Drug Utilization Review Board

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1A
Oklahoma City, Oklahoma 73107
Ponca Room

Wednesday
March 12, 2014
4:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – March 12, 2014**

DATE: March 3, 2014

NOTE: The DUR Board will meet at 4:00 p.m. The meeting will be held in the Ponca Room at the Oklahoma Health Care Authority Offices in Shepherd Mall. (North Entrance)

Enclosed are the following items related to the March meeting. Material is arranged in order of the Agenda.

Call to Order

Public Comment Forum

Action Item – Approval of DUR Board Meeting Minutes – See Appendix A

Update on DUR / Medication Coverage Authorization Unit / FDA Safety Alerts – See Appendix B

Action Item – Vote to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan) – See Appendix C

Action Item – Vote to Prior Authorize Select Cephalosporins – See Appendix D

Annual Review of Erythropoiesis Stimulating Agents – See Appendix E

Annual Review of Insomnia Medications – See Appendix F

Annual Review of Oral Antihistamines – See Appendix G

Annual Review of Smoking Cessation Products – See Appendix H

Annual Review of Benzodiazepine Medications – See Appendix I

60 Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications – See Appendix J

FDA and DEA Updates – See Appendix K

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – March 12, 2014 @ 4:00 p.m.

Oklahoma Health Care Authority
2401 N.W. 23rd Street, Suite 1-A
Oklahoma City, Oklahoma 73107
Ponca Room (North Entrance)

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call To Order
   A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum
   A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A
   A. February 12, 2014 DUR Minutes – Vote
   B. February 12, 2014 DUR Recommendation Memorandum

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:

4. Update on DUR / Medication Coverage Authorization Unit / FDA Safety Alerts – See Appendix B
   A. Medication Coverage Activity for February 2014
   B. Pharmacy Help Desk Activity for February 2014
   C. Updates on FDA Safety Alerts

Items to be presented by Dr. Nawaz, Dr. Muchmore, Chairman:

5. Action Item – Vote to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan) – See Appendix C
   A. COP Recommendations

Items to be presented by Dr. Le, Dr. Muchmore, Chairman:

6. Action Item – Vote to Prior Authorize Select Cephalosporins – See Appendix D
   A. Recommendations

Items to be presented by Dr. Le, Dr. Muchmore, Chairman:

7. Annual Review of Erythropoiesis Stimulating Agents – See Appendix E
   A. Introduction
   B. Utilization of Erythropoiesis Stimulating Agents
   C. Prior Authorization Review
   D. Market News and Updates
   E. Discussion
   F. Recommendations

Items to be presented by Dr. Adams, Dr. Muchmore, Chairman:

8. Annual Review of Insomnia Medications – See Appendix F

A. Current Authorization Criteria
B. Utilization of Insomnia Medications
C. Prior Authorization Review
D. Market News and Updates
E. COP Recommendations
F. Utilization Details

Items to be presented by Dr. Teel, Dr. Muchmore, Chairman:

9. Annual Review of Oral Antihistamines – Appendix G

A. Current Authorization Criteria
B. Utilization of Oral Antihistamines
C. Prior Authorization Review
D. Market News and Updates
E. COP Recommendations
F. Utilization Details

Items to be presented by Dr. Nawaz, Dr. Muchmore, Chairman:

10. Annual Review of Smoking Cessation Products – Appendix H

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Updates
E. Discussion
F. COP Recommendations
G. Utilization Details

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:

11. Annual Review of Benzodiazepine Medications – See Appendix I

A. Current Authorization Criteria
B. Utilization of Benzodiazepines
C. Prior Authorization Review
D. Market News and Updates
E. COP Recommendations
F. Utilization Details

Items to be presented by Dr. Holderread, Dr. Muchmore, Chairman:

12. 60 Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications – See Appendix J

A. Introduction
B. Economic Impact
C. Market Analysis
D. COP Recommendations

Items to be presented by Nico Gomez, Executive Chief, Dr. Muchmore, Chairman:

13. Updates Regarding OHCA

Items to be presented by Dr. Cothran, Dr. Muchmore, Chairman:

14. FDA and DEA Updates – See Appendix K

15. Future Business

A. Annual Reviews

B. New Product Reviews

16. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF FEBRUARY 12, 2014

BOARD MEMBERS:	PRESENT	ABSENT
Mark Feightner, Pharm.D.	x	
Anetta Harrell, Pharm.D.	x	
Evie Knisely, Pharm.D.	x	
John Muchmore, M.D., Ph.D.; Chairman	x	
Paul Louis Preslar, D.O., MBA	x	
James Rhymer, D.Ph.	x	
Bruna Varalli-Claypool, MHS, PA-C		x
Eric Winegardener, D.Ph.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison		x
Bethany Holderread, Pharm. D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator	x	
Jennifer Sipols, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Graduate Students: Tim Pham	x	
Visiting Pharmacy Student(s): Brian Lindsey	x	

	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director	x	
Nico Gomez, Chief Executive Officer		x
Chris Le, Pharm.D.; Clinical Pharmacist Consultant	x	
Sylvia Lopez, M.D., FAAP; Chief Medical Officer	x	
Ed Long, Chief Communications Officer	x	
Jennie Melendez, Marketing Coordinator	x	
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, Deputy State Medicaid Director	x	
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	x	
Jill Ratterman, D.Ph.; Pharmacy Specialist	x	
Garth Splinter, M.D., M.B.A.; Medicaid Director	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Randy McGinley, Bayer	Jon A. Maguire, GSK	Brian Maves, Pfizer
Kim Greenberg, Upsher-Smith	Jim Fowler, Astra Zenca	Jim Chapman, Abbvie
Toby Thompson, Pfizer	Roger Grotzinger, BMS	Janie Huff, Takeda
Ron Cain, Pfizer	Mai Duong, Novartis	
Mark DeClerk, Lilly	Clint Degner, Novartis	

PRESENT FOR PUBLIC COMMENT:	
	None

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: ROLL CALL

Dr. Muchmore called the meeting to order. Roll call by Dr. Cothran established the presence of a quorum.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

NONE

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: **APPROVAL OF DUR BOARD MINUTES**

3A: JANUARY 8, 2014 DUR MINUTES

3B: JANUARY 8, 2014 DUR RECOMMENDATION MEMORANDUM

3C: CORRESPONDENCE

Dr. Harrell moved to approve; seconded by Dr. Knisely

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON DUR / MEDICATION COVERAGE AUTHORIZATION UNIT, SOONERPSYCH PROGRAM UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2014

4B: PHARMACY HELP DESK ACTIVITY FOR JANUARY 2014

4C: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE PROCYSBI™ (CYSTEAMINE BITARTRATE)**

5A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Preslar moved to approve; seconded by Dr. Feightner

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE RAVICTI® (GLYCEROL PHENYLBUTYRATE)**

6A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

Dr. Harrell moved to approve; seconded by Dr. Rhymer

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE SIRTURO™ (BEDAQUILINE FUMARATE)**

7A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Preslar moved to approve; seconded by Dr. Feightner

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE INHALED TOBRAMYCIN PRODUCTS AND PULMOZYME® (DORNASE ALFA)**

8A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Le

Dr. Feightner moved to approve; seconded by Dr. Rhymer

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: **DRUG UTILIZATION REVIEW OF PULMONARY ARTERIAL HYPERTENSION MEDICATIONS AND 30 DAY NOTICE TO PRIOR AUTHORIZE ADEMPAS® (RIOCIGUAT) AND OPSUMIT® (MACITENTAN)**

9A: INTRODUCTION

9B: CURRENT AUTHORIZATION CRITERIA

9C: UTILIZATION

9D: PRIOR AUTHORIZATION

9E: MARKET NEWS AND UPDATES

9F: COP RECOMMENDATIONS

9G: UTILIZATION DETAILS

9H: PRODUCT DETAILS OF ADEMPAS®

9I: PRODUCT DETAILS OF OPSUMIT®

Materials included in agenda packet; presented by Dr. Nawaz

Dr. Muchmore recommends *"discontinuing PDE- 5 before starting Adempas."*

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: **DRUG UTILIZATION REVIEW OF CEPHALOSPORIN ANTIBIOTICS AND 30 DAY NOTICE TO PRIOR AUTHORIZE SELECT CEPHALOSPORINS**

10A: INTRODUCTION

10B: UTILIZATION

10C: COP RECOMMENDATIONS

10D: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Le

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **DRUG UTILIZATION REVIEW OF OPHTHALMIC ANTI-INFLAMMATORY MEDICATIONS**

11A: INTRODUCTION

11B: UTILIZATION

11C: MARKET NEWS AND UPDATES

11D: COP RECOMMENDATIONS

11E: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 12:</u> **FDA AND DEA UPDATES**
Materials included in agenda packet; presented by Dr. Cothran.
ACTION: **NONE REQUIRED**

<u>AGENDA ITEM NO. 13:</u> **FUTURE BUSINESS**
13A: **ANNUAL REVIEWS**
13B: **NEW PRODUCT REVIEWS**
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: **NONE REQUIRED**

<u>AGENDA ITEM NO. 14:</u> **ADJOURNMENT**
The meeting was adjourned at 6:41pm

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: February 13, 2014

To: Nancy Nesser, Pharm.D., J.D.
Pharmacy Director
Oklahoma Health Care Authority

From: Bethany Holderread, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of February 12, 2014

Recommendation 1: Vote to Prior Authorize Procysbi™ (Cysteamine Bitartrate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Procysbi™ (cysteamine bitartrate) with the following criteria:

Procysbi™ (Cysteamine Bitartrate) Approval Criteria:

1. An FDA approved diagnosis of nephropathic cystinosis; and
2. A patient specific, clinically significant reason why member cannot use the short-acting formulation Cystagon® (cysteamine bitartrate).

Recommendation 2: Vote to Prior Authorize Ravicti® (Glycerol Phenylbutyrate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Ravicti® (glycerol phenylbutyrate) with the following criteria:

Ravicti® (Glycerol Phenylbutyrate) Approval Criteria:

1. An FDA approved diagnosis of urea cycle disorder (UCD); and
2. Active management with protein restricted diet; and
3. A patient specific, clinically significant reason why member cannot use Buphenyl® (sodium phenylbutyrate).

Recommendation 3: Vote to Prior Authorize Sirturo™ (Bedaquiline)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Sirturo™ (bedaquiline fumarate) with the following criteria:

Sirturo™ (Bedaquiline Fumarate) Approval Criteria:

1. An FDA approved diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB); and
2. Member must be 18 years of age or older; and
3. An alternative, effective treatment regimen cannot otherwise be provided; and
4. Medical supervision by an infectious disease specialist; and
5. Sirturo™ must be used in combination with at least three other drugs to which the patient's MDR-TB isolate has been shown to be susceptible; and
6. Sirturo™ must be administered under direct observation; and
7. Baseline ECG should be obtained and repeated 2, 12, and 24 weeks after starting treatment; and
8. Liver enzymes should be obtained at baseline and monitored monthly.
9. Sirturo™ will not be approved for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis. MDR-TB must be confirmed by sensitivity cultures indicating resistance to at least isoniazid and rifampin.
10. A maximum quantity of 188 tablets for the entire course of treatment will apply.
11. Approvals will be for the duration of 24 weeks.

Recommendation 4: Vote to Prior Authorize Inhaled Tobramycin Products and Pulmozyme® (Dornase Alfa)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. Reserve use of inhaled tobramycin products and Pulmozyme® (dornase alfa) for members who have a diagnosis of cystic fibrosis. These medications will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 24 months of claims history. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Restrict use of inhaled tobramycin products to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy. Use outside of this recommended regimen may be considered for coverage via a manual petition.
3. Access to Tobi® Podhaler™ will remain similar to Tobi® at this time. A study will be conducted over the course of the next year to evaluate and compare the impact of the two products on overall healthcare outcomes including hospitalizations and pharmacy costs. The results of this study may contribute to further recommendations regarding Tobi® Podhaler™.

Recommendation 5: Drug Utilization Review of Pulmonary Arterial Hypertension Medications and 30 Day Notice to Prior Authorize Adempas® (Riociguat) and Opsumit® (Macitentan)

NO ACTION REQUIRED.

Recommendation 6: Drug Utilization Review of Cephalosporin Antibiotics and 30 Day Notice to Prior Authorize Select Cephalosporins

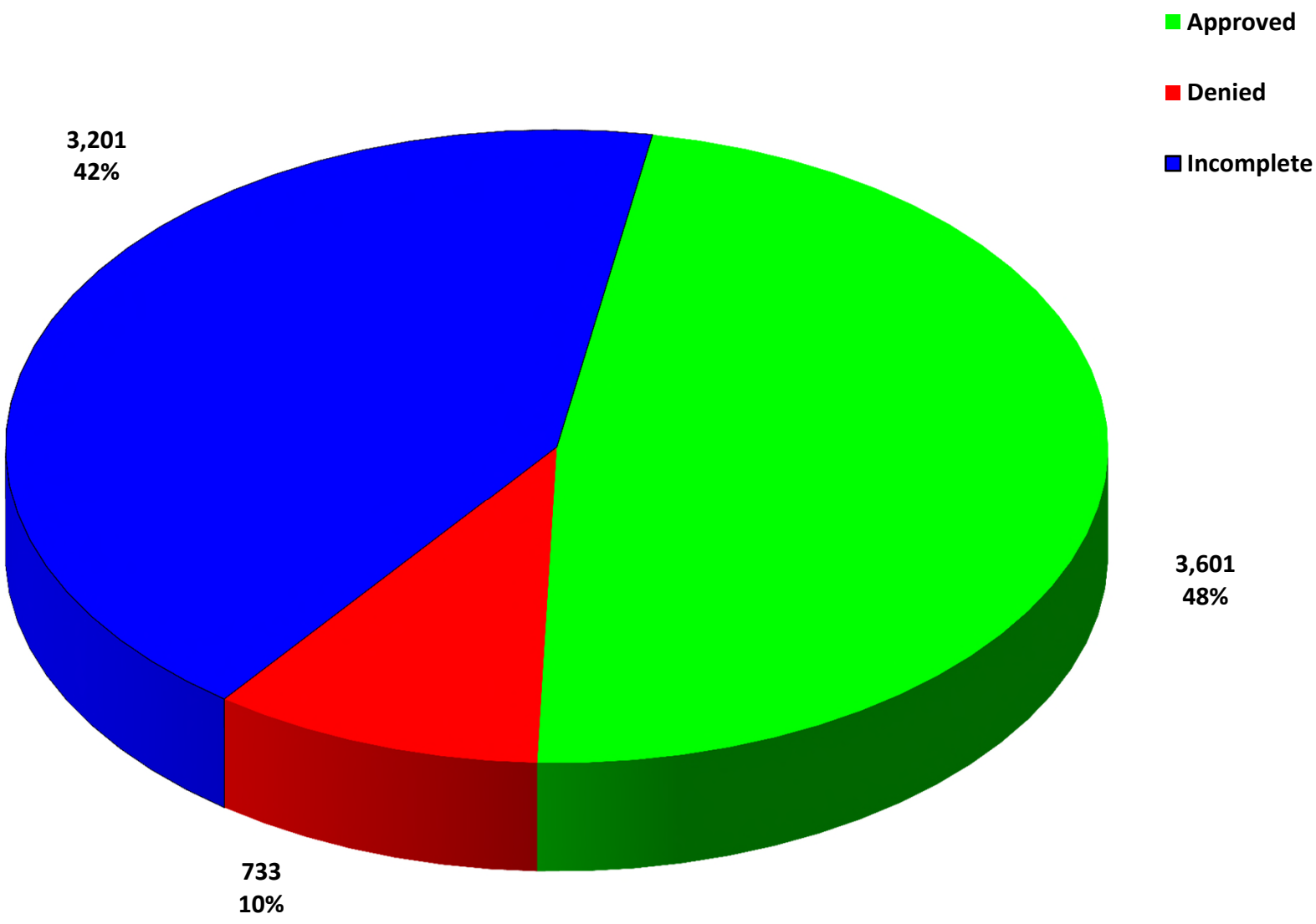
NO ACTION REQUIRED.

Recommendation 7: Drug Utilization Review of Ophthalmic Anti-Inflammatory Medications

NO ACTION REQUIRED.

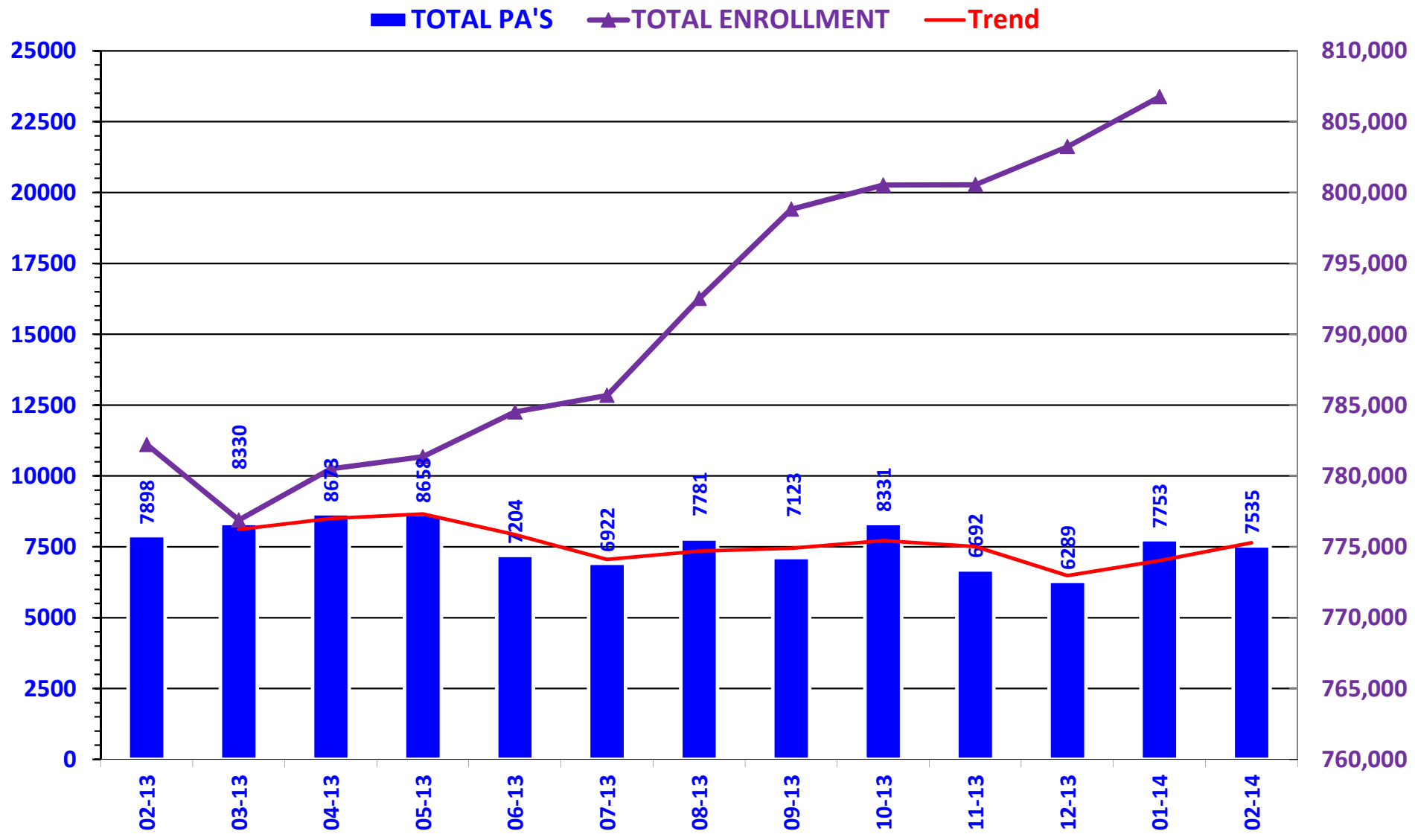
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY



