

**DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
February 16, 2007**

The Executive Formulary Committee convened on Friday, February 16, 2007 in Conference Room 164 - CO Building 2. The meeting was called to order by Dr. Ward, Interim Chair at 9:35 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.	Absent
Lisa Mican, Pharm.D.	√	Nina Muse, M.D.	√
Connie Millhollon, RN,	√	Vacant Medical Director Position	
Victoria B. Morgan, M.D.	√	Vacant Center Position	
Ann L. Richards, Pharm.D.	√	Vacant Center Position	
Bernardo C. Tarin-Godoy, M.D.	Absent	Vacant Center Position	
Robert L. Ward, D.O.	√	Vacant State School Position	
Kenny Dudley	Absent	Vacant DADS Nursing Coordinator	

Guest Present: Sharon Tramonte, Pharm.D., San Antonio State School; Richard Perry, Pharm.D., Resident; Angela Hughes, Pharm.D., Resident; Joseph Jessup, Pharmacy student; Dana Leung, Pharmacy student

Approval of Minutes of October 13, 2006

On a motion of Dr. Heidel, seconded by Ms. Millhollon, the minutes of the October 13th meeting were approved as previously distributed.

Adverse Drug Reaction Reports

The Executive Formulary Committee received numerous adverse drug reaction reports. In the first case, a 46 year-old male was admitted for the treatment of schizoaffective disorder, bipolar type. The patient was treated with divalproex (Depakote®) ER, fluticasone/salmeterol (Advair®) and guaifenesin (Humibid LA) when clozapine (Clozaril®) was started on 8/9/06. The clozapine dose was slowly titrated to 300 mg/day, eleven days after initiation. On 8/22/06, benzotropine (Cogentin®) 2 mg/day was added due to drooling. On 9/1/06, the patient complained of severe abdominal discomfort and vomiting. After an assessment, the patient was transferred to a medical hospital for treatment of severe impaction. The patient was treated at the local facility and returned to the State Hospital on polyethylene glycol (MiraLax®), bisacodyl (Dulcolax®) prn, pantoprazole (Protonix®) and levofloxacin (Levaquin®). Benzotropine was discontinued and clozapine was continued. The patient developed a

subsequent episode of impaction and was transferred to a medical facility. Upon return to the State Hospital, the patient was on lactulose (Chronulac®), polyethylene glycol, docusate sodium and milk of magnesia prn. The clozapine was discontinued and olanzapine (Zyprexa®) was started. Upon discharge the patient was only receiving olanzapine, divalproex ER and docusate sodium.

In the next report, a 41 year-old female was admitted for the treatment of schizoaffective disorder, bipolar type. The patient had been on the same HIV regimen for over two years. This included fosamprenavir (Lexiva®), tenofovir/emtricitabine (Truvada®) and lamivudine (Epivir®). Since 2005, the patient has been on lithium, pantoprazole, omega 3-fatty acids and docusate calcium at steady doses. Paroxetine (Paxil®) was started on 3/23/06, clozapine was started on 8/15/06, clonidine (Catapres®) was started 8/31/06 and lactulose was started on 9/12/06. The clozapine was titrated to 150 mg/day as previous higher doses of clozapine lead to severe constipation and stomach aches requiring the use of laxatives and enemas on several occasions. These symptoms progressed to include difficulty swallowing, vomiting (once) and increased AST and ALT on 10/6/06. The HIV agents were discontinued on 10/13/06 and clozapine was reduced to 100 mg/day and subsequently discontinued. The liver function tests improved after the discontinuation of the HIV medications and clozapine.

An 18 year-old female was admitted for the treatment of schizoaffective disorder. The patient was prescribed oxcarbazepine (Trileptal®), pantoprazole (Protonix®), escitalopram (Lexapro®) and olanzapine (Zyprexa®) during admission in late August. The olanzapine was increased to 30 mg/day on 9/5/06. Lithium was started on 9/25/06 and was increased to 1200 mg/day on 10/2/06. Clozapine was initiated at 12.5 mg/day on 10/9/06. The next day, the dose was increased to 25 mg/day and at the same time the olanzapine dose was decreased to 20 mg/day. Early the next morning (12:52 a.m.) the patient had a grand mal seizure lasting approximately 3.5 minutes followed by an 8 minute postictal state. Clozapine was discontinued and the oxcarbazepine dose was increased. No additional seizures occurred between the time of this incident and the time of submitting the report (about 1 month).

A 37 year-old male was admitted for the treatment of schizoaffective disorder, bipolar type. On admission, it was noted that the patient had been noncompliant with his outpatient medication for approximately 4 days. On admission, the patient was started on the previously prescribed dose of clozapine (Clozaril®) 150 mg at bedtime. In addition, risperidone (Risperdal®) M-tabs 2 mg at bedtime, lithium 1200 mg at bedtime and pantoprazole (Protonix®) 40 mg daily was prescribed. The next day, it was noted that the patient had a tonic-clonic seizure and projectile vomiting. The patient was transferred to a medical facility for four days. The clozapine was discontinued without subsequent seizure event. The patient had no prior history of seizures.

A 55 year-old male was admitted to the State Hospital for the treatment of his first psychotic break. Prior to admission, the patient was taking a product called Relacore™ for several months and he was on no prescription medication at the time of admission. He had no known drug allergies and no known medical conditions. Few weeks before admission, he began experiencing insomnia, delusions, paranoia and decreased appetite. On admission, he had pressured speech, felt paranoid that people are talking in code and untrusting of the admitting physician. The Relacore™ was discontinued and ziprasidone (Geodon®) was initiated.

A 45 year-old male was admitted for the treatment of schizoaffective disorder, bipolar type. He was continued on the medication from his previous hospital stay. These include ziprasidone (Geodon®) 240 mg/day, olanzapine (Zyprexa®) 30 mg/day, lithium controlled release 1350 mg/day, ritonavir (Norvir®) 200 mg/day, saquinavir (Invirase®) 2000 mg/day, stavudine (Zerit®) 80 mg/day, and lamivudine (Epivir®) 300 mg/day. Olanzapine and lorazepam (Ativan®) prn were added later. An EKG completed about a week after admission showed a QTc interval of 490 ms with a left atrial abnormality. Previous EKGs obtained 28 months and 19 months before this one, showed QTc intervals of 408 ms and 428 ms, respectively.

A 52 year-old male was admitted for the treatment of schizoaffective disorder, bipolar type. On admission, the patient was treated with quetiapine (Seroquel®) 900 mg/day, pantoprazole (Protonix®) 40 mg/day and divalproex (Depakote®) ER 1000 mg/day. Three days after admission, the divalproex ER was increased to 2000 mg/day. Ten days after admission, clonazepam (Klonopin®) 1.5 mg/day was added. Fourteen days after admission, oxcarbazepine (Trileptal®) 600 mg/day was added. Around this time, the patient began complaining of sedation and deteriorating eye sight. In addition, the patient was poorly oriented to time. The symptoms progressed and the patient became obtunded and was unresponsive. The patient was transferred to a medical facility where he was

treated for hyperammonemia (ammonia level 440 micromole/L). The patient was treated with IV normal saline and oral lactulose. The divalproex was discontinued.

