedrine (Actifed)

Capsule, extended release: Triprolidine 5 mg/Pseudoephedrine 120 mg
Syrup: Triprolidine 1.25 mg/Pseudoephedrine 30 mg per 10 mL
Tablet: Triprolidine 2.5 mg/Pseudoephedrine 60 mg

Theophylline (Elixophyllin)

Capsule, timed release (12 hour): 130 mg, 260 mg
Capsule, timed release (24 hour): 100 mg, 200 mg, 300 mg
Solution, oral: 80 mg/15 mL, 150 mg/15 mL
Tablet, immediate release [Slo-phyllin]: 100 mg, 125 mg, 200 mg, 250 mg, 300 mg
Tablet, timed release:
Theolair SR (8-12 hour): 100 mg, 200 mg, 250 mg, 300 mg, 500 mg
Theo-Dur (8-24 hour): 100 mg, 200 mg, 300 mg, 450 mg
Theophylline SR (12-24 hour): 100 mg, 200 mg, 300 mg
Uniphyl (24 hour): 400 mg

Triamcinolone (Aristocort, Kenacort, Azmacort, Nasacort)

Aerosol, oral, inhalation: 100 mcg/metered spray
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%
Spray, intranasal: 55 mcg/actuation [100 sprays/canister]

Zafirlukast (Accolate)

Tablet: 10 mg, 20 mg

Levalbuterol
(Xopenex®)

Classification: Respiratory Agents; Bronchodilators

Description: Levalbuterol inhalation solution is a sterile, clear, colorless, preservative-free solution of the (R)-enantiomer of (racemic) albuterol.

Vials must be stored in the protective foil pouch, protected from light and heat. Vials should be used within 2 weeks of removal from the pouch.

Pharmacology: Levalbuterol is an inhaled beta $_2$-adrenergic agonist. Activation of beta $_2$-adrenergic receptors on airway smooth muscle leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic AMP. This increase in cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation. Levalbuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Levalbuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway.

While it is recognized that beta $_2$-adrenergic receptors are the predominant receptors on bronchial smooth muscle, data indicate that there is a population of beta $_2$-receptors in the human heart that comprise between 10% and 50% of cardiac beta-adrenergic receptors. The precise function of these receptors has not been established. However, all beta-adrenergic agonist drugs can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or electrocardiographic changes.

Results from an *in vitro* study of binding to human beta-adrenergic receptors demonstrated that levalbuterol has approximately 2-fold greater binding affinity than racemic albuterol and approximately 100-fold greater binding affinity than (S)-albuterol.

Pharmacokinetics:

- Initial Response: 10 to 17 minutes
- Duration: After 4 weeks of treatment, the duration of bronchodilatory effect (greater than a 15% increase in forced expiratory volume in 1 second (FEV-1) from baseline) is approximately 5 hours after a levalbuterol dose of 0.63 mg and 6 hours after a 1.25-mg dose. The duration of effect may be as long as 8 hours in some patients.

Indications: Xopenex is indicated for the treatment or prevention of bronchospasm in adults, adolescents, and children 6 years of age and older with reversible obstructive airway disease.

Dosage: The recommended starting dose of Levalbuterol is 0.63 mg administered three times a day, every 6 to 8 hours, by nebulization. Patients with more severe asthma or patients who do not respond adequately benefit from a dosage of 1.25 mg three times a day.

Contraindications and Precautions:

- Pregnancy category C
- Like other inhaled beta-adrenergic agonists, Levalbuterol can produce paradoxical bronchospasm, which may be life threatening
- Like all other beta-adrenergic agonists, can produce a clinically significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, ECG changes, and/or symptoms.
- Levalbuterol, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, hypertension, and cardiac arrhythmias; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines.
- Large doses of intravenous racemic albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis. As with other beta-adrenergic agonist medications, levalbuterol may produce significant hypokalemia in some patients, which has the potential to produce adverse cardiovascular effects. The decrease is usually transient, not requiring supplementation.

Interactions:

- Other short-acting sympathomimetic aerosol bronchodilators or epinephrine should be used with caution with Levalbuterol to avoid deleterious cardiovascular effects.
- Beta-blockers: Beta-adrenergic receptor blocking agents not only block the pulmonary effect of beta-agonists such as Levalbuterol, but may also produce severe bronchospasm in asthmatic patients. If there is no acceptable alternative to the use of beta-adrenergic blocking agents in patients with asthma, cardio-selective beta-blockers could be considered.
- Monoamine Oxidase Inhibitors or Tricyclic Antidepressants: Administer with extreme caution to patients being treated with MAOIs or TCAs, or within 2 weeks of discontinuation of such agents, because the action of Levalbuterol on the vascular system may be potentiated.

