Drug Utilization Review Board

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

Wednesday
October 10, 2012
6:00 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Keast, Pharm.D., M.S.

SUBJECT: Packet Contents for Board Meeting – October 10, 2012

DATE: October 6, 2012

NOTE: The DUR Board will meet at 6:00 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 October 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 / MCAU Program – See Appendix B.

Action Item – Vote to Prior Authorize Cialis® – See Appendix C.

Action Item – Vote to Prior Authorize Neupro® – See Appendix D.

Action Item – Annual Review of Bladder Control Medications and 30 Day Notice to Prior Authorize Myrbetriq™ – See Appendix E.

Action Item – Annual Review of Antidepressants and 30 Day Notice to Prior Authorize Forvivo XL™ and Fluoxetine 60mg – See Appendix F.

Action Item – Annual Review of Alzheimer's Medications – See Appendix G.

30 Day Notice to Prior Authorize Miscellaneous Butalbital Products – See Appendix H.

FDA and DEA Updates – See Appendix I.

Future Business

Adjournment

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Oklahoma Health Care Authority
Drug Utilization Review Board
(DUR Board)
Meeting – October 10, 2012 @ 6:00 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. September 12, 2012 DUR Minutes – Vote
- B. September 13, 2012 DUR Recommendation Memorandum

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

4. Update on DUR / Medication Coverage Authorization Unit – See Appendix B.
- A. Retrospective Drug Utilization Review Response for April 2012
- B. Medication Coverage Activity for September 2012
- C. Pharmacy Help Desk Activity for September 2012
- D. Retrospective Drug Evaluation: Focusing on Safety

Items to be presented by Dr. Weber, Dr. Muchmore, Chairman

5. Action Item – Vote to Prior Authorize Cialis® – See Appendix C.
- A. COP Recommendations

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

6. Action Item – Vote to Prior Authorize Neupro® – See Appendix D.
- A. COP Recommendations

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

7. Action Item – Annual Review of Bladder Control Medications and 30 Day Notice to Prior Authorize Myrbetriq™ – See Appendix E.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details
G. Myrbetriq™ Product Details

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

8. Action Item – Annual Review of Antidepressants and 30 Day Notice to Prior Authorize Forfivo XL™ and Fluoxetine 60mg – See Appendix F.

A. Current Authorization Criteria
B. Utilization Review
C. Prior Authorization Review
D. Market News and Update
E. COP Recommendations
F. Utilization Details
G. Forfivo XL™ Product Details

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

9. Action Item – Annual Review of Alzheimer's Medications® – See Appendix G.

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

Items to be presented by Dr. Moore, Dr. Muchmore, Chairman

10. 30 Day notice to Prior Authorize Miscellaneous Butalbital Products – See Appendix H.

A. Overview
B. Cost Comparison
C. COP Recommendations
D. Product Information

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

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. Annual Reviews
B. New Product Reviews
C. Utilization Review of COPD Medications

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of SEPTEMBER 12, 2012

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.: Vice-Chairman	X	
Mark Feightner, Pharm.D.		X
Anetta Harrell, Pharm.D.	X	
Evelyn Knisely, Pharm.D.	X	
Thomas Kuhls, M.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	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	X	
Shellie Keast, Pharm.D, M.S.; DUR Manager	X	
Chris Le, Pharm.D.; Clinical Coordinator	X	
Mark Livesay, Operations Manager	X	
Carol Moore, Pharm.D.; Clinical Pharmacist		X
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research		X
Leslie Robinson, D.Ph.; PA Coordinator		X
Jennifer Sipols, Pharm.D.; Clinical Pharmacist	X	
Jo Nel Weber, Pharm.D.; Clinical Pharmacist	X	
Graduate Students: Amany Hussein, Manish Mittal	X	
Visiting Pharmacy Student(s): Dawood Dawood, John Sutrick	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Garth Splinter, M.D., M.B.A.; Director of Medicaid/Medical Services	X	
Rebecca Pasternik-Ikard, Deputy State Medicaid Director	X	
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director	X	
Lynn Rambo-Jones, J.D.; Deputy General Counsel III		X
Carter Kimble, M.Ph.; Public Affairs- Information Representative		X
Jill Ratterman, D.Ph.; Pharmacy Specialist	X	
Kerri Wade, Senior Pharmacy Financial Analyst	X	
Stacey Hale, Pharmacy Research Analyst	X	