A 52 year-old male on risperidone (Risperdal®) Consta and oral risperidone reported priapism to medical staff that was ongoing for three days. Patient was sent to an emergency room at a local hospital where the urologist inserted a shunt and the penis went flaccid. The patient returned to the State Hospital and began having problems the next day. The patient returned to the medical facility where he underwent saphenous cavernosal shunt. The physician indicated that the patient probably has permanent impairment since the priapism was reported on the third day.

Psychotropic Audit Criteria

Based on the recent changes, the Psychotropic Audit Criteria are being finalized. Once completed these will be distributed to the field and placed on the website.

Psychotropic Dosing in Children and Adolescents

Dr. Mican and Dr. Perry presented the information on psychotropic dosing in children and adolescents. Dr. Mican reviewed the updated “Psychotropic Medication Utilization Parameters for Foster Children.” Previously the Committee recommended that the doses listed in this document could serve as an excellent resource for determining the recommended children and adolescent doses that are listed in the Formulary.

For antidepressants, it was noted that the adolescent maximum dose for citalopram (Celexa®) and paroxetine (Paxil®) were changed from the previous recommendation. Dr. Perry reviewed dosing for duloxetine (Cymbalta®), mirtazapine (Remeron®) and trazodone (Desyrel®) as these were not listed in the Foster Children guidelines. The following are the recommendations based on this review:

- For duloxetine, there is limited data available for the use of duloxetine in children and adolescents, therefore no maximum dosage was recommended.
- For mirtazapine, it was recommended that the maximum dose per day for an adolescent is 45 mg/day. For children, there is insufficient data to recommend a maximum dose.
- For trazodone, the maximum dose for adolescents is 200 mg per day. For children the maximum dose is 100 mg/day for tics, Tourette’s and aggressive behavior. There is no data to support the use of trazodone in children for insomnia. It was recommended that trazodone be listed in both the antidepressant and hypnotic/sedative sections.

For antipsychotics, the maximum doses for adolescents changed for haloperidol (Haldol®) and perphenazine (Trilafon®). For children, the doses changed for haloperidol and quetiapine (Seroquel®). “No data” was added for perphenazine in children. Dr. Perry reviewed the dosing for quetiapine and ziprasidone (Geodon®). The following are recommendations based on this review.

- Since the original document was published, the maximum dose of quetiapine was changed to 300 mg. The literature does support a maximum dose of 350 mg/day. It was recommended to keep the dose of quetiapine in children to 300 mg/day.
- The Foster Care guidelines show that “no data” is available to determine the maximum dose in children for ziprasidone. The literature shows case reports for the use of ziprasidone in children with bipolar disorder and autism. A mixed age study of the efficacy and tolerability of ziprasidone in children and adolescents with Tourette’s Syndrome and chronic tic disorders has been reported in the literature. In addition, a single dose ziprasidone was assessed in children and adolescents with a diagnosis of Tourette’s Syndrome or chronic tic disorder to determine the pharmacokinetic, safety and tolerability data. It was recommended that the maximum dose of ziprasidone in children be 80 mg/day.

For ADHD medications the maximum doses for dexamethylphenidate (Focalin®) and the methylphenidate (Daytrana®) patch were added for both the children and adolescents. For adolescents, the doses for bupropion (Wellbutrin®) and methylphenidate (Ritalin®) were changed from the previous guidelines. Dr. Perry reviewed the dosing of methylphenidate OROS (Concerta®). Based on this review, the following recommendations were made:

- For children, it was recommended that the dose of methylphenidate OROS be 2 mg/kg/day, not to exceed 54 mg/day.
- For adolescents, it was recommended that the dose of methylphenidate OROS be 2 mg/kg/day, not to exceed 72 mg/day.

On a motion of Dr. Morgan, seconded to Dr. Heidel it was recommended that in the Drug Formulary that the maximum dose section be changed from “Stimulants” to “ADHD Medications.”

For mood stabilizers, the maximum dose for lamotrigine (Lamictal®) was changed from the original guidelines. Dr. Perry reviewed the dosing of topiramate (Topamax®) and oxcarbazepine (Trileptal®). From this review, the following recommendations were made:

- For topiramate there is insufficient data to support its efficacy as a mood stabilizer in children and adolescents. For seizure disorder, the maximum dose is 9 mg/kg/day for patients age 2 – 16 years and 400 mg/day for those 17 years old.
- For oxcarbazepine there is insufficient data regarding efficacy and lack of data regarding how doses were determined in the clinical studies, no maximum dose can be recommended. For seizure disorders, in patients age 2-16 years, oxcarbazepine’s maximum recommended dose is 900 mg/day for patients weighing 20 to 29 kg, 1200 mg/day for patients weighing 29.1 to 39 kg and 1800 mg/day for patients weighing over 39 kg. For 17 year old patients, the maximum dose is 2400 mg/day.

Since propranolol (Inderal®) is frequently used in the treatment of psychiatric disorder, this agent was also reviewed. It was recommended that the dose of propranolol be listed under the Miscellaneous Table. It appears that propranolol is effective in the treatment of aggression, rage outbursts and akathisia. Daily dosages appear to differ greatly for each individual patient. Bradycardia, hypotension, somnolence and lethargy appear to be the most common dose-limiting side effects. When using propranolol, it is important to titrate the dose slowly and monitor for side effects. From the published studies, it appears that propranolol is useful as adjunctive therapy to control aggression and rage outbursts. In the treatment of hypertension, the maximum recommended dose of propranolol is 16 mg/kg/day. Based on the hypertension treatment dose, it was recommended that the maximum dose for propranolol for children and adolescents be 16 mg/kg/day.

For those items that there is insufficient data, it was recommended that a footnote be added that states that there is insufficient data to suggest support regarding its efficacy or to provide maximum dose guidelines in this patient group.

The Committee discussed whether or not there are other drugs being used in the adolescent and children population at the State Facilities. If possible, this information will be obtained from the facilities that have this patient population.

Psychotropic Consent List

Dr. Richards presented an updated psychotropic consent list. The new list contains paliperidone (Invega®) under antipsychotics and ramelteon (Rozerem®) under anxiolytic/sedative/hypnotics. Ramelteon is a non-formulary drug

and the status of paliperidone will be determined later in the meeting. On a motion of Dr. Morgan, seconded by Dr. Hood, the recommendation to add these products to the consent list was approved.

FDA Alerts

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

For olanzapine (Zyprexa®), the precautions have been changed to include transaminases elevations. Rare post-marketing reports of hepatitis have been received. Very rare cases of cholestatic or mixed liver injury have also been reported in the post-marketing period. In addition, adverse reactions have changed to include jaundice under post-introduction reports.