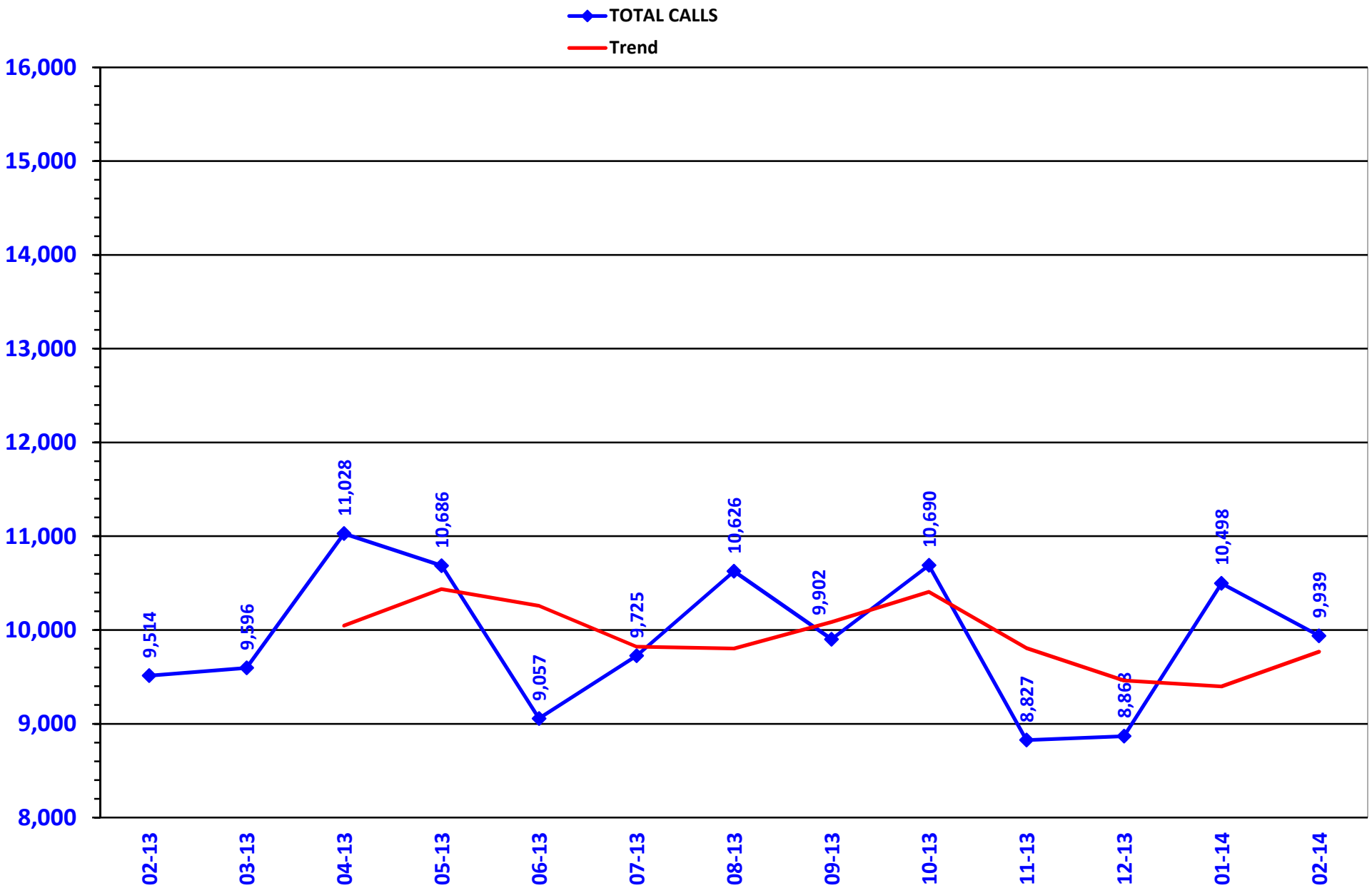
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: FEBRUARY 2013– FEBRUARY 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
FEBRUARY 2013- FEBRUARY 2014



Prior Authorization Activity

2/1/2014 Through 2/28/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	361	163	10	188	357
Analgesic - NonNarcotic	10	1	2	7	360
Analgesic, Narcotic	370	202	20	148	233
Angiotensin Receptor Antagonist	33	4	7	22	360
Antiasthma	291	168	10	113	323
Antibiotic	32	5	3	24	77
Anticoagulant	71	47	0	24	342
Anticonvulsant	71	29	4	38	317
Antidepressant	250	55	28	167	318
Antidiabetic	120	48	10	62	359
Antifungal	12	1	2	9	4
Antihistamine	161	126	3	32	350
Antimigraine	77	29	11	37	347
Antiplatelet	18	13	1	4	302
Antiulcers	229	47	72	110	166
Anxiolytic	97	70	2	25	238
Atypical Antipsychotics	400	203	19	178	341
Benign Prostatic Hypertrophy	10	0	3	7	0
Biologics	69	38	3	28	297
Bladder Control	58	3	18	37	358
Botox	25	17	4	4	341
Calcium Channel Blockers	18	6	0	12	217
Cardiovascular	40	19	3	18	220
Chronic Obstructive Pulmonary Disease	23	7	3	13	311
Dermatological	106	19	30	57	120
Endocrine & Metabolic Drugs	60	45	0	15	144
Erythropoietin Stimulating Agents	29	14	0	15	93
Fibromyalgia	135	34	16	85	342
Gastrointestinal Agents	134	29	19	86	127
Glaucoma	13	4	1	8	229
Growth Hormones	69	50	3	16	147
HFA Rescue Inhalers	60	18	4	38	339
Insomnia	59	11	15	33	209
Multiple Sclerosis	36	18	2	16	245
Muscle Relaxant	97	32	34	31	76
Nasal Allergy	100	9	28	63	183
Neurological Agents	54	33	5	16	351
Nsaids	119	14	15	90	279
Ocular Allergy	28	4	7	17	291
Ophthalmic Anti-infectives	21	0	2	19	0
Osteoporosis	25	7	5	13	360
Other*	153	35	25	93	203
Otic Antibiotic	25	7	2	16	8
Pediculicide	88	36	12	40	15
Prenatal Vitamins	18	0	2	16	0
Statins	65	19	10	36	352
Stimulant	1,234	480	100	654	324
Suboxone/Subutex	163	121	2	40	76
Synagis	143	91	17	35	47
Testosterone	76	13	7	56	357
Topical Antifungal	47	1	23	23	35
Topical Corticosteroids	114	2	39	73	48
Vitamin	50	8	27	15	310
Pharmacotherapy	80	67	0	13	78
Emergency PAs	0	0	0	0	
Total	**6,247**	**2,522**	**690**	**3,035**	

* Includes any therapeutic category with less than 10 prior authorizations for the month.

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Overrides					
Brand	130	114	5	11	96
Cumulative Early Refill	4	4	0	0	156
Dosage Change	326	297	1	28	4
High Dose	2	1	0	1	359
Ingredient Duplication	26	20	0	6	4
Lost/Broken Rx	74	73	0	1	4
NDC vs Age	8	8	0	0	270
Nursing Home Issue	92	86	0	6	5
Other*	28	25	0	3	5
Quantity vs. Days Supply	548	426	20	102	251
Stolen	2	2	0	0	3
Temporary Unlock	28	12	14	2	27
Third Brand Request	22	14	3	5	71
Wrong D.S. on Previous Rx	2	1	0	1	358
Overrides Total	**1,288**	**1,079**	**43**	**166**	
Total Regular PAs + Overrides	**7,535**	**3,601**	**733**	**3,201**	

Denial Reasons	
Unable to verify required trials.	2,862
Does not meet established criteria.	760
Lack required information to process request.	387

Other PA Activity	
Duplicate Requests	475
Letters	3,332
No Process	111
Changes to existing PAs	604
Partials	771

* Includes any therapeutic category with less than 10 prior authorizations for the month.

Retrospective Drug Evaluation: Focusing on Safety

Overview of FDA Safety Alerts

Overview of Safety Alerts

Oklahoma Health Care Authority
March 2014

Introduction[1-10]

The following are recent FDA safety alerts included for the DUR Board's consideration. SoonerCare specific data may be presented where applicable. The College will make recommendations as well as take recommendations from the DUR Board.

Date	Drug	Issue
8/29/2013	**Fingolimod (Gilenya®)**	**Rare and serious brain infection**
Issue Details: The FDA received a report of a European patient developing progressive multifocal leukoencephalopathy (PML) after taking fingolimod. PML is caused by John Cunningham (JC) virus which can cause damage to the myelin sheath covering the brain in people with compromised immune systems. **FDA Recommendations:** Currently the FDA is investigating the issue and will communicate their findings and conclusions upon completion of their evaluation. Patients should not stop taking Gilenya® at this time **Evaluation:** Review of hospital and pharmacy data for calendar year 2013 reveals 194 pharmacy claims for fingolimod for 27 members. Five members were hospitalized with an ICD-9 diagnosis code 046.3 (PML), however, none were taking fingolimod, nor were they diagnosed with multiple sclerosis.		

Date	Drug	Issue
9/25/2013	**Rituximab (Rituxan®), Ofatumumab (Arzerra®)**	**Risk of reactivation of Hepatitis B (HBV) infection.**
Issue Details: A Drug Safety Communication has been issued after continued surveillance showed persistent incidence of reactivation of HBV infections despite the warning already contained in the drug label. **FDA Recommendations:** A Black Box warning has been added to the labels of both drugs. The FDA recommends that all patients be screened for HBV infection before starting either drug. Additionally the FDA recommends expert consultation for at risk patients, monitoring patients with history of HBV for symptoms while on the medications, and discontinuing the drug if reactivation occurs. **Evaluation:** Review of claims data revealed five SoonerCare members with paid claims of rituximab since 1/1/13. One member was noted to have history of Hepatitis C, however none were noted to have history of HBV. There have been no pharmacy claims for ofatumumab since its release in June 2011.		

Date	Drug	Issue
10/31/2013	**Ezogabine (Potiga®)**	**Retinal abnormalities and potential vision loss/skin discoloration**

Issue Details: The FDA has received reports of fundoscopic abnormalities in patients taking ezogabine, a seizure medication, including perivascular pigmentation in the retinal periphery. Ezogabine was also found to cause permanent blue discoloration of the skin after prolonged use.
FDA Recommendations: A Drug Safety Communication issued 4/26/13 has been upgraded to a Boxed Warning regarding the risk of retinal damage. Patients taking ezogabine should have an eye exam before starting the medication and every six months while on treatment. The FDA also advises that ezogabine be limited to patients who have failed alternative therapy, and when the benefit outweighs the risk.
Evaluation: Review of claims data revealed 11 members on ezogabine in calendar year 2013, three with a diagnosis of visual disturbances. Ezogabine was discontinued for two of these members; however the third member continues to be on this medication. The diagnosis in that member's claims was noted to be 368.15 (Other Visual Distortions And Entoptic Phenomena), leading to uncertainty in determining if related to the above issue. All prescribers of ezogabine were neurologists.

Date	Drug	Issue
11/25/2013	**Rosiglitazone (Avandia®)**	**Restrictions removed**

Issue Details: Evaluation of recent data indicates no increased risk of heart attack when compared to metformin and sulfonylurea therapy**.**
FDA Recommendations: FDA requires removal of prescribing and dispensing restrictions for rosiglitazone and rosiglitazone-containing drugs. The rosiglitazone REMS program is also to be modified, removing restrictions on distribution and removing enrollment requirement. Prescribers should be trained regarding the cardiovascular risks of rosiglitazone.

Date	Drug	Issue
12/3/2013	**Clobazam (Onfi®)**	**Serious skin reaction**

Issue Details: A Drug Safety Communication was issued regarding possibility of Stevens-Johnsons Syndrome and toxic epidermal necrosis (TEN) with the use of clobazam. These reactions can occur at any time during treatment, but are seen most often in the first 8 weeks of therapy or when clobazam is stopped and then restarted. All cases reported to the FDA resulted in hospitalization, with one case of blindness, and one death.
FDA Recommendations: The Warnings/Precaution sections of the product label and the Medication Guide have been changed. Health care professionals should closely monitor their patients and should discontinue use of clobazam and consider an alternate therapy at the first sign of rash, unless it is clearly not drug-related.
Evaluation: From 1/1/13 to 12/31/13, 192 SoonerCare members had paid claims for clobazam, written by 63 different prescribers. 24 of the prescribers were neurologists. Examination of hospital diagnosis codes did not reveal any members taking clobazam to have been hospitalized with Stevens-Johnson Syndrome or toxic epidermal necrosis in 2013.

Date	Drug	Issue
12/20/2013	**Ponatinib (Iclusig®)**	**Risk of blood clots and narrowing of blood vessels**
Issue Details: Investigation of the leukemia drug revealed increased frequency of blood clots and narrowing of blood vessels in extremities, heart, and brain. Fatal and serious adverse events have occurred as early as two weeks from initiation of therapy. No determination has been made if this is related to dose or duration. **FDA Recommendations:** 10/31/2013 – The FDA asked the manufacturer to suspend marketing and sales of the drug. 11/5/2013 – The FDA provided instructions for obtaining ponatinib for prescribers whose patients are responding favorably to the drug. 12/20/2013 – The FDA approved resuming of marketing with new required safety measures for use of ponatinib, including limited indications, label changes, medication guide, and REMS program. The manufacturer will continue to monitor.		

Date	Drug	Issue
1/8/2014	**Sodium Phosphate OTC Products (Fleet, Store Brand, And Generic Products)**	**Risk of severe dehydration with damage to kidneys and heart, and possible death**
Issue Details: Reports of use of more than one dose in 24 hours of OTC sodium phosphate oral solutions and enemas, causing severe dehydration and electrolyte imbalance, with resultant damage to kidneys and heart, and in some cases death. **FDA Recommendations:** Consumers and healthcare professionals should always read Drug Facts label for OTC sodium phosphate drugs and use as recommended on the label. Most cases of severe harm occurred when a larger dose than recommended was taken, or a second dose was taken in the same day. Oral products should not be given to children 5 years and younger; rectal formulations should not be given to children younger than 2 years of age.		

Date	Drug	Issue
1/14/2014	**Acetaminophen (APAP)**	**Risk of liver injury**
Issue Details: Severe liver injury can result from unintentional overdoses of APAP. Overdose can occur when patients take more APAP containing medication than prescribed in a 24-hour period. Overdose is more likely when patients take more than one APAP-containing drug at the same time including OTC products. Doses greater than 4 grams per day of APAP have not been found to outweigh the risk of liver injury. **FDA Recommendations:** The FDA recommends that prescribers write for combination drugs containing no more than 325 mg of APAP. The FDA also recommends that drug products containing more than 325 mg of APAP be withdrawn from the market in the near future. **Evaluation:** SoonerCare has initiated ingredient duplication edits when multiple claims for APAP-containing medications are attempted for its members within a designated timeframe. An ingredient duplication petition is now required when the APAP duplication occurs.		

Date	Drug	Issue
1/31/2014	**Testosterone**	**Risk of stroke, heart attack, death**
Issue Details: Two separate studies suggested the possibility of increased risk of stroke, heart attack, and death, in men taking testosterone products. **FDA Recommendations:** The FDA will continue to investigate the possible link between testosterone and the risk of cardiovascular events. Men currently taking testosterone should not stop taking their prescribed medications without discussing with their physician. Health professionals should weigh the benefits versus the risks before prescribing testosterone. **Evaluation:** Currently 346 SoonerCare members are utilizing testosterone products. All testosterone products require prior authorization for SoonerCare members. The petition must be submitted along with laboratory documentation of low testosterone levels.		

Date	Drug	Issue
2/11/2014	**Saxagliptin (Onglyza®, Kombiglyze™ XR)**	**Risk of heart failure (HF)**
Issue Details: Study in NEJM reported increased rate of hospitalization for HF with use of saxagliptin. **FDA Recommendations:** The FDA has requested clinical trial data from the manufacturer of saxagliptin to evaluate possible association between this drug and the incidence of HF. Patients currently taking saxagliptin should not stop taking the drug. **Evaluation:** There were 161 SoonerCare members utilizing these drugs in calendar year 2013; 120 on Onglyza® and 44 on Kombiglyze™ XR. Of those 161 members on a saxagliptin product, 14 had a diagnosis of HF and 4 had hospital claims that included HF.		

[1] FDA Drug Safety Communication (fingolimod) available online at: - http://www.fda.gov/drugs/drugsafety/ucm366529.htm Last revised: 8/30/2013. Last accessed: 2/20/2014

[2] Arzerra (ofatumumab) and Rituxan (rituximab): Drug Safety Communication available online at http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm369846.htm Last revised: 9/25/2013. Last accessed: 2/20/2014

[3] FDA Drug Safety Communication (ezogabine) available online at http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm349847.htm Last revised: 11/18/2013. Last accessed: 2/20/2014.

[4] FDA Drug Safety Communication (rosiglitazone) available online at: http://www.fda.gov/Drugs/DrugSafety/ucm376389.htm Last revised: 1/9/2014. Last accessed: 2/20/2014

[5] FDA Drug Safety Communication (clobazam) available online at http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm377340.htm Last revised: 12/3/2013. Last accessed: 2/20/2014

[6] FDA Drug Safety Communication (ponatinib) available online at http://www.fda.gov/Drugs/DrugSafety/ucm379554.htm Last revised: 1/7/2014. Last accessed: 2/20/2014

[7] FDA Drug Safety Communication (sodium phosphate OTC) available online at http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm380833.htm Last revised: 1/8/2014. Last accessed: 2/25/2014.

[8] FDA Drug Safety Communication (acetaminophen) available online at http://www.fda.gov/Drugs/DrugSafety/ucm381644.htm Last revised: 1/14/2014. Last accessed: 2/25/2014.

[9] FDA Drug Safety Communication (testosterone) available online at http://www.fda.gov/Drugs/DrugSafety/ucm383904.htm Last revised: 2/6/2014. Last accessed: 2/25/2014.

[10] FDA Drug Safety Communication (saxagliptin) available online at http://www.fda.gov/Drugs/DrugSafety/ucm385287.htm Last revised: 2/12/2014. Last accessed: 2/25/2014.

Appendix C

Vote to Prior Authorize Adempas® (Riociguat) And Opsumit® (Macitentan)

Oklahoma Health Care Authority
March 2014

Recommendations

The College of Pharmacy recommends prior authorization of the following medications:

Adempas® (Riociguat) Approval Criteria:

1. FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension
    a. Members with a diagnosis of pulmonary arterial hypertension must have previous failed trials of at least one of each of the following categories:
        i. Revatio® (sildenafil) or Adcirca® (tadalafil); and
        ii. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    b. Members with a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) must currently be on anticoagulation therapy; and
2. Medical supervision by a pulmonary specialist and/or cardiologist; and
3. Member must not be on concurrent PDE-5 inhibitor therapy; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Adempas® REMS program.
5. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

1. FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan), or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist and/or cardiologist; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Opsumit® REMS program.
5. A quantity limit of 30 tablets per 30 days will apply.