Adverse Reactions:

Immediate hypersensitivity reactions have occurred, including angioedema, oropharyngeal edema, urticaria, rash and anaphylaxis

The most frequent (>10%) adverse reactions include: hyperglycemia, hypokalemia, rhinitis, and respiratory infections. Less frequent (2% to 10%) adverse reactions include nervousness, tremor, anxiety, dizziness, migraine, tachycardia, dyspepsia, pharyngitis, cough, and sinusitis.

Costs and Monitoring:
Monitoring should include pulmonary function tests and assessment of symptoms.
Consider periodic blood pressure and pulse rate during chronic therapy.

Product Identification:
Solution, inhalation: 0.31 mg/3mL, 0.63 mg/3 mL, 1.25 mg/3 mL

Efficacy:
- During chronic therapy, nebulized Levalbuterol 0.625 mg three times daily was as effective as nebulized racemic Albuterol 2.5 mg three times daily, and had a similar duration of action. Levalbuterol 1.25 mg three times daily was more effective.
- One small study in patients with chronic obstructive pulmonary disease (COPD) failed to show clear clinical advantages in using Levalbuterol over conventional nebulized bronchodilators.
- Adverse Effects
  a. In a small sample of intensive care (ICU) patients with and without baseline tachycardia, no statistically or clinically significant differences were observed between maximum heart rate increases induced by equipotent doses of Albuterol and Levalbuterol.
  b. With single or multiple dosing, adverse effects of 0.625-mg doses of Levalbuterol were fewer than observed with 2.5-mg doses of racemic Albuterol, including tachycardia, nervousness, tremor, and changes in glucose and potassium levels. Adverse effects were similar with Levalbuterol 1.25 mg and racemic Albuterol 2.5 mg

Conclusions:
Levalbuterol provides a reasonable treatment alternative for patients in whom Albuterol, or another beta-2 agonist, is effective but who experience significant adverse effects. However, many patients with asthma are maintained effectively with racemic Albuterol and switching to Levalbuterol may not be necessary, especially if the cost of the latter is significantly higher. Clinical data is not available on the use of Levalbuterol in severe asthma, but it has proven to be effective in moderate-to-severe asthma in children and adults.

Recommendation: Add to formulary

References:

1. Levalbuterol Monograph. Facts and Comparisons. Facts and Comparisons. St. Louis. 200.
2. Levalbuterol Monograph. MICROMEDEX(R) Healthcare Series Vol. 129 (2006)

Prepared by:
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12 October 2006

Budesonide
(Pulmicort® respules)

Classification: Respiratory agents; steroids

Description: Pulmicort respules is a sterile suspension for inhalation that contains micronized Budesonide.

Pharmacology: Budesonide is an anti-inflammatory corticosteroid that exhibits potent glucocorticoid activity and weak mineralocorticoid activity. The precise mechanism of corticosteroid actions on inflammation in asthma is not known. Corticosteroids have been shown to have a wide range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic and non-allergic-mediated inflammation. These anti-inflammatory actions of corticosteroids may contribute to their efficacy in asthma.

Pharmacokinetics:

Absorption:	Total bioavailability (i.e., lung + oral) was ≅ 6% of the labeled dose.
Distribution:	85-90% bound to plasma proteins.
Metabolism:	Rapidly and extensively metabolized via CYP-450 3A4 to inactive metabolites.
Excretion:	Excreted in urine (≅ 60%) and feces. No unchanged drug was detected in the urine.

Indications: Budesonide is used in maintenance treatment of asthma and for patients requiring oral corticosteroid therapy who may be able to reduce or eliminate their requirement for oral corticosteroids.

Dosage: The recommended starting dose and highest recommended dose is, based on prior asthma therapy

.

Previous Therapy	**Recommended Starting Dose** *(administered either QD or BID in divided doses)*	**Highest Recommended Dose**
Bronchodilators alone	0.5 mg total daily dose	0.5 mg total daily dose
Inhaled Corticosteroids	0.5 mg total daily dose	1 mg total daily dose
Oral Corticosteroids	1 mg total daily dose	1 mg total daily dose

Contraindications and Precautions:

- Pregnancy Category B
- Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals.
- **Do Not Use** for rapid relief of bronchospasm or other acute episodes of asthma.