For nateglinide (Starlix®), an additional post-marketing experience for adverse reactions was made. Cases of jaundice, cholestatic hepatitis and elevated liver enzymes have been reported.

For oseltamivir (Tamiflu®), Roche distributed a correction to a Dear Healthcare notification issued November 13, 2006. The original letter referenced changes to the Precautions Section of prescribing information for oseltamivir about post marketing reports of self-injury and delirium with the use of oseltamivir in patients with influenza. The prescribing information that accompanied the letter contained an incorrect dose chart for the Standard Dosage of oseltamivir oral suspension for prophylaxis of influenza in pediatric patients. The chart incorrectly specified twice daily instead of once daily dosing under "Recommended Dose" for 10 days. Healthcare professional should discard the incorrect version of the package insert included in the November 13, 2006 mailing and refer to the new dosing chart included in the December 26, 2006 letter.

Medicare D

Dr. Richards reported that the third party claims administrator is functioning and provides the facilities with information about rejects.

Quarterly Non-Formulary Drug Justification Report

The Quarterly Non-Formulary drug list was reviewed by facility and generic name. Facilities are still not reporting all the non-formulary drug requests. It was requested that a follow up contact be made for those facilities that are not reporting on a consistent basis.

New Drug Applications

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

trospium (Sanctura®) - discussed by Dr. Hughes

Trospium is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency. It is a quaternary ammonium compound that has antispasmodic and antimuscarinic effects, but minimally crosses the blood-brain barrier. Trospium has low lipophilicity and is positively charged (polar). It antagonizes the effects of acetylcholine on muscarinic receptors in cholinergically innervated organs. Its parasympathetic action reduces the tonus of smooth muscle in the bladder. Trospium increases maximum cystometric bladder capacity and volume at first detrusor contraction. The half-life of trospium is 20 hours but it is normally dosed twice daily due to nocturnal enuresis. The recommended dose is 20 mg twice daily. Trospium should be administered at least one hour before meals or given on an empty stomach.

Following discussion, on motion of Dr. Heidel, seconded by Dr. Mican, the request to add trospium

(Sanctura®) to the formulary was approved. The Formulary CheckList was completed.

paliperidone extended release (Invega®) - discussed by Joseph Jessup and Dana Leung (Pharm.D. students)

Paliperidone is the major active metabolite of risperidone (Risperdal®). Paliperidone contains the racemic mixture of paliperidone. Paliperidone extended release exerts its activity by antagonizing central dopamine (D₂) and serotonin (5HT_{2a}) receptors. It also blocks α_1 and α_2 adrenergic receptors and H₁ receptors. Paliperidone uses the OROS osmotic drug-release technology that delivers the drug at a controlled rate. The drug delivery systems allows for a gradual rise in peak plasma concentration. Peak plasma concentration is reached after 24 hours of dosing. The recommended starting dose is 6 mg day given in the morning. Doses greater than 6 mg/day have not shown any additional benefit. Dose increments should be done in 3 mg increments with the maximum daily dose of 12 mg/day. For patients with creatinine clearance 50 to 80 ml/min, the maximum dose is 6 mg/day. For patients with creatinine clearance 10 to 50 ml/min, the maximum dose is 3 mg/day. Paliperidone should be swallowed whole and it can be taken without regard to food.

Following discussion, on motion of Dr. Hood, seconded by Dr. Heidel, the request to add paliperidone (Invega®) to the formulary was approved. The Formulary CheckList was completed. For the audit criteria, the maximum dose for paliperidone was set at 12 mg/day. In addition, the following will be added as a monitoring parameter for paliperidone: "Serum creatinine baseline and as clinically indicated.

flurazepam (Dalmane®) - discussed by Dr. Mican

Flurazepam is a long acting benzodiazepine that is thought to exert its action by binding to the GABA-A Receptor-Benzodiazepine Receptor-Chloride Ion Channel Complex, which increases the affinity of the receptor for GABA. Flurazepam has not been shown to be superior to other benzodiazepines currently available for the treatment of insomnia. Other long-acting benzodiazepines are already available on the Formulary including chlordiazepoxide (Librium®), clonazepam (Klonopin®), clorazepate (Tranxene®) and diazepam (Valium®). Concerns with using flurazepam include the risk of accumulation and toxicity in patients with hepatic or renal impairment, the elderly, and those receiving concomitant medications that inhibit CYP 3A4.

Based on a lack of a motion to add flurazepam to the Formulary, flurazepam was not added to the Formulary.

Proposed Drug Deletion List -

**Respiratory Agents
Ophthalmic Agents**

The Committee did not receive any comments from the field about the proposed deletions for the respiratory agents and ophthalmic agents. On a motion of Dr. Heidel, seconded by Ms. Millhollon, the motion to delete these agents was approved.

Pharmaceutical Waste

Dr. Tramonte found a pharmaceutical waste containers on the internet. This particular product is called PHARMASAFETY™ Sharps Disposal Container. In the product information it is noted that the waste containers are developed exclusively to meet state regulations for pharmaceutical waste. White with blue lids, they are easily distinguished from other disposal containers. Each has a leak-resistant gasket and absorbent pad to help contain liquid contents. Floor carts and locking wall-mounting brackets offer point-of-use placement and enhance security, stability and mobility. The price of this product was not available. Dr. Heidel noted that HealthCare Logistics has a similar product. This issue will continue to be researched.

Drug Formulary Sectional Review-

**Otics Agents
Nasal, Mouth & Throat Agents
Irrigation Solutions**

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

Dr. Tramonte made the following recommendations:

- Add hydrogen peroxide to the Otics section (currently listed only in miscellaneous dermatologicals)
- Remove Acetasol® and VoSol® as trade names for acetic acid
- Change acetic acid/hydrocortisone/propylene glycol/sodium acetate/benzethonium to acetic acid/hydrocortisone
- Remove volume from mineral oil
- Remove strengths from ingredients in neomycin/polymyxin B/hydrocortisone

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

Dr. Tramonte made the following recommendations:

- Add sodium chloride to this section
- Add Cepacol® and Orajel® as trade names for benzocaine
- Remove strengths from benzocaine lozenges
- Remove strengths from phenol products

Dr. Tramonte recommended that the following products be deleted from Formulary:

Generic Name	Brand Name	Dosage forms to be deleted	Dosage forms still available
Cetylpyridinium	Cepacol®	Lozenges: 0.07% cetylpyridinium/0.03% benzyl alcohol (with tartrazine) Mouthwash: 0.05% cetylpyridinium/14% alcohol (with tartrazine) Troches: 0.07% cetylpyridinium/10 mg benzocaine (with tartrazine)	None See Note*
Triamcinolone in oral adhesive base	Kenalog in Orabase	Paste: triamcinolone 0.1%	None

* - Cepacol® has been re-formulated to include different ingredients.