Appendix D

Vote to Prior Authorize Select Cephalosporins

Oklahoma Health Care Authority
March 2014

Recommendations

Prior authorize cefixime (Suprax®), ceftibuten (Cedax®), and cefditoren (Spectracef®) with the criteria presented below. A pre-emptive educational initiative will be sent to medical as well as pharmacy providers before these prior authorizations become effective.

Suprax® (Cefixime), Cedax® (Ceftibuten), and Spectracef® (Cefditoren) Approval Criteria:

1. Indicated diagnosis or infection known to be susceptible to requested agent; and
2. Patient specific, clinically significant reason why member cannot use cephalexin and cefdinir, or other cost effective therapeutic equivalent medication(s).

Appendix E

Fiscal Year 2013 Annual Review of Erythropoiesis Stimulating Agents

Oklahoma Health Care Authority
March 2014

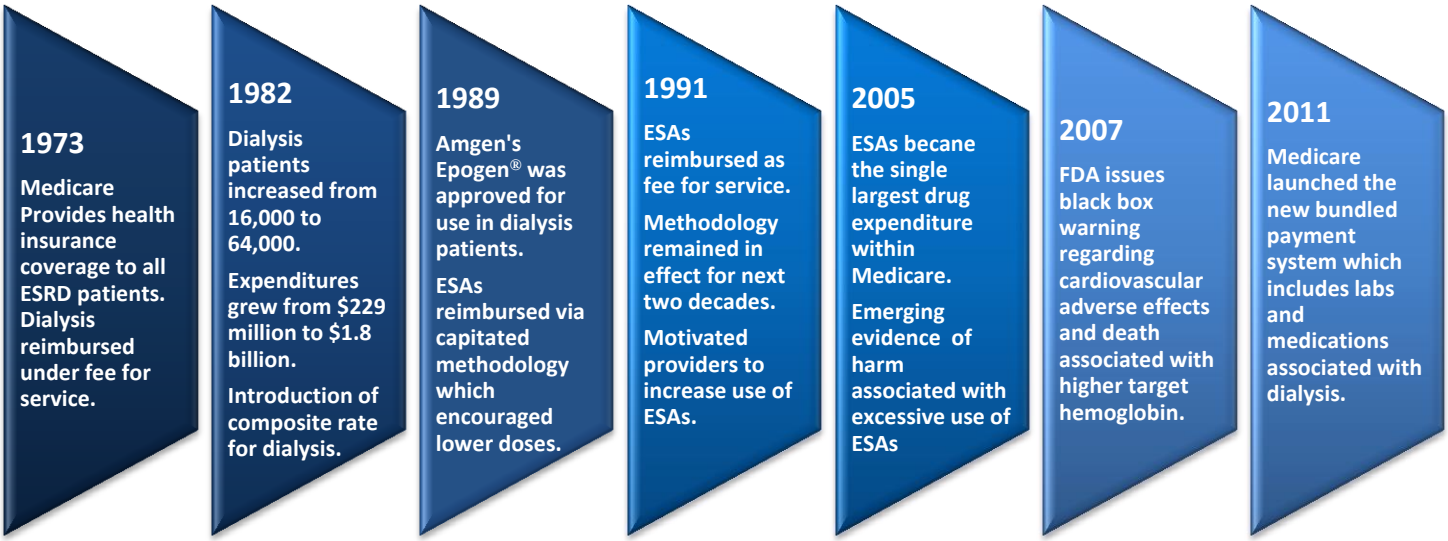
Introduction

This category has been in effect since March 2009. In July 2012 all use of erythropoiesis stimulating agents (ESAs) by members on dialysis for the diagnosis of end stage renal disease (ESRD) became part of a bundled payment with the patient's dialysis and was no longer reimbursed separately. Use of these products for patients on dialysis was no longer under the prior authorization process. The following criteria remain effective for other diagnoses.

Erythropoiesis Stimulating Agents Approval Criteria:

1. FDA approved indication for specific products.
    a. Treatment of anemia in zidovudine-treated HIV-infected patients
    b. Treatment of anemia in cancer patients on chemotherapy
        i. Myelosuppressive chemotherapy-induced anemia (non-curative)
    c. Reduction of allogeneic blood transfusion in surgery patients
2. Initiation Criteria
    a. Most recent hemoglobin level and date obtained must be included on petition.
    b. Hemoglobin (Hb) level less than 10 g/dL.
    c. Each approval will be for 16 weeks in duration. Authorization can be granted for up to 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen. Authorization for surgery patients will be for a maximum of 4 weeks.
3. Continuation Criteria:
    a. Continue dose if Hb is ≤ 11.0 g/dL.
    b. If Hb is increasing and approaching 11.0 g/dL then reduce dose.
    c. If more than 1 g/dL increase (but Hb not greater than upper limits listed below) has occurred in a 2 week period, reduce dose by 25 to 50 %.
4. Discontinuation Criteria:
    a. ESRD – Discontinue treatment if Hb is at or above 11.0 g/dL.
    b. All others – Discontinue treatment if Hb is at or above 11.0 g/dL.
    c. If a minimum increase of 1 g/dL has not been achieved after initial 8 weeks of therapy for anemia associated with chemotherapy and 12 weeks of therapy for ESRD.
5. Reinitiation Criteria:
    a. If Hb decreases to ≤ 10 g/dL then therapy may be reinitiated at 25 to 50% of the prior dose.

Timeline: Medicare Reimbursement of Dialysis Services[1]



Over the years the Oklahoma Health Care Authority has used Medicare's reimbursement methodologies as the guiding standard for reimbursement of dialysis services and associated costs. On July 1, 2012 bundling of pharmacy and laboratory costs into the dialysis reimbursement composite rate was implemented in the SoonerCare population. This report is the first attempt to evaluate the effects of bundling ESAs into the dialysis reimbursement and how this might affect general cost trends and patient factors in the SoonerCare population.

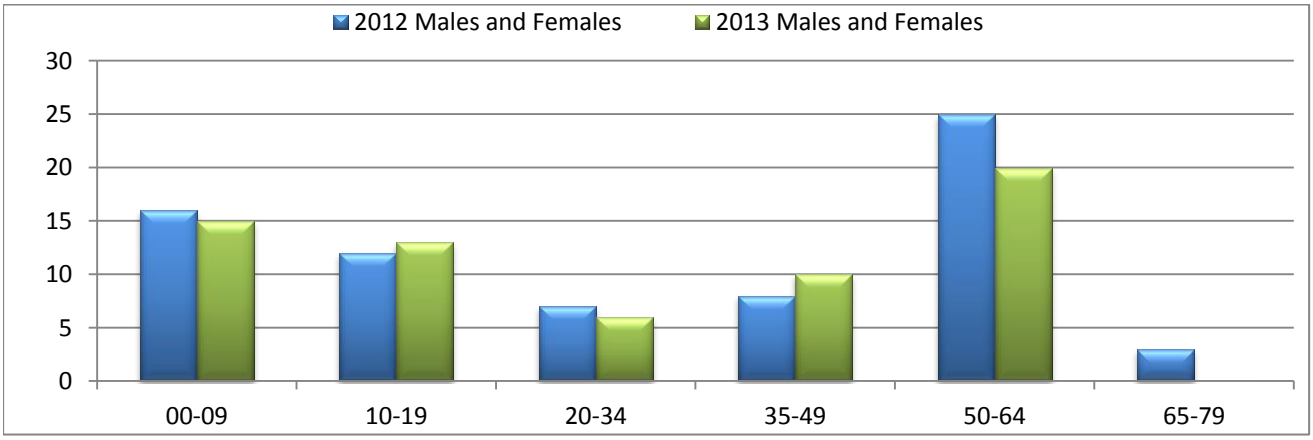
Utilization of Erythropoiesis Stimulating Agents Under the Pharmacy Benefit

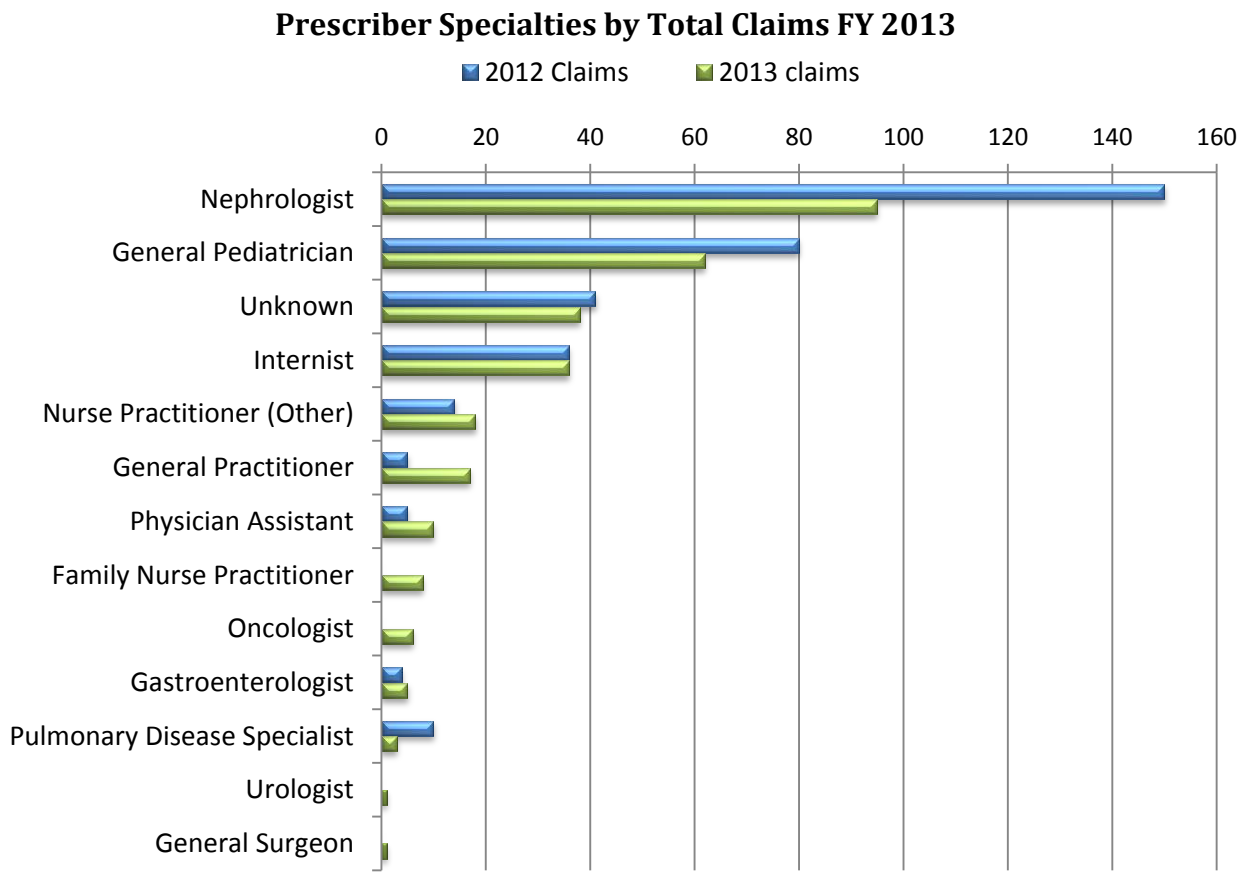
Comparison of Fiscal Years

Fiscal Year	Members*	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2012	71	359	$325,185.23	$905.81	$51.07	732	6,368
2013	64	300	$378,345.98	$1,261.15	$67.43	776	5,611
% Change	-9.90%	-16.40%	16.30%	39.20%	32.00%	6.00%	-11.90%
Change	-7	-59	$53,160.75	$355.34	$16.36	44	-757

*Total number of unduplicated members.

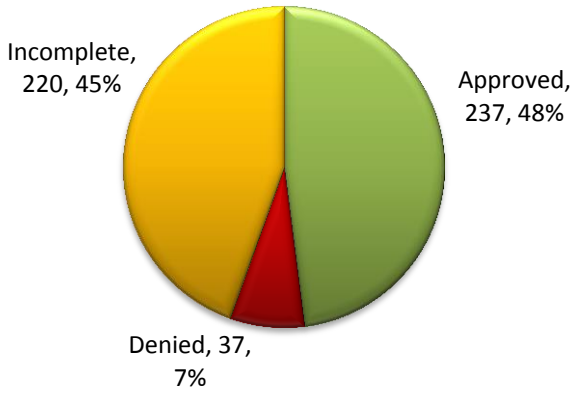
Demographics of Members Utilizing ESAs

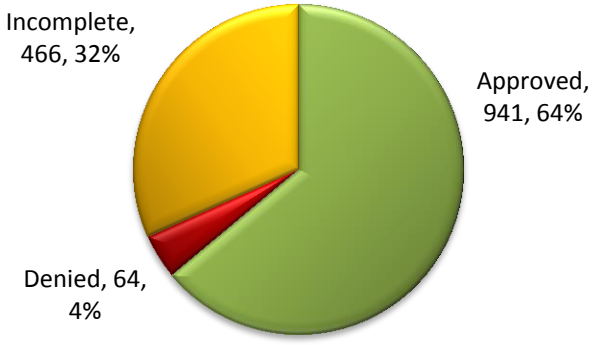




Prior Authorization of Erythropoiesis Stimulating Agents: Pharmacy and Medical

There were a total of 494 petitions submitted for this medication during fiscal year 2013. This is a significant reduction from fiscal year 2012, which totaled 1,471 petitions. The following chart shows the status of the submitted petitions between the fiscal years.





Utilization of Dialysis Services Under the Medical Benefit

Comparison of Fiscal Years

Fiscal Year	Members*	Claims	Cost	Cost/Claim	Cost/Member
2012	371	5,303	$4,535,132.59	$855.20	$12,224.08
2013	328	2,036	$4,802,386.08	$2,358.74	$14,641.42
% Change	-11.5%	-61.6%	5.89%	175.81%	19.78%
Change	-43	-3,267	$267,253.49	$1,503.53	$2,417.34

*Total number of unduplicated members.

Trends in Hospitalizations for Members with ESRD on Dialysis

Fiscal Year	Members*	Claims	Cost	Cost/Visit	Cost/Member	% of Members
2012	260	845	$8,934,301.77	$10,573.14	$34,362.70	70.08%
2013	229	705	$8,352,838.23	$11,848.00	$36,475.28	69.82%
% Change	-11.92%	-16.57%	-6.51%	12.06%	6.15%	-0.37%
Change	-31	-140	-$581,463.54	$1,274.86	$2,112.58	-0.26%

*Total number of unduplicated members.

Trends in Blood Transfusions for Members with ESRD on Dialysis

Fiscal Year	Members*	Claims	Cost	Cost/Claim	Cost/Member	% of Members
2012	31	59	$18,196.93	$308.42	$587.00	8.36%
2013	23	44	$21,261.36	$483.21	$924.41	7.01%
% Change	-25.81%	-25.42%	16.84%	56.67%	57.48%	-16.03%
Change	-8	-15	$3,064.43	$174.79	$337.41	-1.34%

*Total number of unduplicated members.

Trends in Total Costs for Members with ESRD on Dialysis

Fiscal Year 2013 (n=328)		Fiscal Year 2012 (n=371)	
Same Day Services	Total Costs	Same Day Services	Total Costs
B - HCFA 1500 XOVER CLAIMS	$280.76	B - HCFA 1500 XOVER CLAIMS	$309.91
C - UB92 OUTP XOVER CLAIMS	$638.48	C - UB92 OUTP XOVER CLAIMS	$305.62
D - DENTAL CLAIMS	$173.28	D - DENTAL CLAIMS	$207.93
H - HOME HEALTH CLAIMS	$7,734.20	H - HOME HEALTH CLAIMS	$6,832.59
I - INPATIENT CLAIMS	$75,842.66	I - INPATIENT CLAIMS	$166,276.00
L - LONG TERM CARE CLAIMS	$154,598.50	L - LONG TERM CARE CLAIMS	$129,248.91
M - HCFA 1500 CLAIMS	$138,601.00	M - HCFA 1500 CLAIMS	$332,147.56
O - OUTPATIENT CLAIMS	$4,812,548.65	O - OUTPATIENT CLAIMS	$4,725,636.99
P - PHARMACY CLAIMS	$92,248.95	P - PHARMACY CLAIMS	$136,552.87
Q - COMPOUND DRUG CLAIMS	$26.88	Q - COMPOUND DRUG CLAIMS	$1,076.71
Total	$5,282,693.36	Total	$5,498,595.09
Costs /Member	$16,105.77	Costs/Member	$14,821.01

Market News and Updates

Patent Expirations

- Epogen® (Epoietin Alfa) by Amgen Pharmaceuticals – August 2013
- Procrit® (Epoietin Alfa) by Janssen Pharmaceuticals – August 2013
- Aranesp® (Darbepoietin) by Amgen - 2024

Over the past two decades Epogen® has empowered Amgen Pharmaceuticals to become the largest biotech company in the world. In the late 1980s both Amgen and Janssen (now part of Johnson and Johnson) competed to be the first pharmaceutical company to bring erythropoietin to market. After being defeated by Amgen, Janssen entered into an agreement to market their epoietin alfa product, Procrit®, for oncology indications only. However, SoonerCare does not mandate use of a specific epoietin product. Amgen's growth was further increased by the release of Aranesp®, a longer acting version of epoietin, that can be dosed weekly and up to every 4 weeks in some instances.[2]

Several pharmaceutical companies have attempted to challenge the monopoly held by Amgen through the years. Roche pharmaceuticals came close in 2007 when it received FDA approval for its pegylated version of erythropoietin, Mircera® (methoxy polyethylene glycol epoietin beta), which has a duration of action six times longer than Aranesp®. Shortly after Mircera®'s FDA approval, Amgen won its litigation on patent infringement against Roche and Mircera® never came to market. In Europe, where there has been a biosimilar approval process in place for some time, Mircera® has been marketed since 2007. In the United States Mircera® will not be marketed until the middle of 2014.[3]

In 2011, Affymax, a small biotechnology company received FDA approval for Omontys® (peginesatide), which is marketed with Takeda Pharmaceuticals. It faced no patent litigation from Amgen. Unfortunately, it was voluntarily withdrawn from the market 11 months later, in early 2013, due to reports of serious hypersensitivity reactions, including anaphylaxis that may be life-threatening.[4]

Discussion

1. Before interpreting data regarding ESRD patients, keep in mind that Medicaid, as well as private payers, are required to cover up to approximately 2 years of dialysis treatments before the patient can be transitioned to Medicare. As such, the SoonerCare ESRD population is constantly changing, which makes it difficult to identify clear trends.
2. The utilization of ESAs under the pharmacy benefit revealed slight alterations in utilization parameters after the implementation of bundled payments, such as:
    a. Less claims per member
    b. Higher doses/units per claim
    c. Increases in overall cost of the ESA medications, due partly to the increase of direct costs of the medication

    d. Shift of some utilization from pharmacy to medical by ESRD patients who might have received ESAs via the pharmacy – evidenced by the decrease in prescriptions by nephrologists and slight decrease in the higher aged demographics.
3. Minimal costs savings may have been realized by both OHCA and healthcare providers in bypassing the prior authorization process for ESAs under the bundled payment methodology.
4. Utilization of dialysis and related services under the medical benefit revealed the following trends, some of which may be concerning:
    a. Decrease in overall members utilizing dialysis services
    b. Overall increase in total dialysis related costs
    c. Increase in overall costs per member per year for ESRD patients – evidenced by a 19% increase in dialysis related costs, and approximately 9% increase in same day services.
5. There is a concern that bundling the ESAs into the dialysis reimbursement would de-incentivize the use of ESAs, even when needed, which may result in increases in hospitalizations and/or blood transfusions. However, the FY 2013 data showed that there were actually decreases from FY 2012 in both the percent of patients hospitalized and percent of patients who needed blood transfusions in the dialysis population.
6. The last parameter of consideration is the loss of rebates associated with the bundling methodology. CMS rules indicate that manufacturers cannot be invoiced separately for rebates when the medication is part of a bundled reimbursement.