- Because of the possibility of systemic absorption of inhaled corticosteroids, patients treated with these drugs should be observed carefully for any evidence of systemic corticosteroid effects.

Interactions:

Since inhaled Budesonide has little systemic absorption, interactions should not be clinically relevant. In clinical studies, concurrent administration of Budesonide and other drugs commonly used in the treatment of asthma has not resulted in an increased frequency of adverse events.

Adverse Reactions:

Reaction severity varies by dose and duration. The most common adverse reactions (>10%) include: respiratory infection, rhinitis. Less frequent (1% - 10%) reactions include: syncope, edema, hypertension, dysphoria, insomnia, nervousness, dry mouth, cough, pharyngitis, sinusitis and a flu-like syndrome.

Rare instances of glaucoma, increased intraocular pressure, and cataracts have been reported following the inhaled administration of corticosteroids.

Costs and Monitoring:

Each dose of Budesonide costs $ 4.13 or $ 4.59 depending on dose.

Product Identification:

Solution, inhalation: 0.25 mg/2 mL, 0.5 mg/2 mL

Efficacy:

Inhaled corticosteroids (i.e., Beclomethasone, Budesonide, Flunisolide, Fluticasone, and Triamcinolone) are effective for controlling asthma symptoms; pharmacokinetic properties, potency, and potential for hypothalamic-pituitary- adrenal (HPA) axis suppression differ between agents and product delivery systems. However, studies have shown that all the inhaled corticosteroids demonstrate similar efficacy in the treatment of asthma.

Conclusions:

Current treatment guidelines published by the National Asthma Education and Prevention Program (NAEPP), the National Institutes of Health (NIH), National, Heart, Lung, Blood Institute (NLBHI), as well as the Global Initiative for Asthma (GINA), Global Strategy for Asthma Management and Prevention, emphasize the use of inhaled corticosteroids (ICS) as first-line therapy for managing persistent asthma symptoms in both children and adults. Compared to as needed use of beta-agonists, ICS have been shown to increase forced expiratory volume in 1 second (FEV1), decrease airway hyperresponsiveness, symptom scores and frequencies, decrease beta-agonists use and need for oral corticosteroids, and reduce hospitalizations and urgent care visits.

Budesonide is the only inhaled steroid available for nebulization.

Recommendation: Add to formulary

References:

1. Budesonide Monograph. Facts and Comparisons. Facts and Comparisons. St. Louis. 2002.
2. Budesonide Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Asthma & Inhaled Corticosteroids (ICS)

Recommended Medications by Level of Severity

All Levels: In addition to regular daily controller therapy, rapid-acting inhaled beta2-agonist* should be taken as needed to relieve symptoms, but should not be taken more than 3 to 4 times a day. Patient education is essential at every level.		
Level of Severity:**	**Daily Controller Medications:**	**Other Treatment Options:*****
Step 1. Intermittent asthma****	None necessary	
Step 2. Mild Persistent Asthma	Low-dose ICS	♦ Sustained-release theophylline, OR ♦ Cromone, OR ♦ Leukotriene modifier
Step 3. Moderate Persistent Asthma	Low-to-medium ICS + long-acting inhaled beta2-agonist	♦ Medium-dose ICS + sustained-release theophylline, OR ♦ Medium-dose ICS + long-acting oral beta2-agonist, OR ♦ High-dose ICS, OR ♦ Medium-dose ICS + leukotriene modifier
Step 4. Severe Persistent Asthma	High-dose ICS + long-acting inhaled beta2-agonist, + ≥ 1 of the following, if needed: Sustained-release theophylline Leukotriene modifier Long-acting oral beta2-agonist Oral glucocorticosteroid Immunoglobulin E (IgE)*****	
All Levels: Once control of asthma is achieved and maintained for at least three months, a gradual reduction of the maintenance therapy should be tried in order to identify the minimum therapy required to maintain control.		

Other options for reliever medications are (in increasing order of cost) inhaled anticholinergic, short-acting oral beta2-agonist, and short-acting theophylline.

** See Figure 5-6, above, and Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document for information regarding classification of severity.