On a motion of Dr. Heidel, seconded by Ms. Millhollon, the recommendation to delete these products was approved. Feedback will be obtained from the field.

Dr. Tramonte provided the review of the irrigation solutions. Attachment D. The comparative cost index and dosage availability of these agents was reviewed (included in Attachment D). There were no recommendations made.

Sectional Review for Next Meeting

The first part of dermatological agents will be reviewed at the next meeting.

Next Meeting Date

The next meeting was scheduled for June 15, 2007. The one month delay was necessary due to difficulties in finding the time to prepare for the meeting.

Adjourn

There being no further business, the meeting was adjourned at 1:40 p.m.

APPROVED:



Robert Ward, D.O., Interim Chairman

Attachments

Attachment A – New Drug Applications & Monographs

A - 1 trospium (Sanctura®)

A - 2 paliperidone extended release (Invega®)

A - 3 flurazepam (Dalmane®)

Attachment B – Otic Agents Class Review & Cost Review and Alphabetical Listing

Attachment C – Nasal, Mouth and Throat Agents Class Review & Cost Review and Alphabetical Listing

Attachment D – Irrigation Solution Class Review & Cost Review and Alphabetical Listing

Minutes Prepared by:

Ann L. Richards, Pharm.D., BCPP

APPENDIX 1: NEW DRUG APPLICATION FORM

415 — C
EXHIBIT A

TEXAS DEPARTMENT OF MENTAL HEALTH AND MENTAL RETARDATION

NEW DRUG APPLICATION
(for inclusion in the DSHS/DADS Drug Formulary)

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

Date: 1/18/07

Name of practitioner submitting the application: Angela Hughes, PharmD / ^{Faculty} preceptor Lisa Mican Ph.D

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

Information regarding new drug:

Therapeutic Classification	Antimuscarinic agent
Generic Name	Tropium chloride
Trade Name(s)	Sanctura TM
Manufacturer(s)	Esprit & Indevus
Dosage Form(s)	20mg tablets

Explain the pharmacological action or use of this drug:

Antimuscarinic agent for the treatment of overactive bladder

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

Quaternary amine vs. tertiary amine with lower lipophilicity & less transfer of drug across the blood brain barrier.

State which drugs this new drug would replace or supplement:

Detrol, Detrol LA, Ditropan, Ditropan XL

application is approved

J. Bawls MD

signature of chairman of facility pharmacy and therapeutics committee

OR

application is appropriate and complete

signature of clinical/medical director or designee

Trospium Chloride (Sanctura®)

Classification: Antimuscarinic agent

Pharmacology:

Trospium is a quaternary ammonium compound that has antispasmodic and antimuscarinic effects, but minimally crosses the blood-brain barrier. Trospium has low lipophilicity and is positively charged (polar). It antagonizes the effects of acetylcholine on muscarinic receptors in cholinergically innervated organs. Its parasympathetic action reduces the tonus of smooth muscle in the bladder. Trospium increases maximum cystometric bladder capacity and volume at first detrusor contraction.

Pharmacokinetics:

Oral bioavailability	< 10%
Protein binding	50-85%
Volume of distribution	395 (\pm 140) L
Metabolism	Hypothesized as ester hydrolysis with subsequent conjugation of benzylic acid to form azoniaspironortropanol with glucuronic acid. CYP450 not expected to contribute significantly to the elimination of trospium.
Excretion	Feces (85.2%) Urine (5.8%)
Half-Life	20 hours

Indications:

Trospium is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency.

Dosage:

The recommended dose is 20 mg twice daily. Trospium should be dosed at least one hour before meals or given on an empty stomach.

For patients with severe renal impairment (CrCl < 30 mL/min), the recommended dose is 20mg once daily at bedtime.

In patients \geq 75 years of age, the dose may be decreased to 20 mg once daily based upon tolerability.

Contraindications:

- Hypersensitivity to drug or its ingredients
- Urinary retention
- Gastric retention
- Uncontrolled narrow-angle glaucoma

Precautions:

- Bladder outflow obstruction
- Gastrointestinal obstructive disorders
- Controlled narrow-angle glaucoma
- Renal or hepatic dysfunction

Interactions:

Trospium is metabolized by esterases and excreted by the kidneys by a combination of tubular secretion and glomerular filtration. Based on *in vitro* data, no clinically relevant interactions with the metabolism of trospium are expected. However, medications which are actively secreted may interact with trospium by competing for renal tubular secretion (e.g., digoxin, metformin).

The concomitant use of trospium with other anticholinergic agents that produce dry mouth, constipation, and other anticholinergic pharmacologic effects may increase the frequency and/or severity of such effects. Anticholinergic agents may potentially alter the absorption of some concomitantly administered medications due to anticholinergic effects on gastrointestinal motility.

Comparison of Drug Interaction Potential:

Tolterodine is a substrate of CYP2C9 (minor), 2C19 (minor), 2D6 (major), and 3A4 (major); possible interactions with warfarin, fluoxetine, chlorpromazine, paroxetine, and ropinirole.

Oxybutynin is a substrate of CYP 3A4 (minor), and an inhibitor of CYP 2C8 (weak), 2D6 (weak), and 3A4 (weak); may cause additive sedation when used with other CNS depressants.

Adverse Events:

The two most common adverse events reported by patients receiving trospium 20mg twice daily were dry mouth and constipation. Dry mouth, the most commonly reported adverse event occurred in 20.1% of patients treated with trospium compared with 5.8% of patients receiving placebo.

Adverse events reported in $\geq 1\%$ of all patients:

Body system/Adverse event (AE)	Percentage of patients	
	Placebo (n=590)	SANCTURA (n=591)
Gastrointestinal disorders		
Dry mouth	5.8	20.1
Constipation	4.6	9.6
Constipation aggravated	0.8	1.4
Abdominal pain upper	1.2	1.5
Dyspepsia	0.3	1.2
Flatulence	0.8	1.2
Nervous system disorders		
Headache	2.0	4.2
General disorders		
Fatigue	1.4	1.9
Renal and urinary disorders		
Urinary retention	0.3	1.2
Eye disorders		
Dry eyes not otherwise specified	0.3	1.2
Total discontinuations	12.7	14.4
Due to AE	5.3	8.1

Incidence of other typical anticholinergic adverse events (placebo vs. trospium)

- abnormal vision: 0.0% vs 0.0%
- blurred vision: 0.0% vs 0.8%
- somnolence: 0.3% vs 0.2%
- dizziness: 1.5% vs 1.0%
- anxiety: 0.2% vs 0.0%

Adverse event information and chart obtained online at <http://www.sanctura.com>

Cost Comparison:

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	AWP COST (per tablet)	NET COST (per tablet)
Trospium	Sanctura	Esprit & Indevus	20 mg tablets	\$2.159	\$1.674
Tolterodine*	Detrol	Pfizer	2 mg tablets	\$2.23	\$1.6469
Tolterodine	Detrol LA	Pfizer	4 mg capsules	\$3.0959	\$2.8580
Oxybutynin*	Oxybutynin	Watson	5 mg tablets	\$0.4459	\$0.1086
Oxybutynin*	Ditropan XL	Janssen	5 mg tablets	\$3.6535	\$2.8331
Oxybutynin*	Ditropan XL	Janssen	10 mg tablets	\$3.6573	\$2.8360

*Formulary item

Recommended Monitoring: BUN, SCr, LFTs

Product Identification:

Tablet 20mg

Efficacy and Safety:

Most randomized, controlled studies with trospium have been in comparison with placebo. The few available comparison studies will be reviewed. One randomized, double-blind study compared trospium 20mg twice daily with oxybutynin 5 mg three times daily for the treatment of detrusor hyper-reflexia (Madersbacher, et al. 1995). There were no statistically significant differences between treatment groups with regard to efficacy. Trospium showed an advantage with regard to a lesser incidence of severe dry mouth versus oxybutynin (4% vs. 23%). Withdrawal from treatment was also less frequent in those receiving trospium (6%) than in those receiving oxybutynin (16%).

Another randomized, controlled trial investigated the tolerability and efficacy of trospium 20mg twice daily in comparison with oxybutynin 5mg twice daily over 52 weeks in patients with detrusor instability (Halaska M, et al. 2003). General health, laboratory values, and vital signs did not change significantly during the 52-week period for either treatment group. ECG changes were noted in both groups, which returned to normal by study end. In the trospium group, at 26 and 52 weeks of treatment, 49% and 63% respectively of the trial physicians assessed tolerability as very good. In the oxybutynin group, the assessment by the trial physicians at the same points showed very good tolerability in 36% and 42% of patients, respectively.

Adverse Events:

	Trospium (n = 267)	Oxybutynin (n = 90)
Abdominal pain	5 (2%)	–
Constipation	18 (7%)	4 (4%)
Diarrhea	2 (1%)	2 (2%)
Dyspepsia	13 (5%)	3 (3%)
Dysphagia	9 (3%)	3 (3%)
Dry mouth	87 (33%)	45 (50%)
Nausea	6 (2%)	2 (2%)
Urinary tract infection	33 (12%)	10 (11%)
Headache	11 (4%)	8 (9%)
Visual disturbances	9 (3%)	5 (6%)
Viral infection	9 (3%)	4 (4%)
Insomnia	10 (4%)	3 (3%)

Another randomized, parallel-group study evaluated the potential CNS adverse events of trospium 15mg three times daily, tolterodine 2mg twice daily, and oxybutynin 5mg three times daily in comparison with placebo (Todorova A, et al. 2001). A quantitative-topographical EEG (qEEG) was recorded for each subject prior to and up to 4 hours after each intake of the trial medication (a total of 10 qEEG sessions). In comparison to placebo, tolterodine and trospium did not induce changes of the qEEG in 5/6 frequency bands. Oxybutynin caused significant reductions in 4/6 frequency bands. Tolerability was similar between groups. The authors concluded that oxybutynin, a tertiary amine which crosses the blood-brain barrier, causes significant qEEG activity changes and implicates a higher risk of CNS effects. Although tolterodine is also a tertiary amine, it showed limited effects of qEEG activity, comparable to trospium, a quaternary amine, which barely crosses the blood-brain barrier.

One double-blind, placebo-controlled trial reported the results of 29 healthy volunteers which took single oral doses of trospium up to 360 mg. Blood pressure, heart rate, ECG, papillary diameter, salivary secretion, and subjective reports of tolerance revealed no essential differences between placebo and trospium in doses up to 120 mg. Starting with a single dose of 180mg, anticholinergic effects were observed with increasing intensity i.e., pupil dilation, reduction in salivary flow, and increased heart rate. The study found no concerns with respect to CNS safety.

Conclusions:

Trospium is a relatively unique agent for the treatment of overactive bladder. This medication is a quaternary amine, which crosses the blood-brain barrier to a minimal extent compared to tertiary amines used for urinary incontinence. Trospium undergoes minimal metabolism (therefore minimal drug-drug interactions), demonstrates low serum protein binding, and low lipophilicity (therefore fewer cognitive-related adverse events). These characteristics contribute to the safety and efficacy profile of this medication. Based upon efficacy, cost comparisons, and a more favorable side effect profile, a recommendation is made to consider adding trospium to the formulary.

Recommendation:

Recommended for addition to the formulary.

References:

1. Product Information: Sanctura™, trospium tablets. Esprit Pharmaceuticals, East Brunswick, NJ and Indevus Pharmaceuticals, Inc., Lexington, MA.
2. Madersbacher H, Stohrer M, Richter R, et al. Trospium chloride versus oxybutynin: a randomized, double-blind, multicenter trial in the treatment of detrusor hyper-reflexia. *Br J Urol* 1995; 75: 452-456.
3. Halaska M, Ralph G, Wiedemann A, et al. Controlled, double-blind multicenter clinical trial to investigate long-term tolerability and efficacy of trospium chloride in patients with detrusor instability. *World J Urol* 2003; 20: 392-399.
4. Todorova A, Vonderheid-Guth B, Dimpfel W. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. *J Clin Psychopharmacol* 2001; 41: 636-644.
5. Breuel HP, Murtz G, Bondy S, et al. Safety and tolerance of trospium chloride in the high dose range. *Arneimittelforschung*. 1993; 43: 461-464.
6. McKesson Online Catalog
7. Scheife R, Takeda M. Central Nervous System Safety of Anticholinergic Drugs for the treatment of overactive bladder in the elderly. *Clin Ther* 2005; 27: 144-153.

Prepared by:

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February 16, 2007

Paliperidone Extended-Release (Invega®)

Classification: Atypical Antipsychotic Agent

Pharmacology:

Paliperidone is the major active metabolite of risperidone. Invega® contains the racemic mixture of paliperidone. Paliperidone ER exerts its activity by antagonizing central dopamine (D₂) and serotonin (5HT_{2a}) receptors. It also blocks α_1 and α_2 adrenergic receptors and H₁ receptors.

Pharmacokinetics:

Absorption Paliperidone ER uses the OROS osmotic drug-release technology that delivers the drug at a controlled rate. The drug delivery systems allows for a gradual rise in peak plasma concentration. Peak plasma concentration is reached after 24 hours of dosing. The oral bioavailability of paliperidone ER is 28%. If 12 mg of paliperidone ER was given with a high fat and high caloric meal, the C_{max} and AUC will increase by 60% and 54% respectively.

Distribution Racemic paliperidone is 74% bound to plasma protein. The volume of distribution of paliperidone is 487 L.

Metabolism Paliperidone is not extensively metabolized by the liver. *In vitro* studies showed CYP2D6 and 3A4 to play a role in paliperidone metabolism, but *in vivo* studies indicate a limited role in the elimination of paliperidone.