Conclusions and Recommendations

From the analysis of data presented above it appears that the recent transition to the bundled reimbursement methodology has resulted in an overall increase in costs for OHCA. Specific to the bundling of ESAs this increase in cost is exacerbated by the loss of rebates that would have been received had the medications been billed separately and could be invoiced to the manufacturer.

It is recommended that OHCA explore ways to implement reimbursement methodologies that take quality of care and clinical endpoints into consideration similar to CMS's novel payment reduction reimbursement structure based on Hb and urea reduction fractions. However, OHCA should proceed with caution and consider altering this methodology to incentivize healthcare providers to achieve clinical/quality targets, as the current CMS methodology has been criticized for having "all sticks and no carrots."[5]

It is also recommended that OHCA explore the possibility of carving ESAs out of the bundled payment package, at least until the impending generic competition is well under way for this class of medications. This will allow for a more cost-effective pricing standard to be used, even if OHCA chooses to include it as part of the bundled payment methodology in the future.

[1] Shailender Swaminathan, Vincent Mor, Rajnish Mehrotra, and Amal Trivedi. Medicare's Payment Strategy For End-Stage Renal Disease Now Embraces Bundled Payment And Pay-For-Performance To Cut Costs. Health Aff (Millwood). Sep 2012; 31(9): 2051–2058. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3766315/. Last revised 09/2013. Last accessed 2/27/14.

[2] Aranesp Product Information. Amgen Pharmaceuticals. Available online at: http://pi.amgen.com/united_states/aranesp/ckd/aranesp_pi_hcp_english.pdf. Last revised 12/2013. Last accessed 2/27/14.

[3] Victor Lamin, MD, Medical Director, Comprehensive Kidney Care (CKC) Management. Battling Anemia in Chronic Kidney Disease: A Look at the Challenges and the Challengers. Available at: http://www.inventivmm.com/news/events/blog/2013/10/17/battling-anemia-a-look-at-the-challenges-and-the-challengers/. Last revised October 2013. Last accessed 2/27/2013.

[4] Affymax and Takeda Announce a Nationwide Voluntary Recall of All Lots of Omontys® (Peginesatide) Injection. Available online at: http://www.takeda.com/news/2013/20130224_5664.html. Last revised 03/2013. Last accessed 2/27/14.

[5] Shailender Swaminathan, Vincent Mor, Rajnish Mehrotra, and Amal Trivedi. Medicare's Payment Strategy For End-Stage Renal Disease Now Embraces Bundled Payment And Pay-For-Performance To Cut Costs. Health Aff (Millwood). Sep 2012; 31(9): 2051–2058. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3766315/. Last revised 09/2013. Last accessed 2/27/14.

Appendix F

Calendar Year 2013 Annual Review of Insomnia Medications

Oklahoma Health Care Authority
March 2014

Current Prior Authorization Criteria

Tier 1 products are available without a prior authorization for all members 19 years of age or older. Members 18 years of age or younger are required to submit a prior authorization for consideration. All products have a quantity limit of 30 per 30 days.

Tier 2 Authorization Criteria:

1. An FDA Approved Indication; and
2. Minimum of 30 day trial with at least two Tier 1 products and documentation of attempts to correct any primary cause for insomnia; and
3. No concurrent anxiolytic benzodiazepine therapy greater than TID dosing.
4. Approval duration will be for 6 months.

Tier 3 Authorization Criteria:

1. An FDA Approved Indication; and
2. Minimum of 30 day trial with all available Tier 2 products and documentation of attempts to correct any primary cause for insomnia; and
3. No concurrent anxiolytic benzodiazepine therapy greater than TID dosing.
4. Approval duration will be for 6 months.

Insomnia Medications		
Tier 1	**Tier 2**	**Tier 3**
Estazolam (ProSom®) Flurazepam (Dalmane®) Temazepam (Restoril® 15mg & 30 mg) Triazolam (Halcion®) Zaleplon (Sonata®) Zolpidem (Ambien®)	Zolpidem CR (Ambien CR®)	Doxepin (Silenor®) Eszopiclone (Lunesta®) Temazepam[+] (Restoril® 7.5 & 22.5 mg) Ramelteon (Rozerem®) Zolpidem[+] oral spray (Zolpimist®) Zolpidem[+] SL Tabs (Edluar®) Zolpidem[+] SL Tabs (Intermezzo®)

[+] Requires special reason for use.

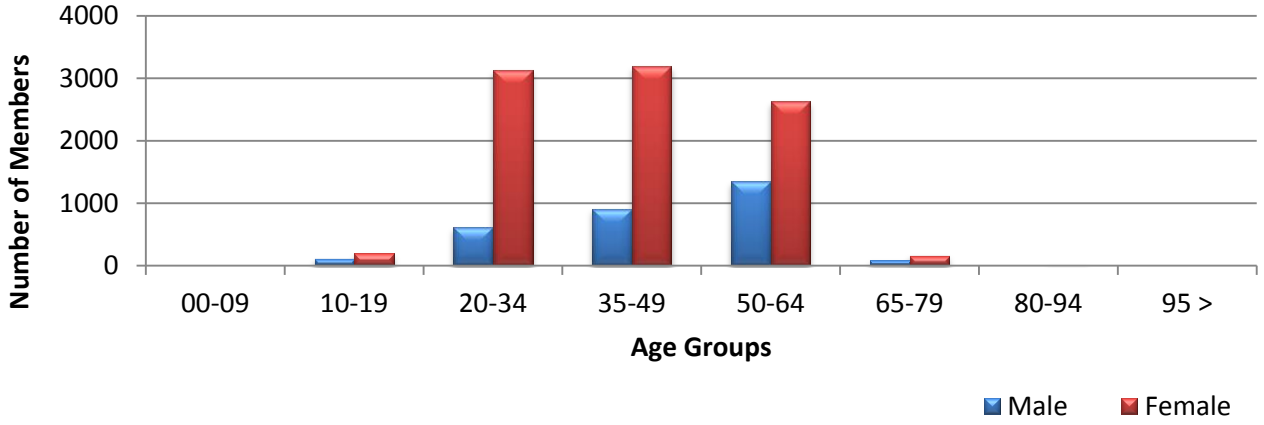
Utilization of Insomnia Medications

Comparison of Calendar Years

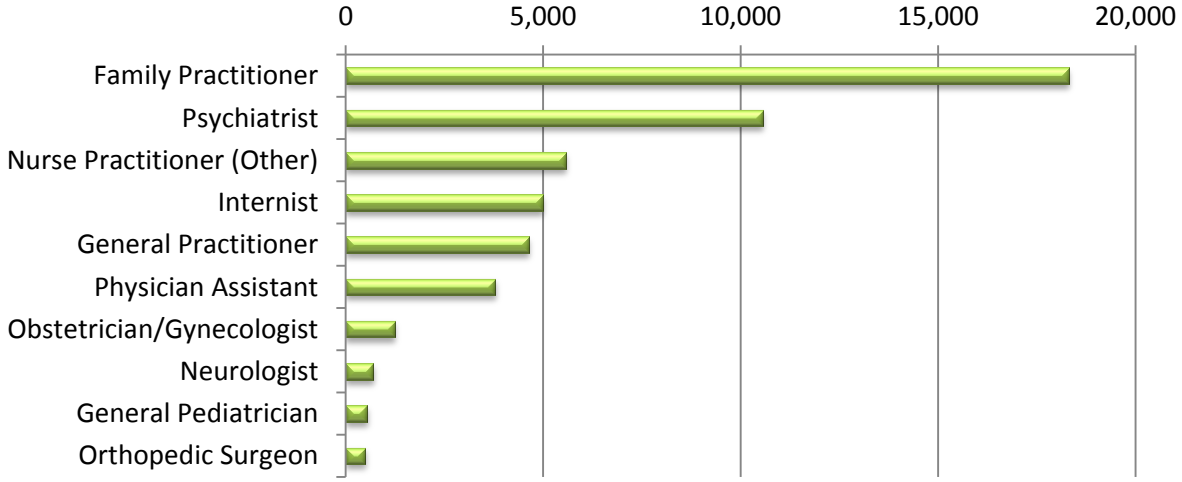
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Per-Diem Cost	Total Units	Total Days
2012	17,570	80,210	$948,700.17	$11.83	$0.41	2,328,827	2,325,864
2013	12,419	54,655	$702,236.40	$12.85	$0.45	1,574,846	1,576,539
% Change	-29.30%	-31.90%	-26.00%	8.60%	9.80%	-32.40%	-32.20%
Change	-5,151	-25,555	-$246,463.77	$1.02	$0.04	-753,981	-749,325

*Total number of unduplicated members.

Demographics of Members



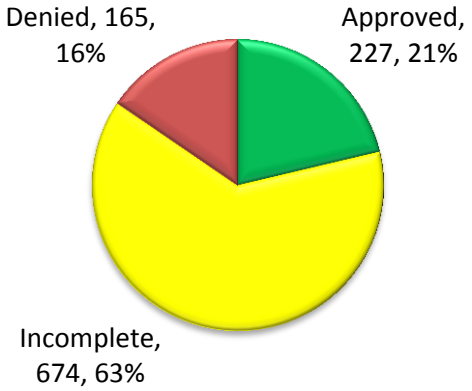
Top Prescriber Specialties of Insomnia Medications by Number of Claims



Prior Authorization of Insomnia Medications

There were a total of 1,066 petitions submitted for this category during calendar year 2013. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,2,3]

Effective January 1, 2013, Medicare Part D prescription drug plans are required to cover benzodiazepines, and to cover barbiturates used in the treatment of epilepsy, cancer, or a chronic mental disorder. Medicaid plans (including SoonerCare) were required to stop covering these products for members who are also eligible for Medicare. The effects of this change in coverage are apparent in the utilization comparison of calendar year 2012 and 2013.

Anticipated Patent Expirations

- Lunesta® (eszopiclone)- 8/2014
- Zolpimist® (zolpidem oral spray)- 10/2017
- Rozerem® (ramelteon)- 7/2019
- Edluar® (zolpidem SL tabs)- 9/2019
- Intermezzo® (zolpidem SL tabs)- 8/2029
- Silenor® (doxepin)- 4/2030

Merck & Co has one medication, suvorexant (formerly known as MK-4305), that has completed Phase 3 Clinical Trials and is currently under review by the FDA. Suvorexant has a novel mechanism of action, as it is an orexin receptor antagonist that helps facilitate sleep by blocking the action of orexins, which are neurotransmitters in the brain that regulate wakefulness, arousal, and appetite.

Recommendations

The College of Pharmacy does not recommend any changes at this time.

Utilization Details of Insomnia Medications: Calendar Year 2013

CHEMICAL NAME	BRAND NAME	CLAIMS	MEMBERS	COST	COST/ DAY	COST/ CLAIM	% COST
Zolpidem	Zolpidem 10mg tabs	31,187	7,377	$153,377.35	$0.17	$4.92	21.84%
Zolpidem	Zolpidem 5mg tabs	6,225	2,392	$31,981.99	$0.18	$5.14	4.55%
	Subtotal	**37,412**	**9,081***	**$185,359.34**	**$0.17**	**$4.95**	**26.40%**
Temazepam	Temazepam 30mg caps	7,750	1,814	$56,752.24	$0.25	$7.32	8.08%
Temazepam	Temazepam 15mg caps	3,745	1,294	$25,219.90	$0.23	$6.73	3.59%
	Subtotal	**11,495**	**2,874***	**$81,972.14**	**$0.24**	**$7.13**	**11.67%**
Triazolam	Triazolam 0.25mg tabs	1,345	628	$11,908.29	$0.44	$8.85	1.70%
Triazolam	Triazolam 0.125mg tabs	45	20	$508.00	$0.47	$11.29	0.07%
	Subtotal	**1,390**	**646***	**$12,416.29**	**$0.44**	**$8.93**	**1.77%**
Zaleplon	Zaleplon 10mg caps	951	350	$17,228.61	$0.62	$18.12	2.45%
Zaleplon	Zaleplon 5mg caps	193	117	$2,748.32	$0.62	$14.24	0.39%
	Subtotal	**1,144**	**453***	**$19,976.93**	**$0.62**	**$17.46**	**2.84%**
Flurazepam	Flurazepam 30mg caps	248	58	$1,567.79	$0.22	$6.32	0.22%
Flurazepam	Flurazepam 15mg caps	63	14	$389.78	$0.21	$6.19	0.06%
	Subtotal	**311**	**67***	**$1,957.57**	**$0.22**	**$6.29**	**0.28%**
Estazolam	Estazolam 2mg tabs	112	32	$1,336.02	$0.41	$11.93	0.19%
Estazolam	Estazolam 1mg tabs	15	6	$175.62	$0.39	$11.71	0.03%
	Subtotal	**127**	**37***	**$1,511.64**	**$0.41**	**$11.90**	**0.22%**
	TIER 1 SUBTOTAL	**51,879**	**12,204***	**$303,193.91**	**$0.20**	**$5.84**	**43.18%**
Zolpidem	Zolpidem 12.5mg ER tabs	1,644	296	$154,941.04	$3.17	$94.25	22.06%
Zolpidem	Zolpidem 6.25mg ER tabs	171	51	$15,867.32	$3.12	$92.79	2.26%
Zolpidem	Ambien CR® 12.5mg tabs	13	1	$3,512.04	$9.01	$270.16	0.50%
	Subtotal	**1,828**	**325***	**$174,320.40**	**$3.21**	**$95.36**	**24.82%**
	TIER 2 SUBTOTAL	**1,828**	**325***	**$174,320.40**	**$3.21**	**$95.36**	**24.82%**
Eszopiclone	Lunesta® 3mg tabs	590	81	$146,455.89	$8.35	$248.23	20.86%
Eszopiclone	Lunesta® 2mg tabs	138	29	$34,229.56	$8.43	$248.04	4.87%
Eszopiclone	Lunesta® 1mg tabs	17	3	$4,250.52	$8.33	$250.03	0.61%
	Subtotal	**745**	**107***	**$184,935.97**	**$8.36**	**$248.24**	**26.34%**
Ramelteon	Rozerem® 8mg tabs	176	26	$35,392.47	$6.70	$201.09	5.04%
	Subtotal	**176**	**26***	**$35,392.47**	**$6.70**	**$201.09**	**5.04%**
Temazepam	Temazepam 7.5mg caps	15	4	$1,978.84	$4.40	$131.92	0.28%
	Subtotal	**15**	**4***	**$1,978.84**	**$4.40**	**$131.92**	**0.28%**
Zolpidem	Intermezzo® 3.5mg SL tabs	9	3	$1,899.56	$7.31	$211.06	0.27%
Zolpidem	Intermezzo® 1.75mg SL tabs	1	1	$219.16	$7.31	$148.05	0.03%
Zolpidem	Edluar® 10mg SL tabs	2	2	$296.09	$4.93	$219.16	0.04%
	Subtotal	**12**	**6***	**$2,414.81**	**$6.90**	**$201.23**	**0.34%**
	TIER 3 SUBTOTAL	**948**	**140***	**$224,722.09**	**$7.97**	**$237.05**	**32.00%**
	TOTAL	**54,655**	**12,419***	**$702,236.40**	**$0.45**	**$12.85**	**100.00%**

*Total number of unduplicated members

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 2/20/14. Last accessed 2/20/14.
[2] Merck & Co.: Research Pipeline. Available online at: http://www.merck.com/research/pipeline/home.html. Last revised 10/31/13. Last accessed 2/20/14.
[3] National Sleep Foundation: Orexin receptor antagonists: A new class of sleeping pill. Available online at: http://www.sleepfoundation.org/article/orexin-receptor-antagonists-new-class-sleeping-pill. Last revised 10/2013. Last accessed 2/20/14.

Appendix G

Calendar Year 2013 Annual Review of Oral Antihistamines

Oklahoma Health Care Authority
March 2014

Current Prior Authorization Criteria

Tier 1 products are covered with no authorization necessary for members under 21 years of age. Members 21 years and older require a prior authorization with appropriate diagnosis for approval of Tier 1 products.

Tier 2 Approval Criteria:

1. A 14 day trial with all Tier 1 products within the last 30 days; and
2. Diagnosis must be for a chronic allergic condition or asthma.
3. Prior authorization will be for 360 days.

Tier 3 Approval Criteria:

1. A 14 day trial with all Tier 2 products within the last 60 days (unless no age-appropriate Tier 2 product exists); and
2. Diagnosis must be for a chronic allergic condition or asthma.
3. Prior authorization will be for 360 days.