*** Other treatment options listed in order of increasing cost. Relative medication costs may vary from country to country.

**** Those with intermittent asthma but severe exacerbations should be treated as having moderate persistent asthma (**Evidence D**).

*****Current evidence supports use in adults and children aged 12 years and above only.

Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2005. 184 p. [1372 references]

Estimated Comparative Adult Daily Doses for Inhaled Corticosteroids			
Drug	Low Daily Dose	Medium Daily Dose	High Daily Dose
Beclomethasone-CFC	200 - 500	500 – 1,000	> 1,000
Beclomethasone-HFA	100 - 250	250 - 500	> 500
Budesonide –DPI	200 - 600	600 – 1,000	> 1,000
Budesonide-neb	500 – 1,000	1000 – 2,000	> 2,000
Flunisolide	500 – 1,000	1000 – 2,000	> 2,000
Fluticasone	100 - 250	250 - 500	> 500
Mometasone	200 - 400	400 - 800	> 800
Triamcinolone	400 – 1,000	1,000 - 2000	> 2,000

Inhaled Steroid Availability & Cost

	Trade Name	Strength	Doses	Cost	Cost/actuation
Beclomethasone	QVAR	40 mcg 80 mcg	100 100	$ 50.99 $ 64.25	$ 0.51 $ 0.64
Budesonide	Pulmicort respules*	0.25 mg/2 mL 0.5 mg/2 mL	30	$ 123.95 $ 137.79	$ 4.13 $ 4.59
	Pulmicort turbohaler	200 mcg	200	$ 136.12	$ 0.68
Flunisolide	Aerobid	250 mcg	100	$ 58.71	$ 0.59
Fluticasone	Flovent	44 mcg 110 mcg 220 mcg	120 120 120	$ 55.38 $ 74.14 $ 115.17	$ 0.46 $ 0.62 $ 0.96
	Flovent-HFA	44 mcg 110 mcg 220 mcg	120 120 120	$ 66.73 $ 89.34 $ 138.77	$ 0.56 $ 0.75 $ 1.16
Fluticasone/Salmeterol	Advair	100 mcg-50 mcg 250 mcg-50 mcg 500 mcg-50 mcg	60 60 60	$ 118.36 $ 149.84 $ 206.95	$ 1.97 $ 2.50 $ 3.45
	Advair-HFA	45 mcg-21 mcg 115 mcg-21 mcg 230 mcg-21 mcg	120 120 120	$ 117.16 $ 148.33 $ 204.86	$ 0.98 $ 1.24 $ 1.71
Mometasone	Asmanex	220 mcg	30 60 120	$ 79.66 $ 79.66 $ 123.74	$ 2.66 $ 1.33 $ 1.03
Triamcinolone	Azmacort	100 mcg	240	$ 103.09	$ 0.43

*Pulmicort respules is the only steroid available for nebulization.

Fluticasone/Salmeterol
(Advair®)

Classification: Respiratory agents; Miscellaneous

Description: Advair is a combination of Fluticasone propionate, a corticosteroid, and Salmeterol xinafoate, a beta $_2$-adrenergic bronchodilator.

ADVAIR DISKUS 100/50, ADVAIR DISKUS 250/50, and ADVAIR DISKUS 500/50 are specially designed plastic devices containing a double-foil blister strip of a powder formulation of Fluticasone and Salmeterol intended for oral inhalation only. Each blister on the double-foil strip within the device contains 100, 250, or 500 mcg of microfine Fluticasone and 72.5 mcg of microfine Salmeterol salt, equivalent to 50 mcg of Salmeterol base, in 12.5 mg of formulation containing lactose (which contains milk proteins). Each blister contains 1 complete dose of both medications. After a blister containing medication is opened by activating the device, the medication is dispersed into the airstream created by the patient inhaling through the mouthpiece.

DATA FROM A LARGE PLACEBO-CONTROLLED SAFETY STUDY THAT WAS STOPPED EARLY SUGGEST THAT SALMETEROL, A COMPONENT OF ADVAIR DISKUS, MAY BE ASSOCIATED WITH RARE SERIOUS ASTHMA EPISODES OR ASTHMA-RELATED DEATHS.

Pharmacology:

Fluticasone is a synthetic trifluorinated corticosteroid with potent anti-inflammatory activity. Corticosteroids have been shown to inhibit multiple cell types (e.g., mast cells, eosinophils, basophils, lymphocytes, macrophages, and neutrophils) and mediator production or secretion (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in the asthmatic response. These anti-inflammatory actions of corticosteroids contribute to their efficacy in asthma.