Elimination Paliperidone is extensively excreted by the kidney unchanged. The elimination half-life of paliperidone is 23 hours.

Indication:

Indicated for the treatment of Schizophrenia in adults. No studies have been done on patients less than 18 years of age.

Dosage:

The recommended starting dose is 6 mg once daily. The dose should be given in the morning. There is no need for initial dose titration. Doses greater than 6 mg/day have not shown any additional benefit. Dose increases should be done in increments of 3 mg. The maximum daily dose is 12 mg. Paliperidone ER needs to be swallowed whole and it can be taken without regard to food. There is no dosage adjustment needed for patients with mild to moderate hepatic impairment. For patients with creatinine clearance 50 to 80 ml/min, the maximum dose is 6 mg/day. For patients with creatinine clearance 10 to 50 ml/min, the maximum dose is 3 mg/day.

Contraindications:

- Patients with known hypersensitivity to paliperidone, risperidone, or any component of the paliperidone formulation

Precautions:

- Block box warning: atypical antipsychotic drugs have a higher risk of death compared to placebo when used for the treatment of elderly patients with dementia-related psychosis
- Pregnancy category C
- Patients with QT prolongation
- Patients with orthostatic hypotension, hyperprolactinemia, or dysphagia

Interactions:

- Paliperidone ER may block the effects of dopamine agonists and levodopa.
- The use of paliperidone ER with other agents that can cause orthostatic hypotension may have an additive effect
- Combination of other centrally acting drugs and alcohol should be used with caution with paliperidone ER

Adverse Reactions:

Possible side effects are headache, akathisia, extrapyramidal disorders, sedation, agitation, anxiety, tachycardia, increased blood sugar, and QT prolongation. Clinical trials show no significant difference in weight gain between placebo, 3mg paliperidone ER, and 6mg paliperidone ER. There was a higher incidence of weight gain in patients taking 9 mg or 12 mg compared to placebo. A rare, but serious side effect is neuroleptic malignant syndrome which is characterized by muscle rigidity, fever, altered mental status, acute renal failure, rhabdomyolysis, and irregular blood pressure.

Costs and Monitoring:

Invega® 3mg & 6mg: \$9.46 per tablet
 Invega® 9mg: \$14.19 per tablet
 Invega® 12mg: \$18.92 (given as two 6mg tablets)
 Invega® is not currently available in unit dose.

Like other atypical antipsychotics baseline BMI, FPG or HbgA1c, fasting lipid panel, EPS evaluation and TD assessment should be conducted and ongoing BMI, FPG or HbgA1c, fasting lipid panel, inquiry for prolactin elevation, EPS evaluation, and TD assessment should be performed.

Product Identification:

Tablets: 3 mg (white), 6 mg (beige), and 9 mg (pink)

Efficacy:

The efficacy of paliperidone ER for the treatment of acute schizophrenia episodes in adults (n=630) was demonstrated in a placebo-controlled, active-controlled (olanzapine), 6-week, fixed-dose study.¹ Patients were randomized to receive a fixed-dose of 6 mg, 9 mg, or 12 mg paliperidone ER, or 10 mg olanzapine, or placebo once daily in the morning. Total scores on the Positive and Negative Syndrome Scale (PANSS) decreased by -17.9, -17.2, and -23.3 for the 6mg, 9mg, and 12mg paliperidone ER groups respectively (p<0.001 for all paliperidone ER groups versus placebo), and -19.9 for the olanzapine group; the PANSS score changed by -4.1 for the placebo group. The adverse events with a higher incidence in the paliperidone ER groups compared to placebo are EPS (7% vs. 1%), hyperkinesia (7% vs. 3%), hypertonia (3% vs. 0%), tachycardia (18% vs. 10%), increased saliva (3% vs. 1%), vomiting (3% vs. 2%), ECG abnormalities (5% vs. 2%), postural hypotension (4% vs. 1%). Prolactin levels increased from 17.4 ng/ml at baseline to 45.3 ng/ml at the end of the trial in males receiving paliperidone ER; in females receiving paliperidone ER, the prolactin levels rose from 38.0 ng/ml to 145.3 ng/ml. Prolactin levels slightly decreased in both males and females receiving placebo or olanzapine. No significant increases in glucose, insulin, or serum lipid levels were seen in any of the paliperidone ER groups. A weight increase of ≥7% was observed in 2% of the placebo group, 3-7% of the paliperidone ER groups, and 13% of the olanzapine patients.

The efficacy of paliperidone ER for the treatment of schizophrenia in adults age 18-65 was

demonstrated in a 8 week run-in open-label flexible dose (3-15 mg/day, starting dose 9mg) phase, followed by a 6 week open-label fixed dose phase (effective dose established during the run-in phase continued), then subjects entered the double-blind treatment phase of variable duration (patients remained in the double-blind phase until they experienced a recurrent event, withdrew, or study was completed- average length 24 weeks).² For the patients in the paliperidone ER group, 38% were stabilized on 9 mg/day, 22% on 12 mg/day, 28% on 15 mg/day, and 12% were tapered down to 3 mg/day or 6 mg/day. The primary measure, rate of recurrence, was significantly higher in the placebo group (52%) versus the paliperidone ER group (22%) with a significance level of $p < 0.001$. Treatment-emergent adverse events (TEAEs) occurring most often with paliperidone ER in the open-label phases were tremors (16%), tachycardia (15%), headache (14%), hyperkinesias (12%), and insomnia (10%). During the double-blind portion of the trial, 7% of patients receiving paliperidone ER reported extrapyramidal symptoms compared to 3% receiving placebo. Prolactin levels were elevated in the paliperidone ER group; the prolactin levels had a slight decrease in the placebo group (exact values not disclosed). Prolactin related adverse events (amenorrhea, nonpuerperal lactation) were more common with paliperidone ER (4%) vs. placebo (0%). One report of possible NMS in the paliperidone ER group. After following the patients for an average of 24 weeks, those in the paliperidone ER group gained an average of 1.8 kg, the placebo group averaged a 0.2 kg weight gain. Clinically significant weight gain ($\geq 7\%$) occurred in 12% of placebo treated patients and 20% of paliperidone ER treated patients. There were no statistically significant differences in C-peptide, glucose, insulin, or lipid levels between the paliperidone ER and placebo group at endpoint.