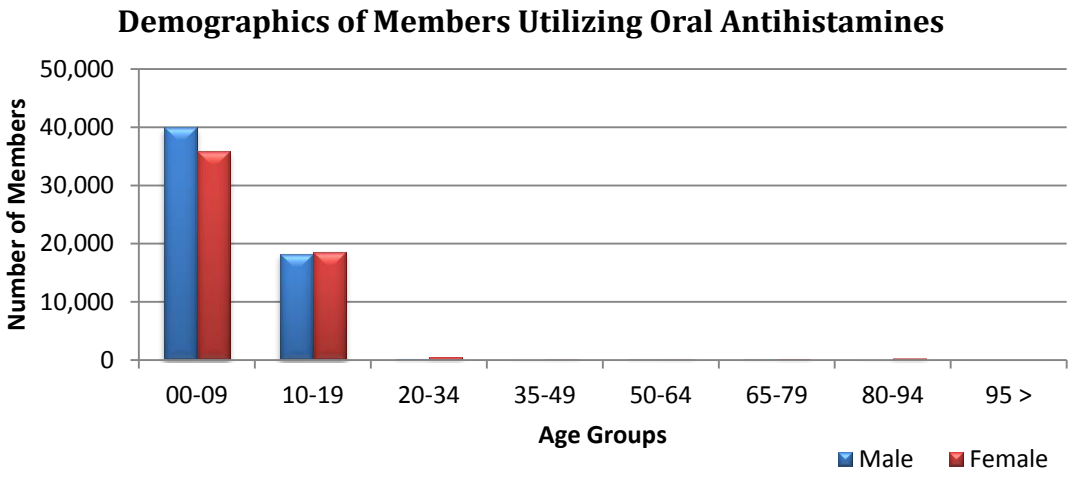
Oral Antihistamines		
Tier 1	**Tier 2**	**Tier 3**
OTC Loratadine (Claritin®)	levocetirizine (Xyzal®)	desloratadine (Clarinex®)
OTC Cetirizine (Zyrtec®)		clemastine (Tavist®)

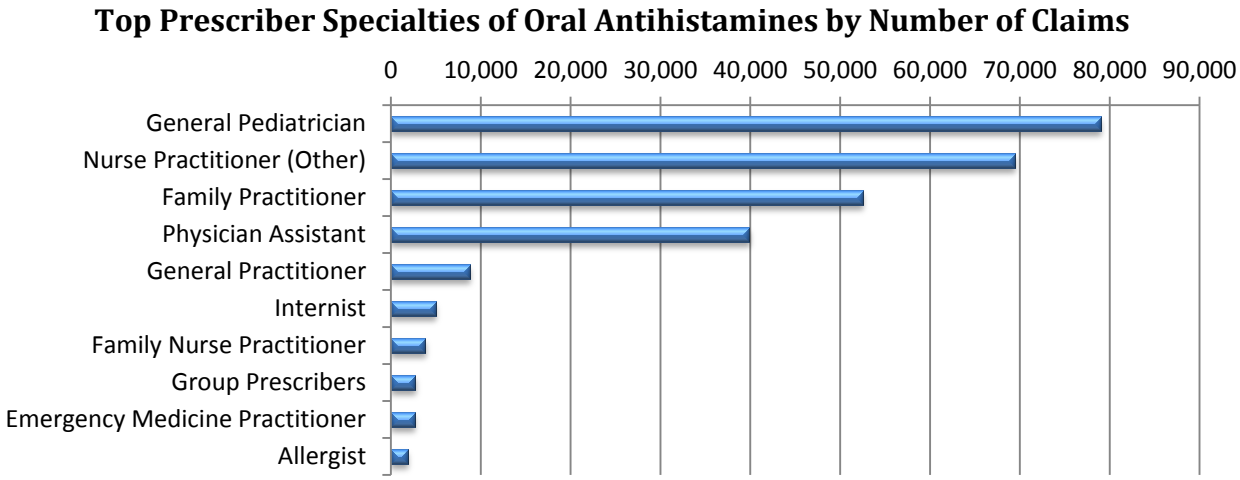
Utilization of Oral Antihistamines

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	113,003	268,336	$2,370,159.12	$8.83	$0.30	22,591,990	8,028,552
2013	115,168	274,450	$2,599,667.41	$9.47	$0.31	23,459,576	8,313,651
% Change	**1.90%**	**2.30%**	**9.70%**	**7.20%**	**3.30%**	**3.80%**	**3.60%**
Change	**2,165**	**6,114**	**$229,508.29**	**$0.64**	**$0.01**	**867,586**	**285,099**

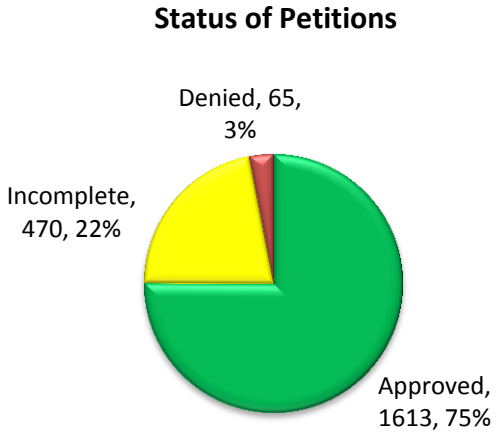
*Total number of unduplicated members.





Prior Authorization of Oral Antihistamines

There were a total of 2148 petitions submitted for this medication during calendar year 2013. The following chart shows the status of the submitted petitions.



Market News and Updates

FDA Update:

- November 2013: FDA added postmarketing adverse reactions to levocetirizine dosing. These include movement disorders, tics, myoclonus, and extrapyramidal symptoms.

Recommendations

The College of Pharmacy does not recommend any changes at this time.

Utilization Details of Oral Antihistamines

Chemical Name	Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Percent Cost	Cost/ Claim
Cetirizine	CETIRIZINE SYP 1MG/ML	85,248	43,782	$888,033.10	1.95	34.16%	$10.42
Cetirizine	CETIRIZINE TAB 10MG	66,944	26,394	$475,915.71	2.54	18.31%	$7.11
Cetirizine	CETIRIZINE SYP 5MG/5ML	15,754	8,270	$167,575.87	1.9	6.45%	$10.64
Cetirizine	CETIRIZINE SOL 5MG/5ML	9,739	5,735	$82,994.68	1.7	3.19%	$8.52
Cetirizine	CETIRIZINE TAB 5MG	4,702	2,033	$39,856.87	2.31	1.53%	$8.48
Cetirizine	ALL DAY ALLG TAB 10MG	1,797	972	$10,781.50	1.85	0.41%	$6.00
Cetirizine	ALL DAY ALLG SOL 5MG/5ML	1,534	773	$14,780.28	1.98	0.57%	$9.64
Cetirizine	ALL DAY ALLG SYP 1MG/ML	997	569	$8,960.43	1.75	0.34%	$8.99
Cetirizine	ALL DAY ALLG SOL 1MG/ML	665	343	$6,150.42	1.94	0.24%	$9.25
Cetirizine	ALLERGY SOL 1MG/ML	402	239	$3,136.24	1.68	0.12%	$7.80
Cetirizine	GNP ALL DAY TAB ALLERGY	105	53	$840.66	1.98	0.03%	$8.01
Cetirizine	SM ALL DAY TAB ALLERGY	47	33	$329.04	1.42	0.01%	$7.00
Subtotal		**187,934**	**89,196**	**$1,699,354.80**	**2.11**	**65.36%**	**$9.04**
Loratadine	LORATADINE TAB 10MG	44,794	17,994	$369,622.87	2.49	14.22%	$8.25
Loratadine	LORATADINE SOL 5MG/5ML	23,931	13,984	$299,310.01	1.71	11.51%	$12.51
Loratadine	LORATADINE SYP 5MG/5ML	10,700	6,490	$138,411.37	1.65	5.32%	$12.94
Loratadine	ALLERGY RELF TAB 10MG	2,141	1,122	$15,204.89	1.91	0.58%	$7.10
Loratadine	ALAVERT TAB 10MG	2,033	841	$26,930.77	2.42	1.04%	$13.25
Loratadine	ALLERGY TAB 10MG	968	401	$8,416.13	2.41	0.32%	$8.69
Loratadine	ALLERGY RELF SYP 5MG/5ML	859	554	$11,713.22	1.55	0.45%	$13.64
Loratadine	ALLERGY RELF TAB 10MG	255	149	$3,173.77	1.71	0.12%	$12.45
Loratadine	ALLERGY TAB 10MG	87	43	$1,298.98	2.02	0.05%	$14.93
Loratadine	LORATADINE TAB 10MG	55	38	$861.95	1.45	0.03%	$15.67
Loratadine	LORATADINE 10MG TAB	1	1	$6.15	1	0.00%	$6.15
Subtotal		**85,824**	**41,617**	**$874,950.11**	**2.06**	**33.64%**	**$10.19**
Tier 1 Subtotal		**273,758**	**130,813**	**$2,574,304.91**	**2.09**	**99.00%**	**$9.40**
Levocetirizine	LEVOCETIRIZI TAB 5MG	362	79	$5,513.48	4.58	0.21%	$15.23
Levocetirizine	LEVOCETIRIZI SOL 2.5/5ML	242	76	$13,770.01	3.18	0.53%	$56.90
Levocetirizine	XYZAL SOL	3	1	$195.00	3	0.01%	$65.00
Subtotal		**607**	**156**	**$19,478.49**	**3.89**	**0.75%**	**$32.09**
Tier 2 Subtotal		**607**	**156**	**$19,478.49**	**3.89**	**0.75%**	**$32.09**
Desloratadine	CLARINEX SYP 0.5MG/ML	38	8	$3,894.80	4.75	0.15%	$102.49
Desloratadine	DESLORATADIN TAB 5MG	36	5	$1,284.61	7.2	0.05%	$35.68
Desloratadine	CLARINEX TAB 5MG	3	1	$489.90	3	0.02%	$163.30
Desloratadine	DESLORATADIN TAB 2.5 ODT	1	1	$157.80	1	0.01%	$157.80
Subtotal		**78**	**15**	**$5,827.11**	**5.2**	**0.23%**	**$74.71**
Clemastine	CLEMASTINE SYP 0.5/5ML	7	1	$56.90	7	0.00%	$8.13
Subtotal		**7**	**1**	**$56.90**	**7**	**0.00%**	**$8.13**
Tier 3 Subtotal		**85**	**16**	**$5,884.01**	**5.31**	**0.23%**	**$69.22**
Total		**274,450**	**115,168***	**$2,599,667.41**	**2.38**	**100%**	**$9.47**

*Total number of unduplicated members.

Appendix H

Calendar Year 2013 Annual Review of Smoking Cessation Products

Oklahoma Health Care Authority
March 2014

Current Prior Authorization Criteria

Nicotine patches and Zyban® (bupropion) do not require prior authorization and each may be used for up to 180 days per calendar year. Other smoking cessation products including Chantix® (varenicline) are covered without prior authorization for the first 90 days. After 90 days of use in a calendar year, further use of these smoking cessation products requires prior authorization.

Approval Criteria After Initial 90 Days of Therapy:

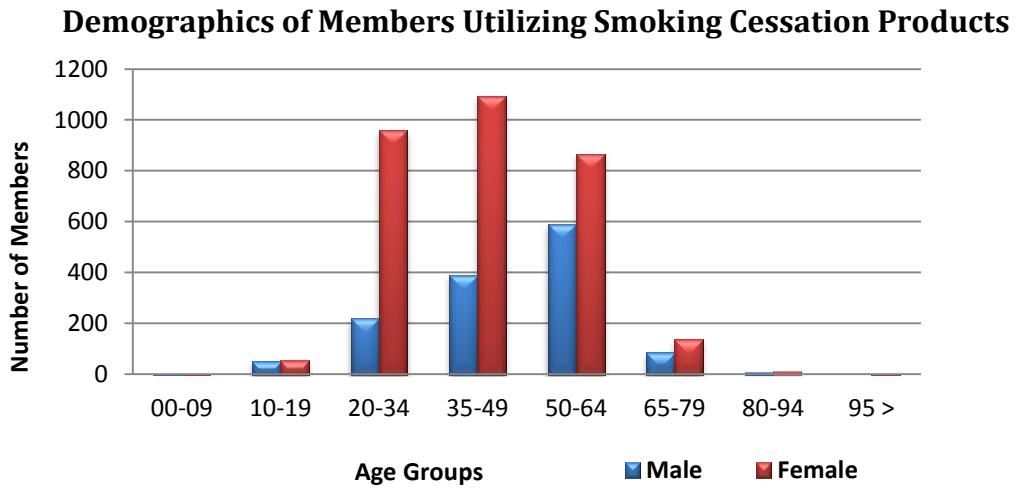
1. Member must be enrolled in a smoking cessation behavior modification program and the name of the program must be stated on the petition.
2. Petition will be approved for another 90 days of therapy.
3. After the member has had 180 days of treatment in a calendar year, the member must wait until the next calendar year before smoking cessation treatment will be covered again.
4. Smoking cessation products do not count against the 6 prescription per month limit. This includes Chantix® and Zyban®.
5. Quantity limits apply.

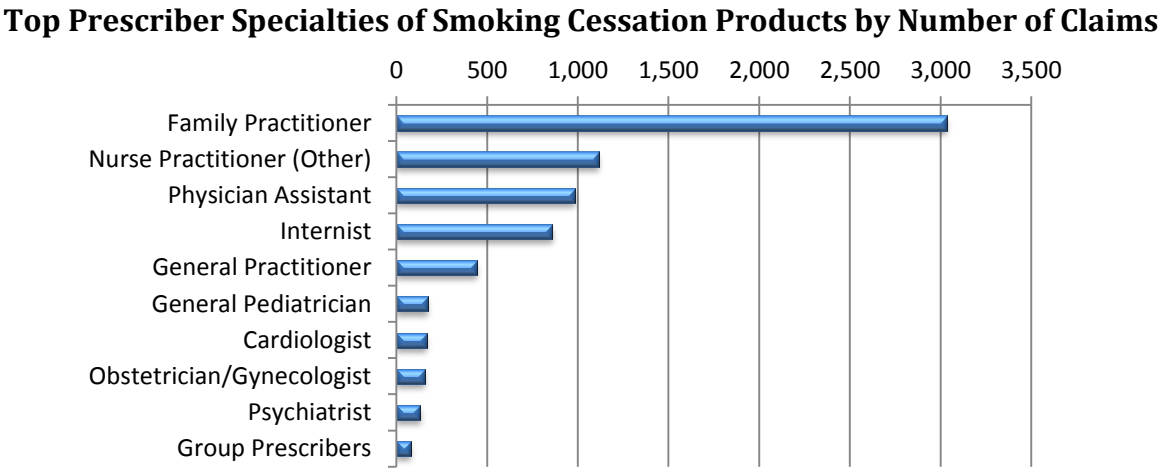
Utilization

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	5,528	8,852	$1,097,620.62	$124.00	$4.86	456,630	225,689
2013	4,461	7,504	$1,018,729.49	$135.76	$5.43	377,727	187,498
% Change	**-19.30%**	**-15.20%**	**-7.20%**	**9.50%**	**11.70%**	**-17.30%**	**-16.90%**
Change	**-1,067**	**-1,348**	**-$78,891.13**	**$11.76**	**$0.57**	**-78,903**	**-38,191**

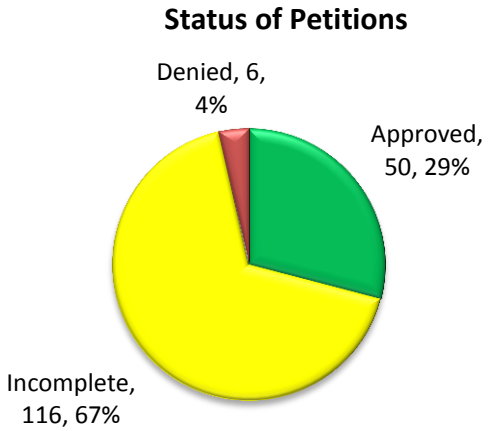
*Total number of unduplicated members





Prior Authorization of Smoking Cessation Products

There were 172 petitions submitted for the smoking cessation product category during calendar year 2013. The following chart shows the status of the submitted petitions.



Market News and Updates

Patent Expirations

1. Nicotrol® Inhaler (nicotine inhalation system) - No current generic available, however, patents have expired.
2. Nicotrol® NS (nicotine nasal spray)- 08/2014
3. Chantix® (varenicline)- 05/2022

Discussion[1]

In January of 2013, prior authorization of Zyban® and nicotine patches after 90 days of therapy was removed to allow members easier access to smoking cessation therapy for up to 180 days per year. This has decreased prior authorizations submitted by approximately 77% compared to the previous calendar year. After evaluating the utilization data from the previous calendar year with the current criteria, it can be concluded that this category is not being over utilized and there may be additional cost savings to consider from fewer administrative costs related to prior authorization submissions.

As a result of the reduced prior authorization requirements for Zyban® and nicotine patches, an increase in utilization was anticipated. The decrease of use in this category may be due to the rising popularity in electronic cigarettes. A recent randomized controlled trial found electronic cigarettes, with or without nicotine, to be modestly effective at helping smokers quit with similar achievement of abstinence as nicotine patches. More research is needed to clearly outline all the risks and benefits associated with electronic cigarettes. Currently, electronic cigarettes are not regulated by the Food and Drug Administration (FDA). Electronic cigarettes do not fall within jurisdiction of the Family Smoking Prevention and Tobacco Control Act that grants the FDA authority to regulate tobacco products.

Recommendations

The College of Pharmacy recommends continuation of current criteria.

[1] Bullen, Christopher, Colin Howe, Murray Laugesen, Hayden Mcrobbie, Varsha Parag, Jonathan Williman, and Natalie Walker. "Electronic Cigarettes for Smoking Cessation: A Randomised Controlled Trial." *The Lancet* 382.9905 (2013): 1629-637.

Utilization Details for Smoking Cessation Products: CY 2013

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/ CLAIM	COST/ DAY	% COST
Chantix Products						
CHANTIX PAK 0.5& 1MG	2,255	2,074	$450,673.04	$199.86	$6.94	44.24%
CHANTIX PAK 1MG	1,073	797	$211,177.11	$196.81	$6.90	20.73%
CHANTIX TAB 1MG	545	361	$105,569.10	$193.70	$6.87	10.36%
CHANTIX TAB 0.5MG	97	71	$17,009.35	$175.35	$6.68	1.67%
SUBTOTAL	**3,970**	**3,303**	**$784,428.60**	**$197.59**	**$4.37**	**77%**
Nicotine Patch						
NICOTINE DIS 21MG/24H	865	626	$38,609.70	$44.64	$2.03	3.79%
NICOTINE DIS 14MG/24H	516	368	$19,724.63	$38.23	$2.11	1.94%
NICODERM CQ DIS 21MG/24H	313	227	$21,246.28	$67.88	$3.13	2.09%
NICOTINE TD DIS 21MG/24H	293	231	$14,479.35	$49.42	$2.09	1.42%
NICOTINE DIS 7MG/24HR	230	151	$7,456.69	$32.42	$2.25	0.73%
NICODERM CQ DIS 14MG/24H	191	148	$11,948.66	$62.56	$3.10	1.17%
NICOTINE TD DIS 14MG/24H	158	136	$7,033.25	$44.51	$2.07	0.69%
SM NICOTINE DIS 21MG	101	86	$6,983.94	$69.15	$2.74	0.69%
NICOTINE TD DIS 7MG/24HR	78	71	$3,105.64	$39.82	$2.05	0.30%
NICODERM CQ DIS 7MG/24HR	69	53	$3,806.86	$55.17	$3.19	0.37%
HM NICOTINE DIS 21MG/24H	25	21	$1,353.96	$54.16	$2.39	0.13%
HM NICOTINE DIS 14MG/24H	15	14	$900.99	$60.07	$2.57	0.09%
SUBTOTAL	**2,854**	**2,132**	**$136,649.95**	**$47.88**	**$3.15**	**13.41%**
Nicotine Gum, Lozenges, etc.						
NICOTROL INH	203	194	$73,140.50	$360.30	$12.97	7.18%
SM NICOTINE GUM 4MG	47	17	$1,630.77	$34.70	$3.43	0.16%
NICOTINE POL GUM 4MG MINT	38	24	$1,640.09	$43.16	$4.04	0.16%
NICORETTE LOZ 4MG CHRY	21	12	$1,765.29	$84.06	$3.85	0.17%
SM NICOTINE GUM 4MG MINT	18	10	$952.88	$52.94	$2.63	0.09%
NICOTROL NS SPR 10MG/ML	18	15	$3,069.04	$170.50	$7.04	0.30%
NICORETTE ST GUM 2MG ORIG	17	2	$767.04	$45.12	$8.62	0.08%
SM NICOTINE LOZ 4MG MINT	16	9	$968.94	$60.56	$3.42	0.10%
NICORETTE GUM 4MG MINT	13	11	$657.84	$50.60	$2.32	0.06%
NICOTINE POL LOZ 4MG MINT	13	9	$700.62	$53.89	$2.94	0.07%
NICOTINE POL GUM 2MG ORIG	10	9	$276.95	$27.70	$1.51	0.03%
NICORETTE GUM 4MG ORIG	10	5	$925.20	$92.52	$4.54	0.09%
SM NICOTINE LOZ 2MG MINT	10	4	$340.26	$34.03	$6.08	0.03%
NICORETTE LOZ 4MG MINT	9	7	$394.85	$43.87	$2.82	0.04%
HM NICOTINE GUM 2MG MINT	8	5	$329.84	$41.23	$2.77	0.03%
SM NICOTINE GUM 2MG MINT	8	6	$515.72	$64.47	$2.38	0.05%