Salmeterol is a long-acting beta $_2$-adrenergic agonist. The pharmacologic effects of beta $_2$-adrenoceptor agonist drugs is attributable to relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

Pharmacokinetics:

Following administration of ADVAIR DISKUS to healthy adult subjects, peak plasma concentrations of Fluticasone were achieved in 1 to 2 hours and those of Salmeterol were achieved in about 5 minutes.

Fluticasone

- Absorption: The majority of the Fluticasone delivered to the lung is systemically absorbed. The systemic bioavailability of Fluticasone from the DISKUS device in healthy volunteers averages 18%.
- Metabolism: In the liver via CYP 450 3A4 to an inactive metabolite
- Elimination: Excreted in the feces as parent drug and metabolites

Salmeterol

- Absorption: Because of the small therapeutic dose, systemic levels of Salmeterol are low or undetectable after inhalation of recommended doses
- Metabolism: Extensively metabolized by hydroxylation
- Elimination: Excreted predominantly in the feces

Indications: ADVAIR is indicated for the long-term, twice-daily, maintenance treatment of asthma and airflow obstruction in patients with COPD associated with chronic bronchitis.

Dosage: ADVAIR DISKUS is administered twice daily.

ADVAIR DISKUS should be administered by the orally inhaled route only. After inhalation, the patient should rinse the mouth with water without swallowing.

Contraindications and Precautions:

- Contraindicated in the primary treatment of status asthmaticus or other acute episodes of asthma or COPD where intensive measures are required
- As with other inhaled asthma and COPD medications, ADVAIR DISKUS can produce paradoxical bronchospasm, which may be life threatening
- Immediate hypersensitivity reactions may occur after administration, as demonstrated by cases of urticaria, angioedema, rash, and bronchospasm.
- ADVAIR DISKUS, like all products containing sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.
- Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals.

Interactions: In the repeat- and single-dose studies, there was no evidence of significant drug interaction in systemic exposure between Fluticasone propionate and Salmeterol when given as ADVAIR.

Adverse Reactions:

The most frequent adverse reactions include: headache, respiratory tract infection, and pharyngitis. Less frequent adverse reactions include: dizziness, nausea, oral candidiasis, cough, hoarseness or dysphonia.

Costs and Monitoring:

Costs of the inhalers depend on the strengths but range from $ 118.36 to $ 206.95 per inhaler.

Product Identification:

Aerosol, inhalation: 100 mg Fluticasone/50 mg Salmeterol, 250 mg Fluticasone /50 mg Salmeterol, 500 mg Fluticasone /50 mg Salmeterol

Conclusions: Both the active agents in this combination product have demonstrated efficacy. Utilizing a combination product has been shown to increase compliance in some patients.

Recommendation: Add to formulary

Prepared by:
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12 October 2006

Memorandum

To: Executive Formulary Committee

From: Sharon M. Tramonte, Pharm.D.

Through: Ann L. Richards, Pharm.D.

Subject: Class Review - Ophthalmics

Date: 10 October 2006

Upon review, the following is a synopsis of recommended changes to the DSHS/DADS Formulary.

Recommended for addition:

- Ophthalmic irrigating solution (BSS, Eye Stream, AK-Rinse)
- Prednisolone ophthalmic

Other Recommendations:

- Add Cromolyn to Decongestant/Antiallergy section

OPHTHALMICS

Agents for Glaucoma

Betaxolol (Betoptic S)	$$$$
Bimatoprost (Lumigan)	$$$$$$$
Brimonidine (Alphagan)	$$$$$$$
Latanoprost (Xalatan)	$$$$$$$
Pilocarpine (Isopto Carpine)	$ - $$$$$$$
Timolol (Timoptic)	$$ - $$$$$$$
Timolol/Dorzolamide (Cosopt)	$$$$$$$
Travoprost (Travatan)	$$$$$$$

Antibiotics

Bacitracin (Baciguent)	$
Ciprofloxacin (Ciloxan)	$$$$$ - $$$$$$$
Erythromycin	$$
Gentamicin (Garamycin)	$$
Polymyxin B/Bacitracin (Polysporin)	$$$$$$
Polymyxin B/Trimethoprim (Polytrim)	$$$
Sulfacetamide Sodium (Sulamyd)	$ - $$$$$$$
Tobramycin (Tobrex)	$$ - $$$$$$$