The potency of Invega® was demonstrated in a “virtual” comparison of paliperidone ER and risperidone.³ Three randomized, placebo-controlled studies for paliperidone ER and for risperidone were pooled. Patients who received either paliperidone ER 6 to 12 mg/day (n=275), risperidone 2 to 4 mg/day (n=173), risperidone 4 to 6 mg/day (n=174), or placebo (n=360), and were aged 18-65, were included in this analysis. The completion rates of paliperidone ER 6 to 12 mg/day and risperidone 4 to 6 mg/day were similar (67.6% and 65.5%), compared to a 40.8% completion rate for the placebo group. The PANSS score changes at endpoint were not significantly different for the paliperidone ER and risperidone groups, -19.0 and -19.7 respectively ($P=0.825$). Mean weight gain with paliperidone ER was 0.7 kg and risperidone 1.3 kg ($P=0.024$). The risperidone 4 to 6 mg/day group was associated with higher rates of akathisia, restlessness, anxiety, insomnia, somnolence, dizziness, and gastrointestinal side effects than the paliperidone ER group. The paliperidone ER 6 to 12 mg/day and risperidone 2 to 4 mg/day groups had completion rates of 67.6% and 53.8%, respectively ($P=0.003$). The paliperidone ER group had a superior mean PANSS reduction of -19.0 compared to the risperidone 2 to 4 mg/day reduction of -11.4 ($P=0.003$). The paliperidone ER group reported fewer incidents of akathisia, restlessness, insomnia, somnolence, dizziness, and gastrointestinal effects, but an increased incidence of tachycardia. Weight gain occurred, but there was no significant difference in weight gain between the groups. This study concluded that paliperidone ER 6 to 12 mg/day is more comparable to risperidone 4 to 6 mg/day.

The studies were conducted throughout North America, Eastern and Western Europe, and Asia. Upon examination, no differences in response were found between population subgroups based on gender, geographic location, or age. Sufficient data was not collected during these studies to determine if a differential response based on race exists.¹

Conclusions:

Studies show paliperidone ER is an effective treatment for schizophrenia. To date, no studies have shown paliperidone ER to be more effective than any other atypical antipsychotics. One advantage of paliperidone ER is the osmotic pressure delivery system, OROS, allowing for effective once daily dosing. While some other antipsychotics are approved for once daily dosing, this is currently the only antipsychotic using OROS technology. Since there have not been any direct head to head comparisons with risperidone it is unclear if paliperidone ER is better tolerated. One disadvantage of paliperidone ER is the price. Comparable effects are achieved from paliperidone ER 6 mg/day and risperidone 4 mg/day, costing \$9.46 and \$9.04, respectively. At the higher comparable doses; however, paliperidone ER 12 mg/day (two 6 mg tablets) is \$18.92, and risperidone 6 mg/day is \$13.46. At this time, paliperidone ER does not come in unit dose form, adding time and cost to repackage the medication. In addition, risperidone is anticipated to be available generically by the end of 2007.

Recommendation:

Not recommended for addition to the formulary.

References:

1. Kane J, et al. Treatment of Schizophrenia With Paliperidone Extended-release Tablets: A 6-Week Placebo-controlled Trial. *Schizophrenia Research* 2007;90(1-3):147-61.
2. Kramer M, Simpson G, Maciulis V, et al. Paliperidone Extended-release Tablets for Prevention of Symptom Recurrence in Patients With Schizophrenia: A Randomized, Double-blind, Placebo-Controlled Study. *Journal of Clinical Psychopharmacology*. 2007;(27)6-14.
3. Schooler N, Gharabawi G, Bossie C, et al. A "Virtual" Comparison of Paliperidone ER and Oral Risperidone in Patients With Schizophrenia [poster]. Presented at: 45th Annual Meeting of the American College of Neuropsychopharmacology 2006; December 3-7, 2006; Hollywood, Fla.
4. Invega Package Insert. Janssen. Titusville, NJ. December 2006.

Prepared by:

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February 15, 2007

Flurazepam
(Dalmane[®], Various)

Classification: Benzodiazepine, psychotropic agent, sedative/hypnotic

Pharmacology:

Flurazepam is a long-acting benzodiazepine, thought to exert its action by binding to the GABA-A Receptor-Benzodiazepine Receptor-Chloride Ion Channel Complex, which increases the affinity of the receptor for GABA.

Pharmacokinetics:

Absorption: Rapidly absorbed

Distribution: 97.2% protein bound

Metabolism: Extensive hepatic metabolism; active metabolites N1-hydroxyethyl-flurazepam and N1-desalkyl-flurazepam

Elimination: Flurazepam elimination t1/2 2.3 hours; Active metabolites N1-hydroxyethyl-flurazepam t1/2 16 hrs and N1-desalkyl-flurazepam (DAFLZ) t1/2 47-100 hrs. Drug accumulation and prolonged t1/2 of DAFLZ may occur in elderly males (t1/2 160 vs. 74 hours) and females (t1/2 120 vs. 90 hours)

Urinary elimination, 22-55% conjugated N1-hydroxyethyl-flurazepam and less than 1% N1-desalkyl-flurazepam

Indications: Indicated as a hypnotic agent for the treatment of short-term/transient insomnia characterized by difficulty falling asleep, frequent nocturnal awakenings, and/or early morning awakenings.

Dosage:

Usual dose 30mg before bedtime, range 15-30mg before bedtime. In elderly or debilitated patients 15mg is recommended as the initial dose.

Contraindications and Precautions:

- Pregnancy category C
- Known hypersensitivity to this product or other benzodiazepines
- Sleep apnea
- Significant hepatic or renal impairment
- Elderly/debilitated patients
- Concomitant CNS depressants
- Severe pulmonary insufficiency

Interactions:

Flurazepam is a substrate of 3A4 (major) and a weak inhibitor of 2E1. Inhibitors of CYP 3A4 (i.e. ciprofloxacin, clarithromycin, doxycycline, erythromycin, fluoxetine, fluvoxamine, isoniazid, protease inhibitors, verapamil) can significantly increase levels/effects of flurazepam and inducers of CYP 3A4 (i.e. carbamazepine, phenobarbital, phenytoin) can decrease levels/effects of flurazepam.

Adverse Reactions:

Dizziness, drowsiness, light-headedness, staggering, ataxia, and falling have occurred, particularly in elderly/debilitated patients. Other side effects include headache, gastrointestinal intolerance, irritability, weakness, and palpitations.

Costs and Monitoring:

Daily costs: 15 mg \$0.10, 30 mg \$0.13

Baseline liver function tests and serum creatinine

Product Identification:

Capsule: 15 mg and 30 mg

Efficacy:

Flurazepam is a long-acting benzodiazepine that typically induces sleep 15 to 45 minutes after ingestion. This medication has a long enough duration of action to provide a hypnotic effect throughout the night and relieve next-day anxiety if needed. However, the DAFLZ metabolite has a long t_{1/2} which can accumulate with continued use contributing to oversedation, impaired daytime functioning, and possible toxicity in susceptible individuals. Controlled trials have not shown flurazepam to be superior to other benzodiazepines currently available for the treatment of insomnia. Many of the trials for insomnia reported next-day impaired cognitive performance and/or daytime sedation with flurazepam compared to other short-acting benzodiazepines such as midazolam, oxazepam, temazepam, and triazolam.