MEDICATION NAME	CLAIMS	MEMBERS	COST	COST/ CLAIM	COST/ DAY	% COST
NICORELIEF GUM 4MG MINT	8	6	$276.83	$34.60	$1.45	0.03%
NICORETTE GUM 2MG ORIG	7	6	$406.64	$58.09	$2.86	0.04%
SM NICOTINE GUM 2MG	6	4	$427.02	$71.17	$5.02	0.04%
HM NICOTINE GUM 4MG MINT	6	5	$236.78	$39.46	$2.89	0.02%
NICORELIEF GUM 4MG ORIG	6	5	$216.71	$36.12	$1.58	0.02%
NICOTINE POL GUM 4MG ORIG	6	5	$385.91	$64.32	$2.88	0.04%
NICORETTE GUM 2MGFRUIT	5	4	$431.86	$86.37	$2.88	0.04%
NICOTINE POL GUM 2MG	5	4	$195.88	$39.18	$1.40	0.02%
NICORETTE LOZ 2MG MINT	5	3	$195.23	$39.05	$4.54	0.02%
NICORETTE LOZ 4MG ORIG	5	5	$380.53	$76.11	$3.07	0.04%
NICOTINE LOZ 4MG MINT	5	3	$544.24	$108.85	$5.44	0.05%
NICORETTE GUM 2MG MINT	4	3	$266.37	$66.59	$2.83	0.03%
NICOTINE POL GUM 2MG MINT	4	3	$196.80	$49.20	$2.73	0.02%
NICORETTE GUM 4MG CINN	4	4	$172.88	$43.22	$3.39	0.02%
GNP NICOTINE LOZ 4MG MINT	4	2	$141.03	$35.26	$2.04	0.01%
NICORELIEF GUM 2MG MINT	3	2	$307.96	$102.65	$3.42	0.03%
NICORELIEF GUM 2MG ORIG	3	2	$78.53	$26.18	$1.21	0.01%
NICORETTE ST GUM 4MG ORIG	3	3	$137.76	$45.92	$2.09	0.01%
NICORETTE LOZ 2MG CHRY	3	3	$448.78	$149.59	$4.99	0.04%
NICORETTE LOZ 2MG ORIG	3	2	$149.23	$49.74	$3.83	0.01%
NICORETTE GUM 4MGFRUIT	2	2	$82.71	$41.36	$2.02	0.01%
HM NICOTINE LOZ 4MG MINT	2	2	$62.36	$31.18	$0.82	0.01%
GNP NICOTINE GUM 2MG MINT	1	1	$39.74	$39.74	$1.32	0.00%
GNP NICOTINE GUM 2MG ORIG	1	1	$14.52	$14.52	$0.58	0.00%
NICORETTE GUM 2MG CINN	1	1	$45.12	$45.12	$5.64	0.00%
NICORETTE ST GUM 2MG MINT	1	1	$47.52	$47.52	$4.75	0.00%
NICOTINE GUM 2MG	1	1	$17.89	$17.89	$8.95	0.00%
GNP NICOTINE GUM 4MG MINT	1	1	$28.23	$28.23	$0.94	0.00%
NICOTINE GUM 4MG	1	1	$20.77	$20.77	$1.38	0.00%
HM NICOTINE LOZ 2MG MINT	1	1	$31.18	$31.18	$1.30	0.00%
NICORELIEF LOZ 2MG MINT	1	1	$31.31	$31.31	$1.04	0.00%
NICOTINE LOZ 2MG MINT	1	1	$39.54	$39.54	$2.64	0.00%
SUBTOTAL	**568**	**427**	**$94,133.69**	**$165.73**	**$3.54**	**9.20%**
Bupropion Products						
BUPROPION TAB 150MG	78	44	$2,321.54	$29.76	$0.96	0.23%
BUPROBAN TAB 150MG	34	26	$1,195.71	$35.17	$1.16	0.12%
SUBTOTAL	**112**	**70**	**$3,517.25**	**$31.40**	**$1.06**	**0.35%**
TOTAL:	**7,504**	**4,461***	**$1,018,729.49**	**$135.76**	**$5.43**	**100%**

*Total number of unduplicated members.

Appendix I

Calendar Year 2013 Annual Review of Benzodiazepine Medications

Oklahoma Health Care Authority
March 2014

Current Prior Authorization Criteria

Benzodiazepine Approval Criteria for Members 19 Years of Age and Older:

1. Currently there are no prior authorizations required however quantity limits are set at maximum of 3 units per day for most products.
2. Approval for dosing greater than 3 times daily requires a chronic physical diagnosis; for these diagnoses the maximum allowed dosing would be 4 times daily.
3. A member may receive more than 3 units per day if the following criteria exist:
    a. The number of units per day is greater than 3, but less than the maximum daily dose for the product (or for a total daily dosing of three times daily).
    b. The member has a chronic diagnosis and a clinical reason for excessive units has been provided.

Benzodiazepine Approval Criteria for Members Under 19 Years of Age:

1. Member must have a chronic behavioral health related diagnosis or a chronic physical diagnosis
2. Approval Criteria for a Chronic Behavior Health Related Diagnosis:
    a. No concurrent stimulant ADHD medications; and
    b. No contraindicated conditions; and
    c. A maximum dosing of 3 times daily will apply.
3. Approval Criteria for a Chronic Physical Diagnosis:
    a. A maximum dosing of 3 times daily will apply if a hypnotic medication is being used concurrently;
    b. A maximum dosing of 4 times daily will apply if no hypnotic medication is being used concurrently.
4. Exceptions can be granted for administration prior to procedures.
5. Members 12 or younger will have the same criteria and the prescription must be originally written by a psychiatrist.

Niravam™ (Alprazolam Orally Disintegrating Tablets) Approval Criteria:

1. An FDA approved diagnosis; and
2. A diagnosis indicating that the member has a condition that prevents him/her from swallowing tablets; and
3. The physician's signature is required for approval.
4. Dosing regimens that involve splitting of tablets will not be covered.

Utilization of Benzodiazepines

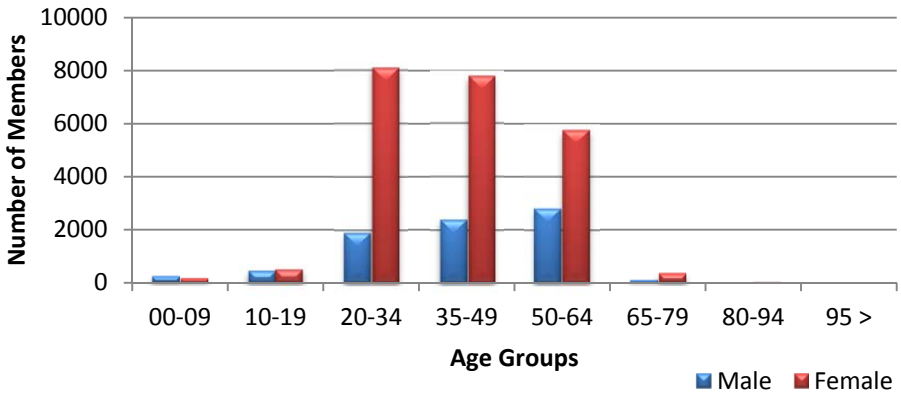
Effective January 1, 2013, Medicare Part D prescription drug plans are required to cover benzodiazepines, and to cover barbiturates used in the treatment of epilepsy, cancer, or a chronic mental disorder. Medicaid plans (including SoonerCare) were required to stop covering these products for members who are also eligible for Medicare. The effects of this change in coverage are apparent in the utilization comparison of calendar year 2012 and 2013.

Comparison of Calendar Years

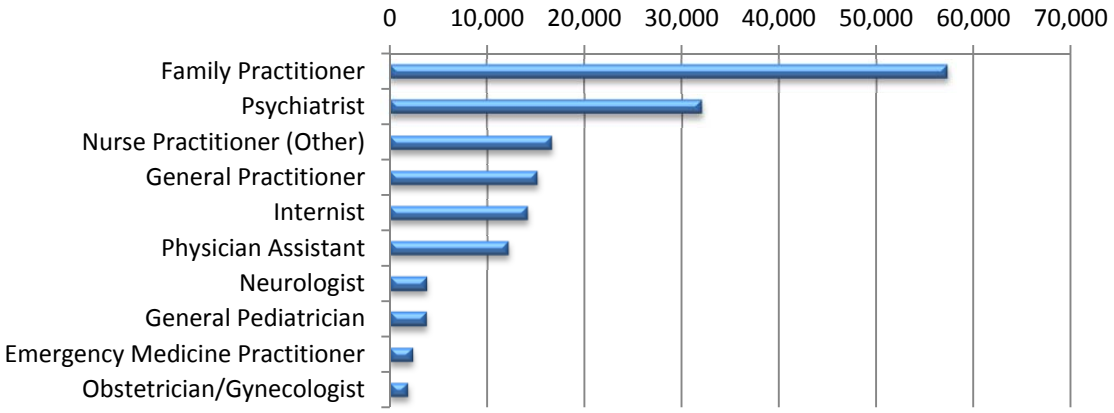
Calendar Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2012	53,354	323,069	$2,798,052.19	$8.66	$0.31	20,280,958	8,979,840
2013	30,879	170,240	$1,444,242.04	$8.48	$0.31	10,685,938	4,703,617
% Change	**-42.10%**	**-47.30%**	**-48.40%**	**-2.10%**	**0.00%**	**-47.30%**	**-47.60%**
Change	**-22,475**	**-152,829**	**-$1,353,810.15**	**-$0.18**	**$0.00**	**-9,595,020**	**-4,276,223**

*Total number of unduplicated members

Demographics of Members Utilizing Benzodiazepines

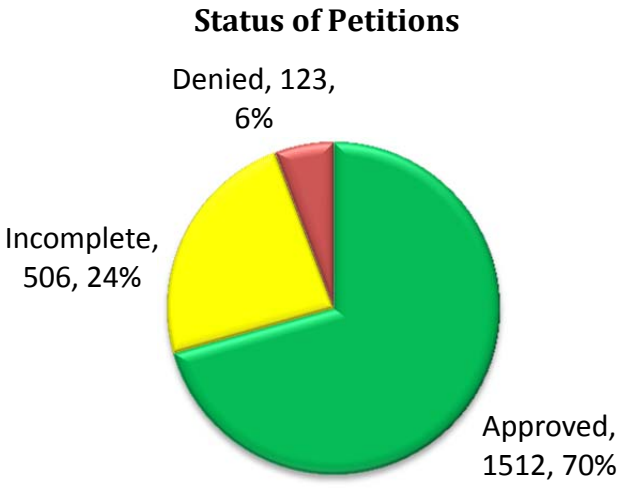


Top Prescriber Specialties of Benzodiazepines by Number of Claims



Prior Authorization of Benzodiazepines

There were a total of 2141 petitions submitted for benzodiazepines during calendar year 2013. The following chart shows the status of the submitted petitions.



Market News and Updates[1]

FDA update:

- July 2013: FDA reminded the public of the potential risks of co-administration of oral ketoconazole with alprazolam. Concomitant use has resulted in elevated plasma concentrations of alprazolam and potentiated hypnotic and sedative effects. Concomitant administration of oral ketoconazole with alprazolam is now contraindicated.

Recommendations

The College of Pharmacy does not recommend any changes at this time.

[1] Nizoral (ketoconazole) Tablets. U.S. Food and Drug Administration. Available online at: http://www.fda.gov/safety/medwatch/safetyinformation/ucm364157.htm. Last revised 08/2013. Last accessed 02/14/2014.

Utilization Details of Benzodiazepines

Chemical Name	Product Utilized	Claims	Members	Units/ Day	Cost	% Cost	Cost/ Claim
Alprazolam	ALPRAZOLAM TAB 0.25MG	4,390	1,686	2.27	$26,432.90	1.86%	$6.02
Alprazolam	ALPRAZOLAM TAB 0.5MG	18,365	4,866	2.34	$127,916.40	8.86%	$6.97
Alprazolam	ALPRAZOLAM TAB 1MG	38,619	6,908	2.55	$345,451.46	23.9%	$8.95
Alprazolam	ALPRAZOLAM TAB 2MG	17,442	2,893	2.01	$190,876.02	13.2%	$10.94
Alprazolam	ALPRAZOLAM TAB 0.5MG ER	63	24	0.99	$792.23	0.05%	$12.58
Alprazolam	ALPRAZOLAM TAB 1MG ER	137	53	1	$2,132.11	0.15%	$15.56
Alprazolam	ALPRAZOLAM TAB 2MG ER	161	56	1.27	$3,237.40	0.22%	$20.11
Alprazolam	ALPRAZOLAM TAB 3MG ER	135	33	1.08	$3,672.09	0.25%	$27.20
Alprazolam	ALPRAZOLAM TAB 0.5MG XR	17	5	1	$238.93	0.02%	$14.05
Alprazolam	ALPRAZOLAM TAB 1MG XR	19	9	1	$334.83	0.02%	$17.62
Alprazolam	ALPRAZOLAM TAB 2MG XR	27	13	1.46	$622.65	0.04%	$23.06
Alprazolam	ALPRAZOLAM TAB 3MG XR	46	9	1	$1,102.85	0.08%	$23.98
Alprazolam	ALPRAZOLAM TAB 1MG ODT	7	2	2.73	$865.24	0.06%	$123.61
Alprazolam	ALPRAZOLAM CON 1 MG/ML	1	1	0.5	$68.90	0.00%	$68.90
	Subtotal	**79,429**	**13,954**	**2.35**	**$703,744.01**	**48.8%**	**$8.86**
Clonazepam	CLONAZEPAM TAB 0.5MG	16,024	4,535	2.04	$102,810.44	7.12%	$6.42
Clonazepam	CLONAZEPAM TAB 1MG	22,552	4,983	2.21	$172,366.73	11.9%	$7.64
Clonazepam	CLONAZEPAM TAB 2MG	6,523	1,255	2	$54,049.13	3.74%	$8.29
Clonazepam	CLONAZEP ODT 0.125MG	174	61	2.46	$9,008.40	0.62%	$51.77
Clonazepam	CLONAZEP ODT 0.25MG	572	187	2.13	$23,973.44	1.66%	$41.91
Clonazepam	CLONAZEP ODT 0.5MG	256	101	2.5	$10,684.33	0.74%	$41.74
Clonazepam	CLONAZEP ODT 1MG	104	39	1.81	$3,489.64	0.24%	$33.55
Clonazepam	CLONAZEP ODT 2MG	74	31	1.67	$2,383.79	0.17%	$32.21
Clonazepam	KLONOPIN TAB 0.5MG	27	3	2.59	$3,999.50	0.28%	$148.13
Clonazepam	KLONOPIN TAB 1MG	17	2	3	$3,506.33	0.24%	$206.25
Clonazepam	KLONOPIN TAB 2MG	6	2	3	$1,694.67	0.12%	$282.45
	Subtotal	46,329	9,710	2.12	$387,966.40	**26.9%**	$8.37
Diazepam	DIAZEPAM TAB 2MG	1,343	486	2.26	$6,701.89	0.46%	$4.99
Diazepam	DIAZEPAM TAB 5MG	10,161	3,231	2.17	$57,822.07	4.00%	$5.69
Diazepam	VALIUM TAB 5MG	2	1	14.4	$10.22	0.00%	$5.11
Diazepam	DIAZEPAM TAB 10MG	13,495	3,164	2.3	$125,375.99	8.68%	$9.29
Diazepam	DIAZEPAM SOL 1MG/ML	295	73	8.08	$6,064.30	0.42%	$20.56
Diazepam	DIAZEPAM CON 5MG/ML	14	6	4.57	$1,602.18	0.11%	$114.44
Diazepam	DIAZEPAM INJ 5MG/ML	23	11	0.91	$684.72	0.05%	$29.77

Chemical Name	Product Utilized	Claims	Members	Units/ Day	Cost	% Cost	Cost/ Claim
	Subtotal	**25,333**	**6,367**	**2.31**	**$198,261.37**	**13.7%**	**$7.83**
Lorazepam	LORAZEPAM TAB 0.5MG	5,285	1,912	2.12	$31,119.93	2.16%	$5.89
Lorazepam	LORAZEPAM TAB 1MG	8,673	2,723	2.26	$55,963.20	3.87%	$6.45
Lorazepam	ATIVAN TAB 1MG	8	1	3	$2,946.26	0.20%	$368.28
Lorazepam	LORAZEPAM TAB 2MG	2,767	726	2.34	$23,240.21	1.61%	$8.40
Lorazepam	LORAZEPAM INJ 2MG/ML	139	71	1.56	$1,074.98	0.07%	$7.73
Lorazepam	LORAZEPAM INJ 2MG/ML	2	2	1.17	$13.58	0.00%	$6.79
Lorazepam	LORAZEPAM CON 2MG/ML	97	49	1.62	$5,098.31	0.35%	$52.56
	Subtotal	**16,971**	**4,909**	**2.23**	**$119,456.47**	**8.26%**	**$7.04**
Clorazepate	CLORAZEPATE TAB 3.75MG	479	74	2.39	$7,729.16	0.54%	$16.14
Clorazepate	CLORAZEPATE TAB 7.5MG	469	114	2.55	$8,397.46	0.58%	$17.91
Clorazepate	CLORAZEPATE TAB 15MG	258	57	2.08	$3,879.60	0.27%	$15.04
Clorazepate	TRANXENE T TAB 3.75MG	6	1	2	$97.11	0.01%	$16.19
	Subtotal	**1,212**	**233**	**2.38**	**$20,103.33**	**1.40%**	**$16.59**
Chlordiazepoxide	CHLORDIAZEPOXIDE 5MG	108	33	2.22	$995.20	0.07%	$9.21
Chlordiazepoxide	CHLORDIAZEPOXIDE 10MG	297	131	2.59	$2,237.66	0.16%	$7.53
Chlordiazepoxide	CHLORDIAZEPOXIDE 25MG	394	205	2.27	$2,868.28	0.20%	$7.28
	Subtotal	**799**	**340**	**2.39**	**$6,101.14**	**0.43%**	**$7.64**
Oxazepam	OXAZEPAM CAP 10MG	49	15	1.53	$1,570.50	0.11%	$32.05
Oxazepam	OXAZEPAM CAP 15MG	75	21	2.11	$5,251.91	0.36%	$70.03
Oxazepam	OXAZEPAM CAP 30MG	21	7	1.84	$1,596.23	0.11%	$76.01
	Subtotal	**145**	**39**	**1.91**	**$8,418.64**	**0.58%**	**$58.06**
	Total	**170,240**	**30,879***	**2.27**	**$1,444,242.04**	**100%**	**$8.48**

*Total number of unduplicated members

Appendix J

60-Day Notice to Prior Authorize Ophthalmic Anti-Inflammatory Medications

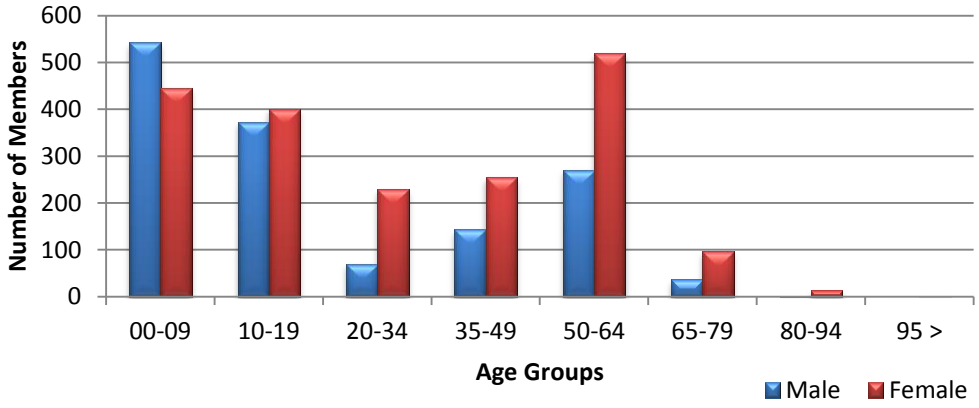
Oklahoma Health Care Authority
March 2014

Introduction

This category was introduced for possible inclusion in the Product Based Prior Authorization program in February 2014. See the February DUR packet for a more complete discussion of the category. This notice and statement of potential economic impact are presented to meet the statutory requirements of 63 O.S. Sec. 5030.5.