Mydriatics	
Atropine Sulfate (Isopto Atropine)	$$
Homatropine (Isopto Homatropine)	$$ - $$$$
Phenylephrine (Neo-Synephrine)	$$ - $$$$
Scopolamine (Isopto Hyoscine)	$$ - $$$
Tropicamide (Mydriacyl)	$$ - $$$$
Lubricants	
Ophthalmic Lubricant (HypoTears, HypoTears PF) [preservative-free, lanolin-free]	$ - $$$$
Decongestant/Antiallergy	
Naphazoline (Naphcon, AK-Con)	$$
Olopatadine (Patanol)	$$$$$$
Tetrahydrozoline (Visine Allergy Relief, Visine Moisturizing)	$$$
Miscellaneous Ophthalmics	
Dexamethasone (Decadron) - **RESERVE USE**	$$
Fluorescein Sodium	$ - $$$
Proparacaine (Alcaine)	$$
Sodium Chloride	$$ - $$$$
Tobramycin/Dexamethasone (TobraDex)- **RESERVE USE**	$$$$$ - $$$$$$

Atropine Sulfate (Isopto Atropine
Ointment, ophthalmic: 1%
Solution, ophthalmic: 1%

Bacitracin (Baciguent)
Injection: 50,000 units
Ointment, ophthalmic: 500 units/g
Ointment, topical: 500 units/g

Bacitracin/Polymyxin B (Polysporin)
Ointment, ophthalmic: Bacitracin 500 units/Polymyxin B 10,000 units/g
Ointment, topical: Bacitracin 500 units/Polymyxin B 10,000 units/g
Powder, topical: Bacitracin 500 units/Polymyxin B 10,000 units/g

Betaxolol (Betoptic S)
Solution, ophthalmic: 0.5%
Suspension, ophthalmic: 0.25%

Bimatoprost (Lumigan)
Solution, ophthalmic: 0.03%

Brimonidine (Alphagan)
Solution, ophthalmic: 0.15%, 0.2%

Ciprofloxacin (Cipro, Ciloxan)
Injection: 200 mg, 400 mg
Solution, ophthalmic: 0.3%
Suspension, oral: 5 gm/100 mL, 10 gm/100 mL
Tablet: 100 mg, 250 mg, 500 mg, 750 mg

Cromolyn (Intal)
Inhalation, oral: 800 mcg/spray
Solution, nebulizing: 10 mg/mL
Solution, nasal: 40 mg/mL
Solution, ophthalmic: 4%

Dexamethasone (Decadron)
Injection, as sodium phosphate: 4 mg/mL, 10 mg/mL, 20 mg/mL, 24 mg/mL
Solution, oral: 0.5 mg/5 mL
Suspension, ophthalmic: 0.1% with methylcellulose 0.5% **- RESERVE USE**
Tablet: 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg

Erythromycin (Erythrocin)
Erythromycin base(Eryc, E-Mycin, Ery-Tab, E-Base, PCE):
Capsule, delayed release: 250 mg
Tablet, enteric coated: 250 mg, 333 mg, 500 mg
Tablet, film coated: 250 mg, 500 mg
Tablet, polymer coated particles: 333 mg, 500 mg
Erythromycin Ethylsuccinate (EryPed, E.E.S.):
Granules/Powder for oral suspension: 200 mg/5 mL, 400 mg/5 mL
Suspension, oral: 200 mg/5 mL, 400 mg/5 mL
Suspension, oral (drops): 100 mg/2.5 mL
Tablet: 400 mg
Tablet, chewable: 200 mg
Ointment, ophthalmic: 5%

Fluorescein Sodium
Injection: 10%
Strip, ophthalmic: 1 mg

Gentamicin (Garamycin)
Cream, topical: 0.1%
Infusion, premixed in D5W: 60 mg, 80 mg, 100 mg
Infusion, premixed in NS: 40 mg, 60 mg, 80 gm, 90 mg, 100 mg, 120 mg
Injection: 10 mg/mL, 40 mg/mL
Injection, intrathecal (preservative free): 2 mg/mL
Ointment, ophthalmic: 0.3% [3 mg/g]
Ointment, topical: 0.1%
Solution, ophthalmic: 0.3% [3 mg/mL]