OTHERS PRESENT:		
Craig Jackson, GSK	Angela Bush, GSK	Jared Theodorakol, GSK
Don Kempir, NovoNordisk	Clint Degner, Novartis	Melissa Parker, Novartis
Jim Fowler, AZ	Tim Burke, AZ	Brent Bumpas, Endo
David Williams, Forest	Crystal Henderson, Forest	Bill Clark, BMS
Greg Klingman, Pfizer	Renee Richard, Sunovion	Warren Tayes, Merck
Brad Clay, Amgen	Michael Spence, Novartis	Russ Wilson, J&J
Roger Grotzinger, BMS	Mark DeClerk, Lilly	Kathy Phillips, Novo Nordisk
Brad Burgstattler , Elan		

PRESENT FOR PUBLIC COMMENT:	
Agenda Item No. 6	Tim Burke, Astra Zeneca

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

Agenda Item No. 6 Tim Burke, Astra Zeneca

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: August 8, 2012 DUR Minutes

Dr. Preslar moved to approve as amended to delete Dr. Kuhls from the Board members present on August 12, 2012; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON DUR/MEDICATION COVERAGE AUTHORIZATION UNIT

4A: Retrospective Drug Utilization Review Response: March 2012

4B: Medication Coverage Activity: August 2012

4C: Pharmacy Help Desk Activity: August 2012

4D: SoonerCare Atypical Rx Program Update

Reports included in agenda packet; presented by Dr. Keast.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE SELECT GONADOTROPIN-RELEASING HORMONE ANALOGS FOR CENTRAL PRECOCIOUS PUBERTY

Materials included in agenda packet; presented by Dr. Keast.

Dr. Kuhls moved to approve as submitted; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: ATYPICAL ANTIPSYCHOTICS ANNUAL REVIEW FOLLOW-UP

For Public Comment: Tim Burke, Astra Zeneca

Materials included in agenda packet; presented by Dr. Le.

The Board decided that "grandfathered" Seroquel XR should require a new PA justifying using the brand instead of the generic; and to send out an educational flyer to all the medical providers and discontinue grandfathering as of January 1, 2013 unless justification can be provided for PA.

Dr. Winegardener moved to approve with removal of Seroquel XR from grandfathering status; seconded by Dr. Harrell.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: ANNUAL REVIEW OF BENIGN PROSTATIC HYPERPLASIA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE CIALIS®

Materials included in agenda packet; presented by Dr. Weber.

The Board recommended only 5 mg Cialis for BPH, not 10 mg.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF ADCIRCA® AND REVATIO®

Materials included in agenda packet; presented by Dr. Sipols.

Dr. Kuhls moved to approve as submitted; seconded by Ms. Varalli-Claypool.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF BENLYSTA®
Materials included in agenda packet; presented by Dr. Sipols.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE NEUPRO®
Materials included in agenda packet; presented by Dr. Nawaz.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: FDA & DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: FUTURE BUSINESS
Materials included in agenda packet; submitted by Dr. Cothran.
A: Annual Reviews
B: New Product Reviews
C: Medical Product Reviews
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ADJOURNMENT
The meeting was adjourned at 6:58 p.m.

The University of Oklahoma
Health Sciences Center
COLLEGE OF PHARMACY
PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: September 13, 2012

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

From: Shellie Keast, Pharm.D., M.S.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of September 12, 2012

Recommendation 1: Vote to Prior Authorize Select Gonadotropin-Releasing Hormone Analogs for Central Precocious Puberty

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends medical and pharmacy prior authorization of select gonadotropin-releasing hormone analogs for central precocious puberty.