Utilization Among SoonerCare Members

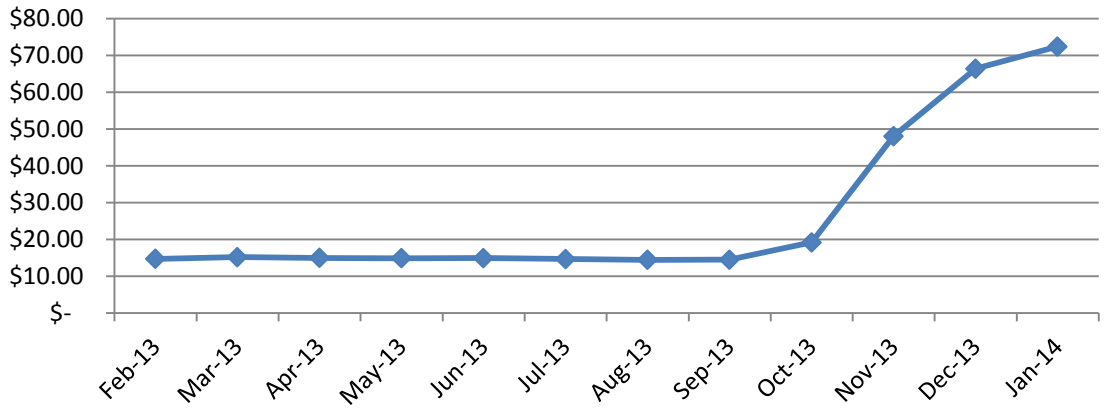
During 2013, there were a total of 3,401 members utilizing ophthalmic anti-inflammatory medications. Within this population there were 74 waiver members and 90 nursing home members.



Medication Cost Trends[1, 2, 3, 4]

A recent price increase for prednisolone acetate 1% has led to a steady rise in the price per bottle from approximately $15.00 to $100.00. The recommended placement of prednisolone acetate 1% into Tier 1 was based on clinical guideline recommendations and the use of prednisolone acetate for acute situations requiring urgent treatment. As a result of the large price increase, the other more cost effective products currently in Tier 2 should be moved to Tier 1 in order to prevent an increase in use of the now more costly product. This change does not allow as significant of savings as previously anticipated. The implementation of tiers for this category is not intended to impede the practice of prescribers, although a lack of difference in clinical efficacy and side effect profiles between many of these products gives way to a potential for savings, particularly as new products become available.

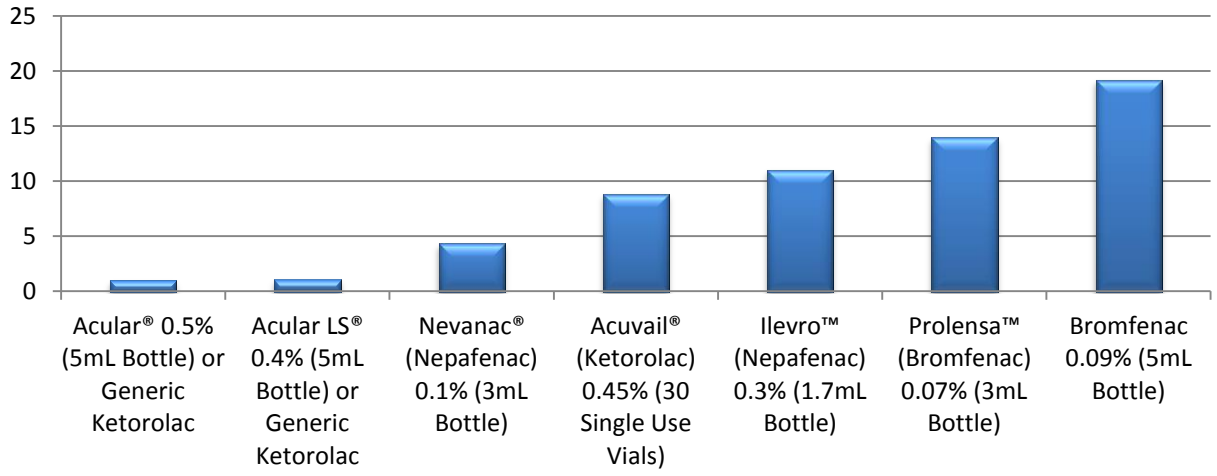
1 Year Trend in Cost/Claim of Prednisolone Acetate 1%

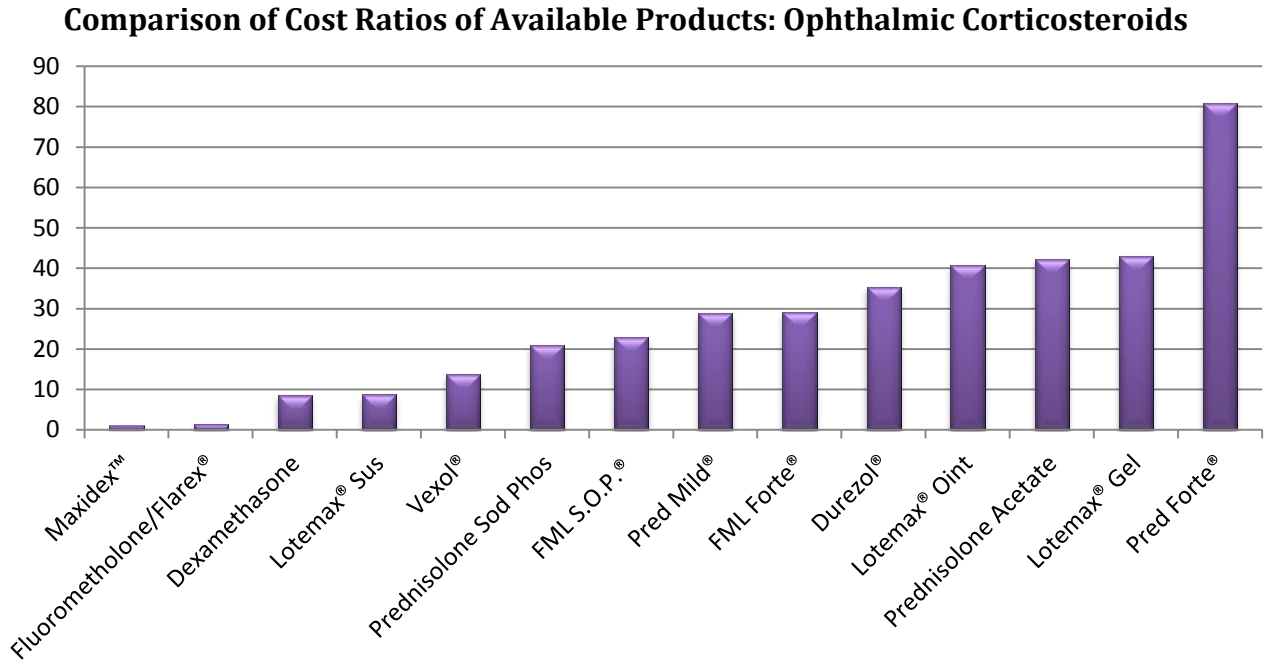


The trend above shows the cost per claim for prednisolone acetate 1% has recently increased approximately five fold.

Cost Ratio Comparison

Comparison of Cost Ratios of Available Products: Ophthalmic NSAIDs





Economic Impact

Potential Secondary Costs

Overall efficacy is considered to be similar across these classes but drug selection requires individual patient history which includes, but is not limited to: etiology of inflammation, severity of inflammation, current symptoms, and other comorbidities.

Potential Administrative Costs

Based on previous use of the final Tier 2 products, it is estimated that approximately 509 petitions annually might be required if step therapy was not initially followed by all members. The proposed Tier changes would affect approximately 15% of the current population for this PBPA category.

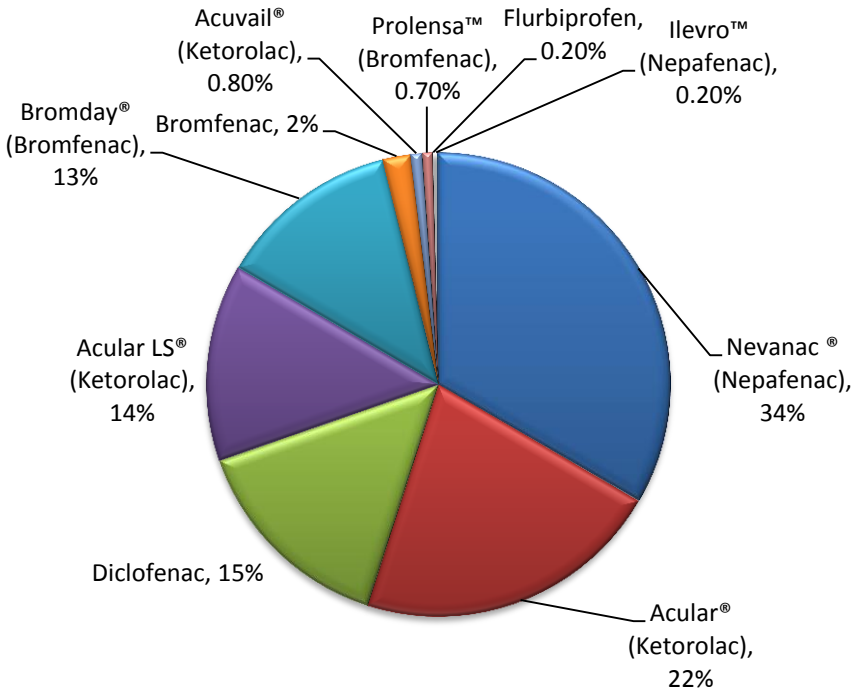
The current estimate of total cost per petition to the *healthcare system* (includes cost to physicians, pharmacists, and program) is between $14.70 and $17.70. Total cost for initial prior authorization of this category to the *healthcare system* is estimated to be between $7,482.30 and $9,009.30 annually. Anticipated actual administrative cost to the program is projected to be less than $6,500.

Potential Program Savings

Potential net ingredient savings to the program after rebates based on the recommended tiers and a potential limited use of Tier 2 products to 25% of current market share is estimated to be 10% of the current reimbursement of approximately $300,000 annually. Potential savings might also be gained as new products come to market.

Market Analysis

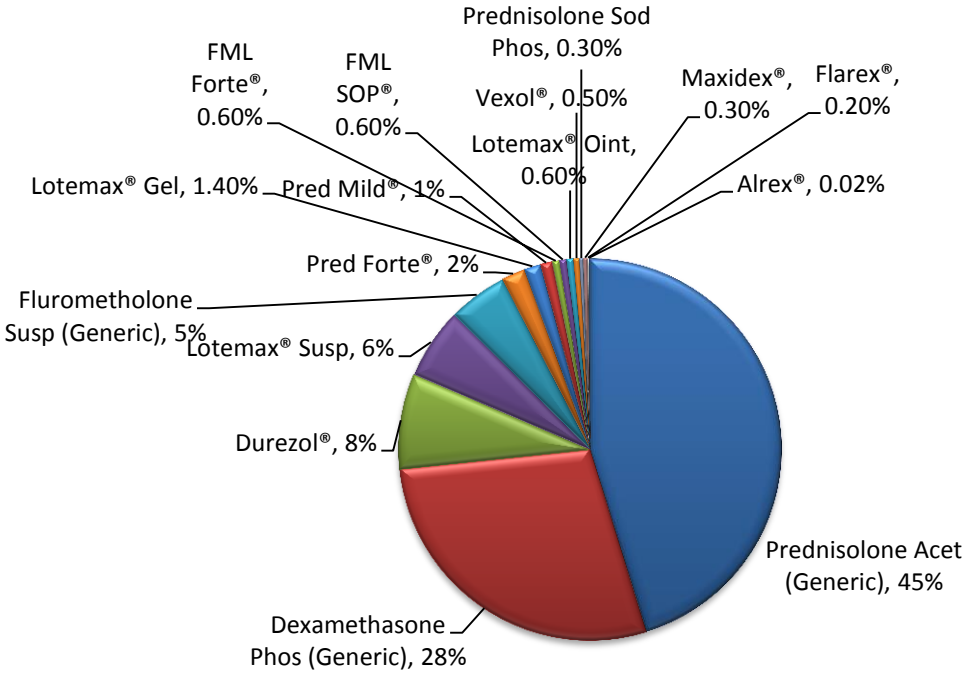
Market Share by Total Claims: Ophthalmic NSAIDs



Market Share by Total Cost: Ophthalmic NSAIDs

Chemical Name	Products Utilized	Total Cost
Nepafenac	Nevanac® 0.1%	$52,464.78
Bromfenac	Bromday® 0.09%	$22,905.14
Ketorolac	Ketorolac 0.5%	$4,158.57
Ketorolac	Ketorolac 0.4%	$2,166.58
Bromfenac	Bromfenac 0.09%	$2,133.12
Ketorolac	Acuvail 0.45%	$1,969.30
Diclofenac	Diclofenac 0.1%	$1,675.76
Bromfenac	Prolensa™ 0.07%	$1,113.48
Nepafenac	Ilevro™ 0.3%	$306.22
Flurbiprofen	Flurbiprofen 0.03%	$21.00

Market Share by Total Claims: Ophthalmic Corticosteroids



Market Share by Total Cost: Ophthalmic Corticosteroids

Chemical Name	Products Utilized	Total Cost
Loteprednol	Lotemax® Sus 0.5%	$47,385.99
Difluprednate	Durezol® 0.05%	$42,786.61
Dexameth Phos	Dexameth Phos 0.1%	$29,216.11
Prednisolone Acet	Prednisolone 1%	$29,047.15
Loteprednol	Lotemax® Gel 0.5%	$7,889.40
Prednisolone Acet	Pred forte® 1%	$4,912.63
Loteprednol	Lotemax® Oint 0.5%	$3,639.05
Fluorometholone	Fluoromethol 0.1%	$2,926.75
Prednisolone Acet	Pred Mild® 0.12%	$1,395.42
Fluorometholone	Fml Oint® 0.1%	$1,211.80
Rimexolone	Vexol® 1%	$1,147.13
Fluorometholone	FML Forte® 0.25%	$1,125.07
Dexamethasone	Maxidex® 0.1%	$889.31
Prednisolone	Pred Sod Pho 1%	$696.60
Fluorometholone	Flarex® 0.1%	$510.85
Loteprednol	Alrex® 0.2%	$277.06

Recommendations

The College of Pharmacy recommends establishing a Product Based Prior Authorization category for ophthalmic NSAIDs and ophthalmic corticosteroids to ensure appropriate cost-effective utilization in accordance with current treatment guidelines. The College of Pharmacy recommends the following tier list and criteria to the Drug Utilization Review Board based on cost and clinical effectiveness for approval before referral to the Oklahoma Health Care Authority.

In addition the College of Pharmacy will implement an educational initiative consisting of a targeted mailing to all prescribers of ophthalmic anti-inflammatory medications in the SoonerCare population in the previous 12 months. The mailing may include information regarding approval criteria of ophthalmic anti-inflammatory medications and a link to the OHCA web page which will contain the updated tier chart.

Ophthalmic Non-Steroidal Anti-Inflammatory Drug (NSAIDs) Tier 2 Approval Criteria:

1. Documented trials of all Tier 1 ophthalmic NSAIDs (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier 1 anti-inflammatories lack.

Ophthalmic NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)	
Tier 1	**Tier 2**
Voltaren® (diclofenac) Solution 0.1%	Nevanac™ (nepafenac) 0.1% Suspension
Acular® (ketorolac) Solution 0.5%	Acuvail® (ketorolac) Solution 0.45%
Acular LS ® (ketorolac) Solution 0.4%	Ilevro™ (nepafenac) 0.3 % Suspension
Ocufen® (flurbiprofen) Solution 0.03%	Prolensa™ (bromfenac) 0.07% Solution
	Bromfenac 0.09% Solution

Ophthalmic Corticosteroid Tier 2 Approval Criteria:

1. Documented trials of all Tier 1 ophthalmic corticosteroids (from different product lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier 1 anti-inflammatories lack.

Ophthalmic Corticosteroids	
Tier 1	**Tier 2**
Dexamethasone Sodium Phosphate Solution 0.1%	Lotemax® (loteprednol) Gel 0.5%
Maxidex™ (dexamethasone) Suspension 0.1%	Lotemax® (loteprednol) Ointment 0.5%
FML Liquifilm® (fluorometholone) Suspension 0.1%	Pred Forte® (prednisolone Acetate) Suspension 1%
Flarex® (fluorometholone) Suspension 0.1%	FML Forte® (fluorometholone) Suspension 0.25%
Lotemax® (loteprednol) Suspension 0.5%	FML S.O.P® (fluorometholone) Ointment 0.1%
Omnipred® (prednisolone Acetate) Suspension 1%	
Durezol® (difluprednate) Emulsion 0.05%	
Pred Mild® (prednisolone Acetate) Suspension 0.12%	
Prednisolone Sodium Phosphate Solution 1%	
Vexol® (rimexolone) Suspension 1%	

[1] Preferred Practice Pattern: Cataract in the Adult Eye. American Academy of Ophthalmology. Available online at: http://one.aao.org/preferred-practice-pattern/cataract-in-adult-eye-ppp--october-2011. Last revised 09/2011. Last accessed 02/24/2014.

[2] Care of the Adult Patient with Cataract. American Optometric Association. Available online at: http://www.aoa.org/documents/optometrists/CPG-8.pdf. Last revised 2004. Last accessed 02/24/2014.

[3] Preferred Practice Pattern: Refractive Errors and Refractive Surgery. American Academy of Ophthalmology. Available online at: http://one.aao.org/preferred-practice-pattern/refractive-errors--surgery-ppp-2013. Last revised 07/2013. Last accessed 02/24/2014.

[4] Optometric Clinical Practice Guideline: Care of the Patient with Conjunctivitis. American Optometric Association. Available online at: http://www.aoa.org/documents/optometrists/CPG-11.pdf. Last revised 11/2002. Last accessed 02/24/14.

Appendix K

FDA & DEA Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: Feb. 18, 2014

FDA approves Northera to treat neurogenic orthostatic hypotension

The U.S. Food and Drug Administration today approved Northera capsules (droxidopa) for the treatment of neurogenic orthostatic hypotension (NOH). NOH is a rare, chronic and often debilitating drop in blood pressure upon standing that is associated with Parkinson's disease, multiple-system atrophy, and pure autonomic failure.

Symptoms of NOH include dizziness, lightheadedness, blurred vision, fatigue and fainting when a person stands.

The FDA is approving Northera under the accelerated approval program, which allows for approval of a drug to treat a serious disease based on clinical data showing that the drug has an effect on an intermediate clinical measure (in this case, short-term relief of dizziness) that is reasonably likely to predict the outcome of ultimate interest (relief of dizziness during chronic treatment). This program provides patient access to promising drugs while the company conducts post-approval clinical trials to verify the drug's clinical benefit, which for this approval is a long-term effect on patient symptoms in NOH, a chronic disease.