Homatropine (Isopto Homatropine)
Solution, ophthalmic: 2%, 5%

Latanoprost (Xalatan)
Solution, ophthalmic: 0.005%

Naphazoline (Naphcon, AK-Con)
Solution, ophthalmic: 0.012%, 0.1%

Olopatadine (Patanol)
Solution, ophthalmic: 0.1%

Ophthalmic Lubricant (HypoTears, HypoTears PF) [preservative-free, lanolin-free]
Ointment, ophthalmic
Solution, ophthalmic

Phenylephrine (Neo-Synephrine)
Solution, nasal, drops: 0.125%, 0.25%, 0.5%
Solution, nasal, spray: 0.25%, 0.5%, 1%
Solution, ophthalmic: 2.5%, 10%

Pilocarpine (Isopto Carpine)
Solution, ophthalmic, as hydrochloride: 1%, 2%, 4%

Polymyxin B/Bacitracin (Polysporin)
Ointment, ophthalmic: Polymyxin B 10,000 units/Bacitracin 500 units
Ointment, topical: Polymyxin B 10,000 units/Bacitracin 500 units
Powder, topical: Polymyxin B 10,000 units/Bacitracin 500 units

Polymyxin B/Trimethoprim (Polytrim)
Solution, ophthalmic: Polymyxin B 10,000 units/Trimethoprim 1 mg/mL

Proparacaine (Alcaine)
Solution, ophthalmic: 0.5%

Scopolamine (Isopto Hyoscine)
Solution, ophthalmic: 0.25%

Sodium Chloride
Drops, nasal: 0.9%
Infusion: 0.2%, 0.45%, 0.9%, 3%, 5%, 20%, 23.4%
Injection, bacteriostatic: 0.9%
Injection, for admixtures: 50 mEq, 100 mEq, 635 mEq
Ointment, ophthalmic: 5%
Solution, irrigation: 0.45%, 0.9%
Solution, nasal: 0.4%, 0.6%, 0.65%
Solution, nebulizing: 0.9%
Solution, ophthalmic: 2%, 5%
Tablet: 650 mg, 1 g
Tablet, enteric coated: 1 g
Tablet, slow release: 600 mg

Sulfacetamide Sodium (Sulamyd, Sebizon)
Lotion: 10%
Ointment, ophthalmic: 10%
Solution, ophthalmic: 10%

Tetrahydrozoline (Visine Allergy Relief, Visine Moisturizing)
Solution, ophthalmic: 0.05%

Timolol (Timoptic)
Gel, ophthalmic: 0.25%, 0.5%
Solution, as maleate, ophthalmic: 0.25%, 0.5%
Solution, as maleate, ophthalmic, preservative free, single use: 0.25%, 0.5%
Tablet: 5 mg, 10 mg, 20 mg

Timolol/Dorzolamide (Cosopt)
Solution, ophthalmic: Timolol 0.5%/Dorzolamide 2%

Tobramycin (Nebcin, Tobrex)
Injection: 10 mg/mL, 40 mg/mL
Ointment, ophthalmic: 0.3%
Powder for injection: 40 mg/mL
Solution, ophthalmic: 0.3%

Tobramycin/Dexamethasone (TobraDex) [contains Benzalkonium] **- RESERVE USE**
Ointment, ophthalmic: Tobramycin 0.3%/Dexamethasone 0.1%
Suspension, ophthalmic: Tobramycin 0.3%/ Dexamethasone 0.1%

Travoprost (Travatan)
Solution, ophthalmic: 0.004%

Tropicamide (Mydriacyl)
Solution, ophthalmic: 0.5%, 1%

Ophthalmic irrigating solution
(BSS, Eye Stream, AK-Rinse)

Classification: Ophthalmics; Miscellaneous ophthalmics

Description: Ophthalmic irrigating solutions are sterile isotonic solutions used to irrigate the eye

Pharmacokinetics: No systemic absorption

Indications: Use to irrigate the eye

Dosage: Irrigate the eye as needed

Contraindications and Precautions:
- To avoid contamination, do not touch the tip of the container to any surface
- Replace cap after using
- Do not use if the solution becomes cloudy or changes color

Interactions: None known

Adverse Reactions: None known

Costs and Monitoring: Costs range from $1.11 to $6.93 depending on the product purchased.