Criteria for Approval

1. FDA approved indication – central precocious puberty (ICD-9 –CM Diagnosis Code 259.1) confirmed by submitting:
    - Documentation of onset of symptoms at ages less than 8 years of age in females and 9 years of age in males.
    - Documentation that bone age is advanced 1 year beyond the chronological age.
    - Lab assessment:
        - Documentation of abnormal basal gonadotropin levels, OR
        - Documentation of pubertal response to a gonadotropin releasing hormone analog stimulation test.

2. Documentation of a failed trial of lower tiered products or FDA approved indication not covered by a lowered tiered product.

Tier 1	Tier 2	Tier 3
Leuprolide (Lupron® Depot, Lupron® Depot-Ped)	Histrelin (Supprelin LA®)	Nafarelin (Synarel®)

Recommendation 2: Atypical Antipsychotic Annual Review Follow-Up

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends an addition to the Atypical Antipsychotics prior authorization criteria to be effective January 1, 2013:

i In addition to applicable tier trials, petitions for Seroquel XR® (quetiapine extended-release) require a clinically significant reason why member cannot use the quetiapine immediate release.

~~Members currently stabilized on Seroquel XR® (quetiapine extended-release) will be grandfathered.~~

Recommendation 3: Annual Review of Benign Prostatic Hyperplasia Medications and 30 Day Notice to Prior Authorize Cialis® (tadalafil)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Adcirca® (sildenafil) and Revatio® (tadalafil)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the criteria:

Revatio® (sildenafil) and Adcirca® (tadalafil) criteria:

1. Member must be age 18 or older.
2. FDA approved diagnosis of pulmonary arterial hypertension.
3. Medical supervision by a pulmonary specialist and/or cardiologist.
4. Quantity limits:
    - Adcirca® (tadalafil) 20mg tabs: #60 tablets per 30 days.
    - Revatio® (sildenafil) 20mg tabs: #90 tablets per 30 days.

Additionally the Drug Utilization Review Board recommends discussions with pediatric cardiologists regarding appropriate use in children under 18 years of age.

Recommendation 5: Annual Review of Benlysta® (belimumab)

NO ACTION REQUIRED.

The College of Pharmacy recommends no changes to this category at this time.

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for April 2012

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 51-60	Hypnotics, Males and Females, Age 60-150	Contraindicated, Normal Pregnancy, Females, Age 30-34	High Dose, Duration, Proton Pump Inhibitors, females, Age 0-10

Response Summary (Prescriber)
Letters Sent: 38
Response Forms Returned: 23

The response forms returned yielded the following results:

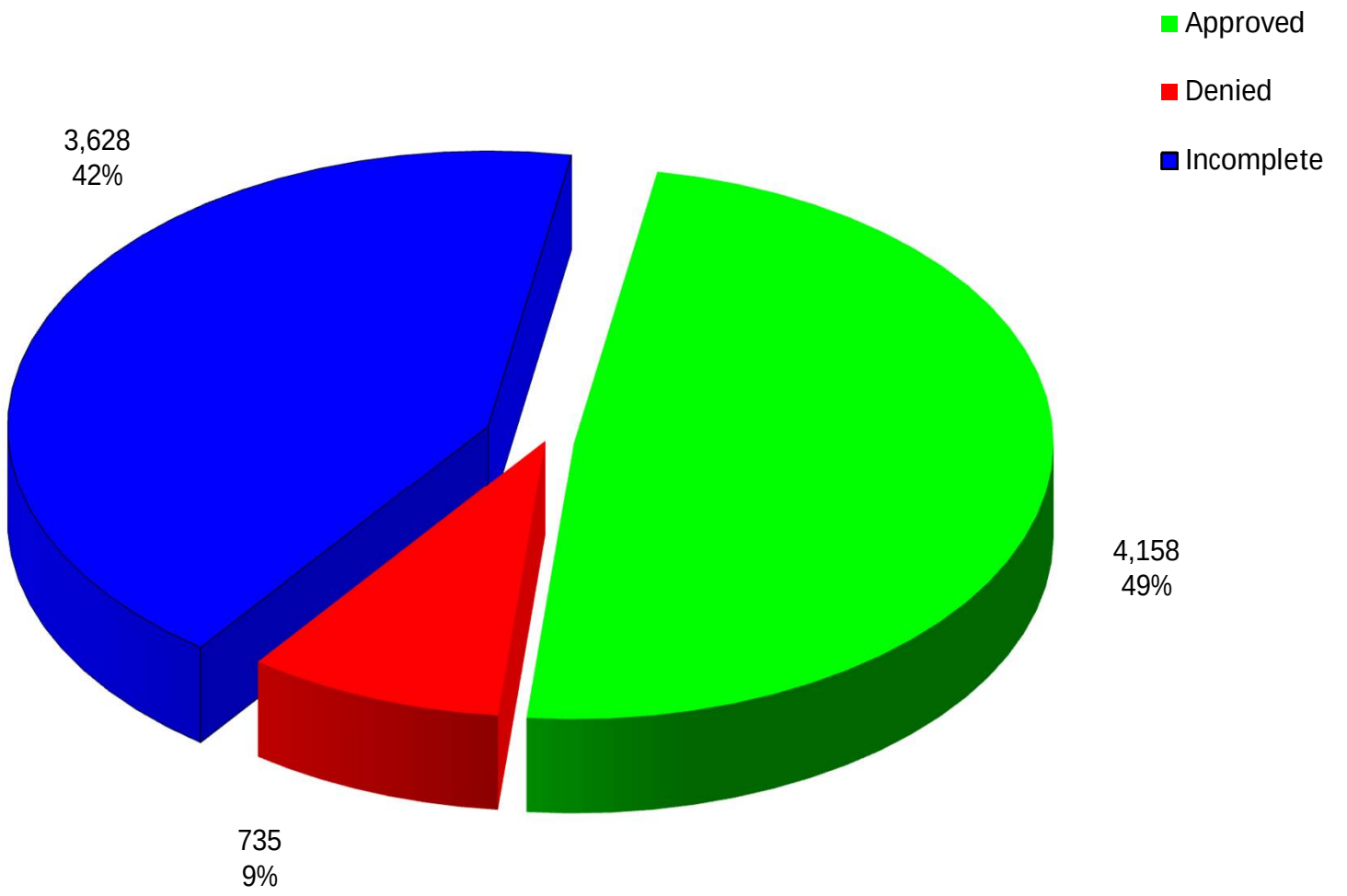
0 (0%)	*Record Error—Not my patient.*
1 (4%)	*No longer my patient.*
4 (17%)	*Medication has been changed prior to date of review letter.*
3 (13%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
14 (61%)	*I am aware of this situation and will plan to continue monitoring therapy.*
1 (4%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 4
Response Forms Returned: 2

The response forms returned yielded the following results:

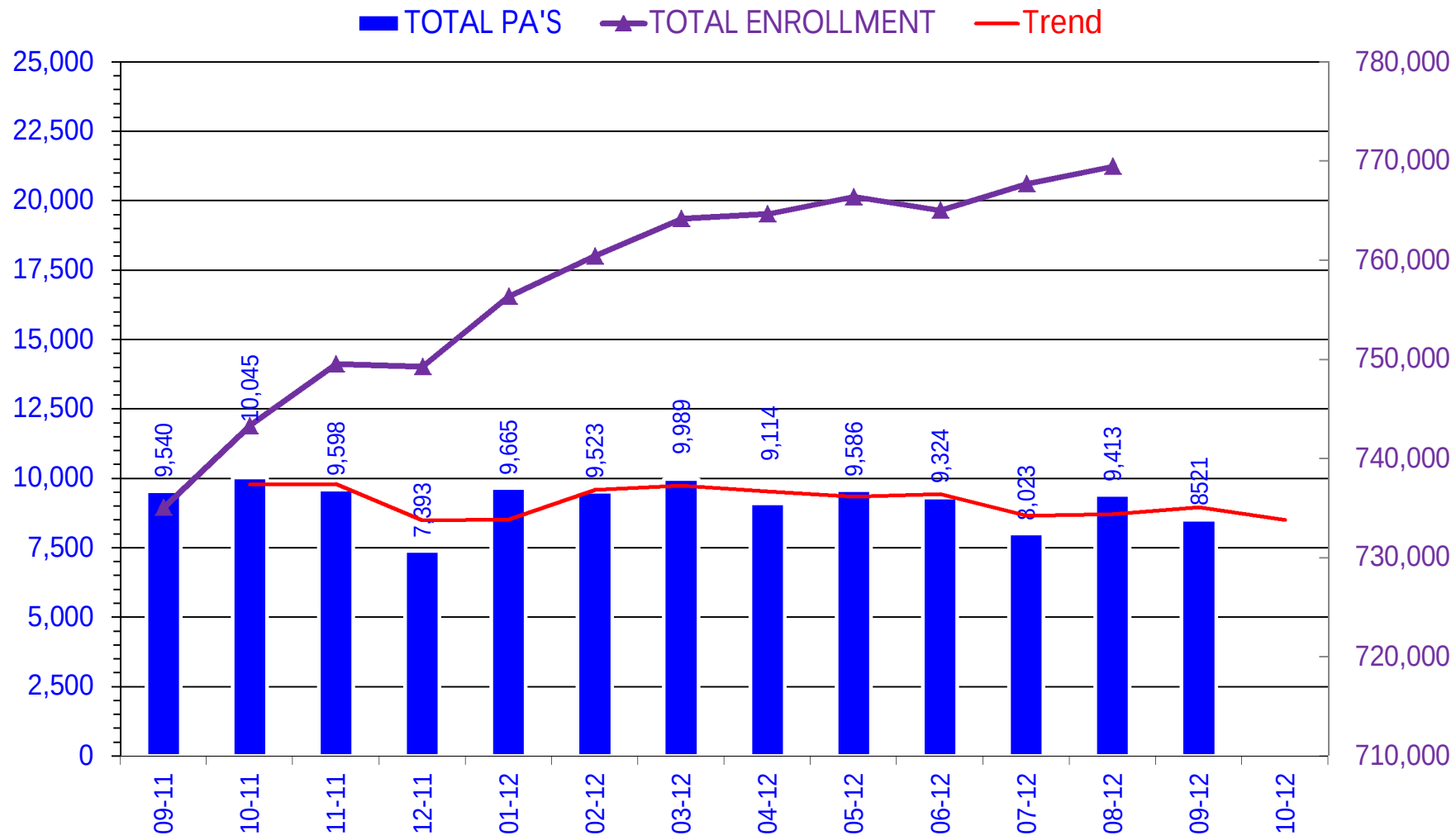
0 (0%)	*Record Error—Not my patient.*
0 (0%)	*No longer my patient.*
0 (0%)	*Medication has been changed prior to date of review letter.*
1(50%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
0 (0%)	*I am aware of this situation and will plan to continue monitoring therapy.*
1(50%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT: September 2012



PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: September 2011 – September 2012