Northera has a boxed warning to alert health care professionals and patients about the risk of increased blood pressure while lying down (supine hypertension), a common problem that affects people with primary autonomic failure and can cause stroke. It is essential that patients be reminded that they must sleep with their head and upper body elevated. Supine blood pressure should be monitored prior to and during treatment and more frequently when increasing doses.

The most common adverse events reported by clinical trial participants taking Northera were headache, dizziness, nausea, high blood pressure (hypertension) and fatigue.

The effectiveness of Northera was shown through two-weeks in two clinical trials in people with NOH. People taking Northera reported a decrease in dizziness, lightheadedness, feeling faint, or feeling as if they might black out compared to those taking an inactive pill (placebo). Durability of the improvement in patient symptoms beyond two weeks has not been demonstrated.

Northera received orphan-product designation from the FDA because it is intended to treat a rare disease or condition.

Northera is made by Charlotte-based Chelsea Therapeutics Inc.

FDA NEWS RELEASE

For Immediate Release: Feb. 25, 2014

FDA approves Myalept to treat rare metabolic disease

On Feb. 24, 2014, the U.S. Food and Drug Administration approved Myalept (metreleptin for injection) as replacement therapy to treat the complications of leptin deficiency, in addition to diet, in patients with congenital generalized or acquired generalized lipodystrophy.

Generalized lipodystrophy is a condition associated with a lack of fat tissue. Patients with congenital generalized lipodystrophy are born with little or no fat tissue. Patients with acquired generalized lipodystrophy generally lose fat tissue over time. Because the hormone leptin is made by fat tissue, patients with generalized lipodystrophy have very low leptin levels. Leptin regulates food intake and other hormones, such as insulin.

Patients with both types of generalized lipodystrophy often develop severe insulin resistance at a young age and may have diabetes mellitus that is difficult to control or very high levels of triglycerides in the blood (hypertriglyceridemia) that can lead to inflammation of the pancreas.

The safety and effectiveness of Myalept, an analog of leptin made through recombinant DNA technology, were evaluated in an open-label, single-arm study that included 48 patients with congenital or acquired generalized lipodystrophy who also had diabetes mellitus, hypertriglyceridemia, and/or elevated levels of

fasting insulin. The trial showed reductions in HbA1c (a measure of blood sugar control), fasting glucose, and triglycerides.
Anti-drug antibodies with neutralizing activity to leptin and/or Myalept may develop, which could result in severe infections or loss of treatment effectiveness. T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, both treated and not treated with Myalept, so healthcare professionals should carefully consider the benefits and risks of treatment with Myalept in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy. Myalept is contraindicated in patients with general obesity. Myalept is not approved for use in patients with HIV-related lipodystrophy or in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of generalized lipodystrophy.
Because of the risks associated with the development of neutralizing antibodies and lymphoma, Myalept is available only through the Myalept Risk Evaluation and Mitigation Strategy (REMS) Program. Under this REMS program, prescribers must be certified with the program by enrolling in and completing training. Pharmacies must be certified with the program and only dispense Myalept after receipt of the Myalept REMS Prescription Authorization Form for each new prescription.
Myalept is also approved with a Medication Guide and instructions for use that provides patients with important information about the medication. The guide will be distributed each time a patient fills a prescription.
The FDA is requiring seven studies (post-marketing requirements) for Myalept, including a long-term prospective observational study (product exposure registry) of patients treated with Myalept, a study to assess for the immunogenicity (antibody formation) of Myalept, and an assessment and analysis of spontaneous reports of potential serious risks related to the use of Myalept. Eight additional studies are being requested as post-marketing commitments.
In clinical trials, the most common side effects observed in patients treated with Myalept were low blood sugar (hypoglycemia), headache, decreased weight, and abdominal pain.
Myalept is marketed by San Diego-based Amylin Pharmaceuticals, L.L.C.

FDA NEWS RELEASE

For Immediate Release: Feb. 14, 2014

FDA approves Vimizim to treat rare congenital enzyme disorder

First drug to receive Rare Pediatric Disease Priority Review Voucher

The U.S. Food and Drug Administration today approved Vimizim (elosulfase alfa), the first FDA-approved treatment for Mucopolysaccharidosis Type IVA (Morquio A syndrome). Morquio A syndrome is a rare, autosomal recessive lysosomal storage disease caused by a deficiency in N-acetylgalactosamine-6-sulfate sulfatase (GALNS). Vimizim is intended to replace the missing GALNS enzyme involved in an important metabolic pathway. Absence of this enzyme leads to problems with bone development, growth and mobility. There are approximately 800 patients with Morquio A syndrome in the United States.
Vimizim was granted priority review. An FDA priority review provides for an expedited review of drugs for serious diseases or conditions that may offer major advances in treatment. Vimizim is also the first drug to receive the Rare Pediatric Disease Priority Review Voucher - a provision that aims to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases.
The safety and effectiveness of Vimizim were established in a clinical trial involving 176 participants with Morquio A syndrome, ranging in age from 5 to 57 years. Participants treated with Vimizim showed greater improvement in a 6-minute walk test than participants treated with placebo. On average, patients treated with Vimizim in the trial walked 22.5 meters farther in 6 minutes compared to the patients who received placebo.
The most common side effects in patients treated with Vimizim during clinical trials included fever, vomiting, headache, nausea, abdominal pain, chills and fatigue. The safety and effectiveness of Vimizim have not been established in pediatric patients less than 5 years of age. Vimizim is being approved with a boxed warning to include the risk of anaphylaxis. During clinical trials, life-threatening anaphylactic reactions occurred in some patients during Vimizim infusions.
Vimizim is marketed by Novato, Calif.-based BioMarin Pharmaceutical Inc.

FDA NEWS RELEASE

For Immediate Release: Feb. 12, 2014

FDA approves Imbruvica to treat chronic lymphocytic leukemia

The U.S. Food and Drug Administration today expanded the approved use of Imbruvica (ibrutinib) for chronic lymphocytic leukemia (CLL) patients who have received at least one previous therapy.

CLL is a rare blood and bone marrow disease that usually gets worse slowly over time, causing a gradual increase in white blood cells called B lymphocytes, or B cells. The National Cancer Institute estimates that 15,680 Americans were diagnosed and 4,580 died from the disease in 2013.

Imbruvica works by blocking the enzyme that allows cancer cells to grow and divide. In November 2013, the FDA granted Imbruvica accelerated approval to treat patients with mantle cell lymphoma, a rare and aggressive type of blood cancer, if those patients received at least one prior therapy.

Under the agency's accelerated approval process, the FDA may approve a drug based on a surrogate or intermediate endpoint that is reasonably likely to predict clinical benefit. Drugs receiving accelerated approval are usually subject to an agreement to conduct confirmatory trials verifying and describing clinical benefit. Imbruvica for CLL also received priority review and orphan-product designation because the drug demonstrated the potential to be a significant improvement in safety or effectiveness in the treatment of a serious condition and is intended to treat a rare disease, respectively.

The FDA's accelerated approval of Imbruvica for CLL is based on a clinical study of 48 previously treated participants. On average, participants were diagnosed with CLL 6.7 years prior to the study and had received four previous therapies. All study participants received a 420 milligram orally administered dose of Imbruvica until the treatment reached unacceptable toxicity or the disease progressed. Results showed nearly 58 percent of participants had their cancer shrink after treatment (overall response rate). At the time of the study, the duration of response ranged from 5.6 to 24.2 months. An improvement in survival or disease-related symptoms has not been established.

The most common side effects observed in the clinical study include low levels of platelets in the blood (thrombocytopenia), diarrhea, bruising, a decrease in infection-fighting white blood cells (neutropenia), low red blood cells (anemia), upper respiratory tract infection, fatigue, pain in the muscles and bones (musculoskeletal pain), rash, fever (pyrexia), constipation, swelling of tissues (peripheral edema), joint pain (arthralgia), nausea, mouth sores (stomatitis), sinus infection (sinusitis) and dizziness.

Imbruvica is manufactured by Sunnyvale, Calif.-based Pharmacyclics.

FDA NEWS RELEASE

For Immediate Release: Jan. 31, 2014

FDA approves Hetlioz: first treatment for non-24 hour sleep-wake disorder in blind individuals

The U.S. Food and Drug Administration today approved Hetlioz (tasimelteon), a melatonin receptor agonist, to treat non-24- hour sleep-wake disorder ("non-24") in totally blind individuals. Non-24 is a chronic circadian rhythm (body clock) disorder in the blind that causes problems with the timing of sleep. This is the first FDA approval of a treatment for the disorder.

Non-24 occurs in persons who are completely blind. Light does not enter their eyes and they cannot synchronize their body clock to the 24-hour light-dark cycle.

Those with the disorder may have difficulty falling asleep or staying asleep, and may wake up groggy or feeling as if they need more rest. People with non-24 may find their sleep patterns reversed -- needing to sleep during the day and to be awake at night.

Although most people who are totally blind still can perceive light well enough to prevent non-24, there may be as many as 100,000 individuals in the United States with this condition, who can't perceive enough light to establish a normal night sleep schedule. Non-24 can occur at any age.

The effectiveness of Hetlioz was evaluated in 104 participants in two clinical trials of totally blind individuals with non-24 disorder. In the trials, treatment with Hetlioz resulted in significant improvement compared to placebo (inactive pill), both in increasing nighttime sleep and decreasing daytime sleep duration.

In clinical trials, the most common side effects reported by patients treated with Hetlioz were headache, elevated liver enzymes (alanine aminotransferase) in the blood, nightmares or unusual dreams, disturbed night's sleep, upper respiratory or urinary tract infection, and drowsiness.
Hetlioz can impair activities that require complete mental alertness. Hetlioz should be taken at the same time every night before bedtime and activities should be limited after taking the drug.
Hetlioz was reviewed under priority review. Priority review provides for an expedited review of drugs that treat serious conditions and have the potential to provide significant improvement in safety or effectiveness of the treatment, diagnosis, or prevention of such serious conditions. Hetlioz also received orphan-product designation by the FDA because it is intended to treat a rare disease or condition.
Hetlioz is manufactured by Vanda Pharmaceuticals, Inc. of Washington, D.C.

Safety Announcements

FDA evaluating risk of stroke, heart attack and death with FDA-approved testosterone products

[January 31, 2014] FDA announced that it is investigating the risk of stroke, heart attack, and death in men taking FDA approved testosterone products. We have been monitoring this risk and decided to reassess this safety issue based on the recent publication of two separate studies that each suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy. We are providing this alert while we continue to evaluate the information from these studies and other available data, and will communicate our final conclusions and recommendations when the evaluation is complete.
At this time, FDA has not concluded that FDA approved testosterone treatment increases the risk of stroke, heart attack, or death. Health care professionals should consider whether the benefits of FDA approved testosterone treatment is likely to exceed the potential risks of treatment. The prescribing information in the drug labels of FDA-approved testosterone products should be followed.
Testosterone products are FDA-approved only for use in men who lack or have low testosterone levels in conjunction with an associated medical condition. Example conditions include failure of the testicles to produce testosterone because of reasons such as genetic problems or chemotherapy. Other examples include problems with the hypothalamus and pituitary that control the testicles' production of testosterone. None of the FDA-approved testosterone products are approved for use in men with low testosterone levels who lack an associated medical condition.
An observational study of older men in the U.S. Veteran Affairs health system published in the *Journal of the American Medical Association* in November 2013 prompted FDA to reassess the cardiovascular safety of testosterone therapy. This study suggested a 30 percent increased risk of stroke, heart attack, and death in the group that had been prescribed testosterone therapy.
A second observational study reported an increased risk of heart attack in older men 65 years and older, as well as younger men less than 65 years, with pre-existing heart disease, who filled a prescription for testosterone therapy.

Safety Announcements

FDA to review heart failure risk with diabetes drug saxagliptin (marketed as Onglyza and Kombiglyze XR)

[02-11-2014] The U.S. Food and Drug Administration (FDA) has requested clinical trial data from the manufacturer of saxagliptin to investigate a possible association between use of the type 2 diabetes drug and heart failure. Our request resulted from a study published in the *New England Journal of Medicine* (NEJM), which reported an increased rate of hospitalization for heart failure, when the heart does not pump blood well enough, with use of saxagliptin (marketed as Onglyza and Kombiglyze XR) compared to an inactive treatment. The study did not find increased rates of death or other major cardiovascular risks, including heart attack or stroke, in patients who received saxagliptin. The manufacturer is expected to submit the trial data to FDA by early March 2014, after which we will conduct a thorough analysis and report our findings publicly.
At this time, we consider information from the NEJM study to be preliminary. Our analysis of the saxagliptin clinical trial data is part of a broader evaluation of all type 2 diabetes drug therapies and cardiovascular risk.

Patients should not stop taking saxagliptin and should speak with their health care professionals about any questions or concerns. Health care professionals should continue to follow the prescribing recommendations in the drug labels.
Type 2 diabetes is a disease in which there is a high level of sugar, or glucose, in the blood because the body does not make or properly use the hormone insulin. If left untreated, type 2 diabetes can lead to serious problems. Saxagliptin is used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. It works by increasing the amount of insulin produced by the body after meals, when blood sugar is high.
We urge health care professionals and patients to report side effects involving saxagliptin products to the FDA MedWatch program.

Current Drug Shortages Index (as of February 28, 2014):

The information provided in this section is provided voluntarily by manufacturers.

Amikacin Injection
Ammonium Chloride Injection (initial posting date 3/8/2013)
Amytal Sodium Injection (initial posting date 1/31/2013)
Atropine Sulfate Injection
Barium Sulfate for Suspension (initial posting date 10/12/2012)
Bumetanide Injection (initial posting date 6/21/2012)
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection UPDATED 2/25/2014
Buprenorphine Hydrochloride (Buprenex) Injection
Caffeine and Ergotamine Tartrate (Cafergot) Tablets (initial posting date 3/8/2012)
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection
Calcium Chloride Injection (initial posting date 12/13/2012)
Calcium Gluconate Injection (initial posting date 1/10/2013) UPDATED 2/25/2014
Chloramphenicol Sodium Succinate Injection (initial posting date 1/7/2014)
Chromic Chloride Injection
Cidofovir Injection (initial posting date 2/15/2013)
Citric Acid; Gluconolactone; Magnesium Carbonate (Renacidin) Solution for Irrigation (initial posting date 6/30/2012)
Clindamycin phosphate (Cleocin) Injection (initial posting date 10/2/2013) UPDATED 2/27/2014
Copper Injection (initial posting date 4/25/2013)
Cyanocobalamin Injection (initial posting date 1/25/2013) UPDATED 2/25/2014
Daunorubicin Hydrochloride Solution for Injection
Desmopressin Acetate (DDAVP) Injection (initial posting date 5/7/2013)
Dexamethasone Sodium Phosphate Injection (initial posting date 1/15/2013) UPDATED 2/25/2014
Dexmethylphenidate Hydrochloride (Focalin) (initial posting date 2/13/2014)
Dextrose Injection (initial posting date 5/23/2012) UPDATED 2/25/2014
Dipyridamole Injection (initial posting date 7/24/2012)
Dobutamine Hydrochloride Injection (initial posting date 4/26/2013) UPDATED 2/25/2014
Doxorubicin (Adriamycin) Lyophilized Powder (initial posting date 12/2/2011)
Epinephrine Injection (initial posting date 4/27/2012) UPDATED 2/25/2014
Epinephrine 1mg/mL (Preservative Free) (initial posting date 6/21/2012)
Ethiodol (Ethiodized Oil) Ampules
Fentanyl Citrate (Sublimaze) Injection UPDATED 2/25/2014
Heparin Sodium Injection (initial posting date 7/5/2012) UPDATED 2/25/2014
Intravenous Fat Emulsion
Ketorolac Tromethamine Injection UPDATED 2/25/2014
Leucovorin Calcium Lyophilized Powder for Injection UPDATED 2/25/2014
Leuprolide Acetate Injection UPDATED 2/18/2014

Lidocaine Hydrochloride (Xylocaine) Injection (initial posting date - 2/22/2012) UPDATED 2/25/2014
Liotrix (Thyrolar) Tablets
Lorazepam (Ativan) Injection UPDATED 2/25/2014
Magnesium Sulfate Injection UPDATED 2/25/2014
Mannitol (Osmitrol, Resectisol) Injection (initial posting date - 12/21/2011)
Mecasermin [rDNA origin] (Increlex) Injection (initial posting date - 4/26/2013)
Methazolamide (Glauctabs, Neptazane) Tablets (initial posting date - 6/29/2012) UPDATED 2/25/2014
Methyldopate Hydrochloride Injection
Methylin Chewable Tablets (initial posting date 2/19/2013)
Methylphenidate Hydrochloride ER Tablets (initial posting date 2/19/2013) UPDATED 2/27/2014
Methylphenidate Hydrochloride Tablets (initial posting date 2/19/2013) UPDATED 2/27/2014
Methylprednisolone Sodium Succinate Injection (initial posting date 2/14/2014)
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free) UPDATED 2/25/2014
Multi-Vitamin Infusion (Adult and Pediatric)
Nalbuphine Hydrochloride (Nubain) Injection (initial posting date 5/15/2012)
Neostigmine Methylsulfate Injection (initial posting date 1/14/2013) UPDATED 2/18/2014
Nitroglycerin in 5% Dextrose Injection (initial posting date 12/20/2013)
Ondansetron (Zofran) 2mg/mL Injection
Pancuronium Bromide Injection UPDATED 2/25/2014
Papaverine Hydrochloride Injection (initial posting date 12/17/2012)
Phosphate (Glycophos) Injection (initial posting date 5/29/2013)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting date 6/1/2012)
Potassium Acetate Injection, USP 2mEq/mL
Potassium Chloride Injection (initial posting date 5/15/2012) UPDATED 2/21/2014
Potassium Phosphate Injection UPDATED 2/25/2014
Procainamide HCL Injection
Prochlorperazine Injection (initial posting date 1/30/2012)
Promethazine Injection (initial posting date 2/10/2012)
Reserpine Tablets (initial posting date 4/17/2013)
Rifampin for Injection (initial posting date 3/22/2013) UPDATED 2/18/2014
Secretin Synthetic Human (ChiRhoStim) Injection (ChiRhoStim) (initial posting date 6/15/2012)
Selenium Injection
Sincalide (Kinevac) Lyophilized Powder for Injection (initial posting date 6/21/2013)
Sodium Chloride 0.9% Injection Bags (initial posting date 1/15/2014) UPDATED 2/25/2014
Sodium Chloride 23.4% UPDATED 2/25/2014
Sodium Phosphate Injection UPDATED 2/25/2014
Succinylcholine (Anectine, Quelicin) Injection (initial posting date 8/17/2012) UPDATED 2/18/2014
Sufentanil Citrate (Sufenta) Injection
Sulfamethoxazole 80mg/ml;Trimethoprim 16mg/ml (SMX/TMP) (Bactrim) Injection
Telavancin (Vibativ) Injection
Tetracycline Capsules
Thiotepa (Thioplex) for Injection
Ticarcillin Disodium/Clavulanic Potassium (Timentin) Injection (initial posting date 8/16/2012)
Tiopronin (Thiola) (initial posting date 10/31/2013)
Tobramycin Solution for Injection UPDATED 2/25/2014
Trace Elements (initial posting date 1/24/2013)
Verapamil Hydrochloride Injection, USP (initial posting date 4/17/2013)
Vitamin A Palmitate (Aquasol A)
Zinc Injection (initial posting date 2/15/2012)