Conclusions:

Flurazepam has not been shown to be superior to other benzodiazepines currently available for the treatment of insomnia. Other long-acting benzodiazepines are already available on the DSHS formulary including chlordiazepoxide, clonazepam, clorazepate, and diazepam. Concerns with using flurazepam include the risk of accumulation and toxicity in patients with hepatic or renal impairment, the elderly, and those receiving concomitant medications that inhibit CYP 3A4.

Recommendation:

Addition to the formulary is not recommended.

References:

1. Flurazepam. In: Klasco RK (Ed): DRUGDEX® System. Thomson Micromedex, Greenwood Village, Colorado (Edition expires 3/2006).
2. Dalmane Package Insert. ICN Pharmaceuticals, Inc. Costa Mesa, CA. Rev. September 2001.

Prepared by:

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February 10, 2006

Otitis Externa Treatments:

Generic	Trade	Cost
Acetic Acid	Generic (15 mL)	\$ 24.53
Acetic Acid/Hydrocortisone	Acetasol HC VoSol HC	\$ 11.47
Neomycin/Polymyxin B/Hydrocortisone <u>solution</u>	Cortisporin (10 mL)	\$ 55.95 (trade) \$ 8.00 (generic)
Neomycin/Polymyxin B/Hydrocortisone <u>suspension</u>	Cortisporin (10 mL) Generic (10 mL)	\$ 55.95 \$ 8.00
Ofloxacin	Floxin Otic	\$ 47.88 (5 mL) \$ 86.56 (10 mL)
Ciprofloxacin/Hydrocortisone	Cipro HC Otic 10 mL	\$ 75.91
Ciprofloxacin/Dexamethasone	Ciprodex 7.5 mL	\$ 75.91

Pricing data current as of 15 February 2007

Memorandum

To: Executive Formulary Committee
From: Sharon M. Tramonte, Pharm.D. 
Through: Ann L. Richards, Pharm.D.
Subject: Class Review – Nasal Mouth Throat
Date: 15 February 2007

The following is a synopsis of recommended changes to the DADS/DHSH Formulary.

Recommended for deletion:

- ◆ Cetylpyridinium
- ◆ Triamcinolone in Oral Adhesive Base (Kenalog in Orabase)

Other Recommendations:

- ◆ Add Sodium Chloride to this section
- ◆ Add “Cepacol” and “Orajel” as trade names for Benzocaine
- ◆ Remove strengths from Benzocaine lozenges
- ◆ Remove strengths from Phenol products

NASAL, MOUTH AND THROAT AGENTS

Benzocaine	\$\$ - \$\$\$
Carbamide Peroxide/Glycerin/Propylene Glycol/ Sodium Stannate (Gly-Oxide)	\$\$\$
Carboxymethylcellulose/Electrolytes (Saliva Substitute, Moi-Stir, Salivart, MouthKote, Salix)	\$ - \$\$\$
Cetylpyridinium (Cepacol)	\$ - \$\$\$
Chlorhexidine (Peridex)	\$\$
Clotrimazole (Mycelex, Fungoid)	\$\$
Doxycycline (Periostat)	\$\$\$
Nystatin (Mycostatin)	\$\$ - \$\$\$
Oxymetazoline (Afrin)	\$
Phenol (Chloraseptic)	\$\$
Phenylephrine (Neo-Synephrine)	\$\$
Sodium Fluoride	\$
Stannous Fluoride (OmniMed, PerioMed)	\$\$\$\$
Triamcinolone in Oral Adhesive Base (Kenalog in Orabase)	\$\$

Benzocaine (Lanacaine)

Topical, for mucous membranes:

Gel: 6%, 20%

Liquid: 20%

Topical, dermatologic:

Cream, topical: 5%, 6%

Lotion: 8%

Ointment: 5%

Spray: 5%, 20%

Mouth/Throat preparations:

Gel: 6.3%, 7.5%, 10%, 15%, 20%

Liquid: 5%, 6.3%, 10%, 20%

Lozenges: ~~5 mg, 6 mg, 10 mg, 15 mg~~

~~Carbamide Peroxide/Glycerin/Propylene Glycol/Sodium Stannate (Debrox, Gly-Oxide)~~

~~Gel, oral: 10%~~

~~Solution, oral: 10%, 15%~~

~~Solution, otic: 6.5%~~

Carboxymethylcellulose/Electrolytes (Saliva Substitute, Moi-Stir, Salivart, MouthKote, Salix)

Solution, oral

~~Cetylpyridinium (Cepacol)~~

~~Lozenges: 0.07% Cetylpyridinium/0.3% Benzyl Alcohol [with tartrazine]~~

~~Mouthwash: 0.05% Cetylpyridinium/14% Alcohol [with tartrazine]~~

~~Troches: 0.07% Cetylpyridinium/10 mg Benzocaine [with tartrazine]~~

Chlorhexidine (Peridex, Hibiclens, Bactoshield)

Liquid, topical, with 4% isopropyl alcohol: 4%

Rinse, oral, with 12% alcohol: 0.12%

Clotrimazole (Lotrimin, Mycelex, Gyne-Lotrimin, Fungoid)

Cream, topical: 1%

Cream, vaginal: 1%, 2%

Lotion: 1%

Solution, topical: 1%

Suppository, vaginal: 100 mg, 200 mg

Tablet, vaginal: 100 mg, 500 mg

Troche: 10 mg

Doxycycline (Vibramycin, Periostat)

Capsule: 50 mg, 100 mg

Powder for injection: 100 mg, 200 mg

Powder for oral suspension: 25 mg/5 mL

Syrup: 50 mg/5 mL

Tablet: 20 mg, 50 mg, 100 mg

Nystatin (Mycostatin)

Cream, topical: 100,000 units/g
Ointment, topical: 100,000 units/g
Powder for oral suspension: 50 million units, 1 billion units, 2 billion units, 5 billion units
Powder, topical: 100,000 units/g
Suspension, oral: 100,000 units/mL
Tablet, oral: 500,000 units
Troche: 200,000 units

Oxymetazoline (Afrin)

Solution, nasal, drops: 0.025%, 0.05%
Solution, nasal, spray: 0.05%

Phenol (Chloraseptic)

Mouthwash/Gargle: 1.4%
Throat Spray: 0.5%

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%

Sodium Fluoride

Liquid, oral: 360 mL, 480 mL, 540 mL
Tablet, chewable: 0.25 mg, 0.5 mg, 1 mg, 1.1 mg, 2.2 mg

Stannous Fluoride (OmniMed, PerioMed)

Solution, oral: 0.4%, 0.63%

~~Triamcinolone in Oral Adhesive Base (Kenalog in Orabase)~~

~~Paste: Triamcinolone 0.1%~~

Memorandum

To: Executive Formulary Committee

From: Sharon M. Tramonte, Pharm.D. 

Through: Ann L. Richards, Pharm.D.

Subject: Class Review – Irrigation Solutions

Date: 15 February 2007

There are no recommended changes to the DADS/DHSH Formulary.

IRRIGATION SOLUTIONS

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

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

Water for Irrigation

- Solution, irrigation