PA totals include approved/denied/incomplete/overrides

Prior Authorization Activity

9/1/2012 Through 9/30/2012

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	355	122	12	221	359
Analgesic, Narcotic	360	165	36	159	250
Angiotensin Receptor Antagonist	53	10	7	36	358
Antiasthma	1,157	513	47	597	233
Antibiotic	20	3	2	15	9
Anticoagulant	32	25	1	6	359
Anticonvulsant	87	38	4	45	340
Antidepressant	327	117	32	178	329
Antidiabetic	139	56	5	78	348
Antihistamine	208	149	14	45	352
Antihyperlipidemic	15	3	2	10	360
Antimigraine	88	23	19	46	325
Antiplatelet	27	15	2	10	333
Antiulcers	357	107	76	174	97
Anxiolytic	121	84	5	32	235
Atypical Antipsychotics	360	214	8	138	344
Biologics	54	25	3	26	293
Bladder Control	76	12	4	60	358
Cardiovascular	31	7	6	18	254
Dermatological	105	24	31	50	105
Endocrine & Metabolic Drugs	209	136	15	58	353
Erythropoietin Stimulating Agents	43	23	1	19	95
Fibromyalgia	143	32	24	87	349
Gastrointestinal Agents	74	27	10	37	132
Genitourinary Agents	10	2	2	6	19
Growth Hormones	50	40	2	8	168
HFA Rescue Inhalers	116	14	25	77	311
Insomnia	69	14	9	46	164
Multiple Sclerosis	15	9	0	6	163
Muscle Relaxant	91	32	29	30	93
Nasal Allergy	179	13	62	104	150
Neurological Agents	46	34	5	7	358
Nsaids	138	21	18	99	304
Ocular Allergy	65	11	6	48	108
Ophthalmic	31	10	2	19	19
Osteoporosis	28	6	6	16	326
Other*	144	30	18	96	214
Otic Antibiotic	49	14	1	34	8
Pediculicide	97	34	7	56	11
Prenatal Vitamins	16	1	1	14	86
Smoking Cess.	52	16	0	36	35
Statins	75	32	6	37	359
Stimulant	798	392	57	349	336
Suboxone/Subutex	149	118	1	30	79
Topical Antibiotic	11	0	3	8	0
Topical Antifungal	14	3	2	9	39

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

Topical Corticosteroids	53	1	15	37	91
Vitamin	32	11	16	5	226
Pharmacotherapy	69	57	3	9	169
Emergency PAs	4	4	0	0	
Total	**6,842**	**2,849**	**662**	**3,331**	
Overrides					
Brand	94	70	3	21	344
Dosage Change	525	484	3	38	7
High Dose	6	5	0	1	196
Ingredient Duplication	12	11	0	1	9
Lost/Broken Rx	119	112	1	6	7
NDC vs Age	2	2	0	0	360
Nursing Home Issue	128	125	1	2	8
Other	36	32	1	3	8
Quantity vs. Days Supply	747	459	63	225	282
Stolen	9	8	1	0	6
Third Brand Request	1	1	0	0	5
Overrides Total	**1,679**	**1,309**	**73**	**297**	
Total Regular PAs + Overrides	**8,521**	**4,158**	**735**	**3,628**	

Denial Reasons	
Unable to verify required trials.	3,164
Does not meet established criteria.	697
Lack required information to process request.	473
Drug Not Deemed Medically Necessary	2