Product Identification:
Solution, ophthalmic

Conclusions: There are often instances when an ophthalmic irrigation solution is needed to wash debris from the eye or to irrigate the eye secondary to irritation.

Recommendation: Add to formulary

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9 October 2006

Prednisolone ophthalmic
(Pred-Forte, AK-Pred)

Classification: Ophthalmics; miscellaneous ophthalmics

Description: Prednisolone ophthalmic is a sterile topical anti-inflammatory agent for ophthalmic use.

Pharmacology: Corticosteroids diffuse across cell membranes and complex with specific cytoplasmic receptors. These complexes then enter the cell nucleus, bind to DNA, and stimulate transcription of mRNA and subsequent protein synthesis of enzymes ultimately responsible for anti-inflammatory effects of topical application of corticosteroids to the eye. In high concentrations, which may be achieved after topical application, corticosteroids may exert direct membrane effects. Corticosteroids decrease cellular and fibrinous exudation and tissue infiltration, inhibit fibroblastic and collagen-forming activity, retard epithelial regeneration, diminish post-inflammatory neovascularization, and reduce toward normal levels the excessive permeability of inflamed capillaries.

Pharmacokinetics: Absorbed into aqueous humor, cornea, iris, choroid, ciliary body, and retina. Systemic absorption occurs, but may be significant only at higher dosages or in extended pediatric therapy.

Indications: Prednisolone ophthalmic is indicated for the treatment of steroid-responsive inflammation of the conjunctiva, cornea and anterior segment of the globe.

Dosage: Instill one to two drops into the conjunctival sac two to four times daily.

- Shaking suspensions vigorously before applying
- Increasing the frequency of administration is usually as effective as, or more effective than, using higher concentrations of the medication.
- The duration of treatment may vary from a few days to several weeks or months in some cases, depending on the condition being treated. Daily or alternate-day therapy may be indicated for extended periods in certain situations, such as following penetrating keratoplasty

Contraindications and Precautions:

- Pregnancy category C
- Contraindicated in most infectious diseases of the cornea and conjunctiva
- Contraindicated in individuals with known or suspected hypersensitivity to corticosteroids
- Prolonged use may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in cataract formation
- Prolonged use may suppress the host immune response and thus increase the hazard of secondary ocular infections
- Long-term use of topical corticosteroids has been known to cause corneal and scleral thinning. Use of topical corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation
- The risk of infection is increased in patients wearing contact lens

Interactions:

- Antiglaucoma agents (chronic or intensive use of ophthalmic corticosteroids may increase intraocular pressure and decrease the efficacy of antiglaucoma agents)
- Anticholinergics, especially atropine and related compounds (risk of intraocular hypertension may be increased with prolonged corticosteroid therapy; may be more likely to occur during use of cycloplegic/mydriatic agents in patients predisposed to acute angle closure)

Adverse Reactions:

- Adverse reactions include, in decreasing order of frequency, elevation of intraocular pressure (IOP) with possible development of glaucoma and infrequent optic nerve damage, posterior subcapsular cataract formation, and delayed wound healing.
- Although systemic effects are extremely uncommon, there have been rare occurrences of systemic hypercorticoidism after use of topical steroids.
- Corticosteroid-containing preparations have also been reported to cause acute anterior uveitis and perforation of the globe. Keratitis, conjunctivitis, corneal ulcers, mydriasis, conjunctival hyperemia, loss of accommodation and ptosis have occasionally been reported following local use of corticosteroids.
- The development of secondary ocular infection (bacterial, fungal, and viral) has occurred. Fungal and viral infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroid. The possibility of fungal invasion should be considered in any persistent corneal ulceration where steroid treatment has been used.
- Transient burning and stinging upon instillation and other minor symptoms of ocular irritation have been reported.

Costs and Monitoring:

Ophthalmologic examinations, especially tonometry and slit-lamp examination (initial ophthalmologic examinations should be performed 2 to 3 weeks following onset of chronic therapy; subsequent examinations are performed at intervals as determined by patient status or risk factors.

Individual bottles range in price from $ 3.49 to $ 38.42 depending on size, strength and manufacturer.

Product Identification:

Solution, ophthalmic, as sodium phosphate: 1%
Suspension, ophthalmic, as acetate: 0.12%, 1%

Recommendation: Add to formulary with reserve criteria of “Consultation with an Ophthalmologist prior to initiation”.

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