Other PA Activity

Duplicate Requests: 595

Letters: 2,216

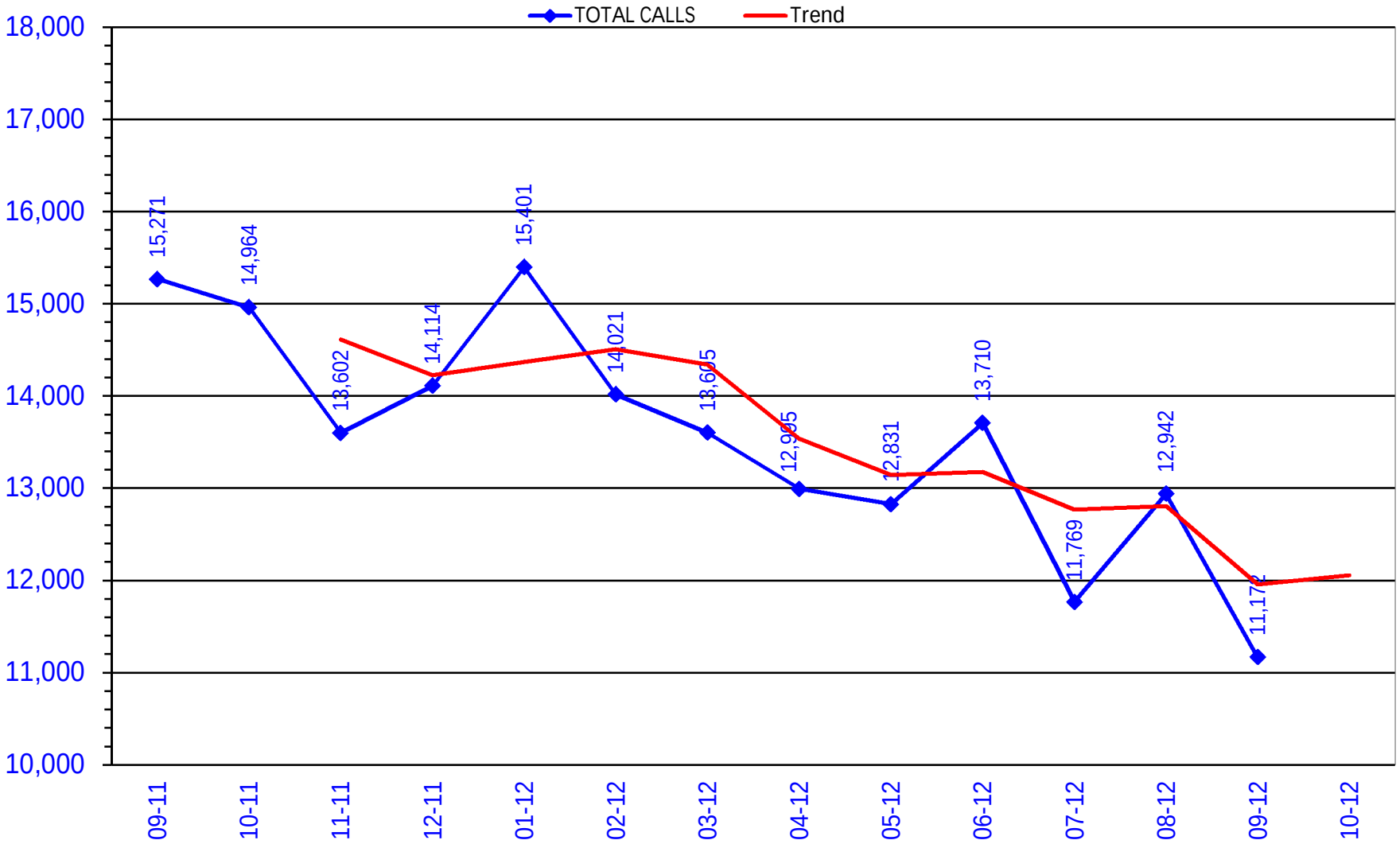
No Process: 296

Changes to existing PAs: 461

Partials: 915

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

CALL VOLUME MONTHLY REPORT:
September 2011 – September 2012



Retrospective Drug Evaluation: Focusing on Safety

1. Alisken Intervention Results
2. Sildenafil Use in Pediatrics
3. Overview of FDA Safety Alerts

1. Aliskiren Safety Intervention Results

Oklahoma Health Care Authority
October 2012

Background

In January of 2012, Novartis, the maker of aliskiren products sent out letters to healthcare professionals[1] regarding the results of the ALTITUDE study. In April of 2012 the FDA also issued a safety alert[2] regarding the risks of using aliskiren with angiotensin converting enzyme inhibitors (ACEIs) inhibitors and angiotensin receptor blockers (ARBs). In ALTITUDE, the risks of renal impairment, hypotension, and hyperkalemia in a group of patients taking aliskiren plus an ARB or ACEI increased relative to a group of patients taking placebo plus an ARB or ACEI. The risk of stroke and death were also numerically higher in aliskiren treated patients. Tekturna®, Tekturna HCT®, Tekamlo®, and Amturnide® will continue to be available for the treatment of high blood pressure in appropriate patients. Novartis decided to voluntarily cease marketing of Valturna® by July 2012. The labels for the aliskiren drugs have been updated with the following:

1. A new contraindication against the use of aliskiren with ARBs or ACEIs in patients with diabetes because of the risk of renal impairment, hypotension, and hyperkalemia.
2. A warning to avoid use of aliskiren with ARBs or ACEIs in patients with moderate to severe renal impairment (i.e., where glomerular filtration rate [GFR] < 60 mL/min).

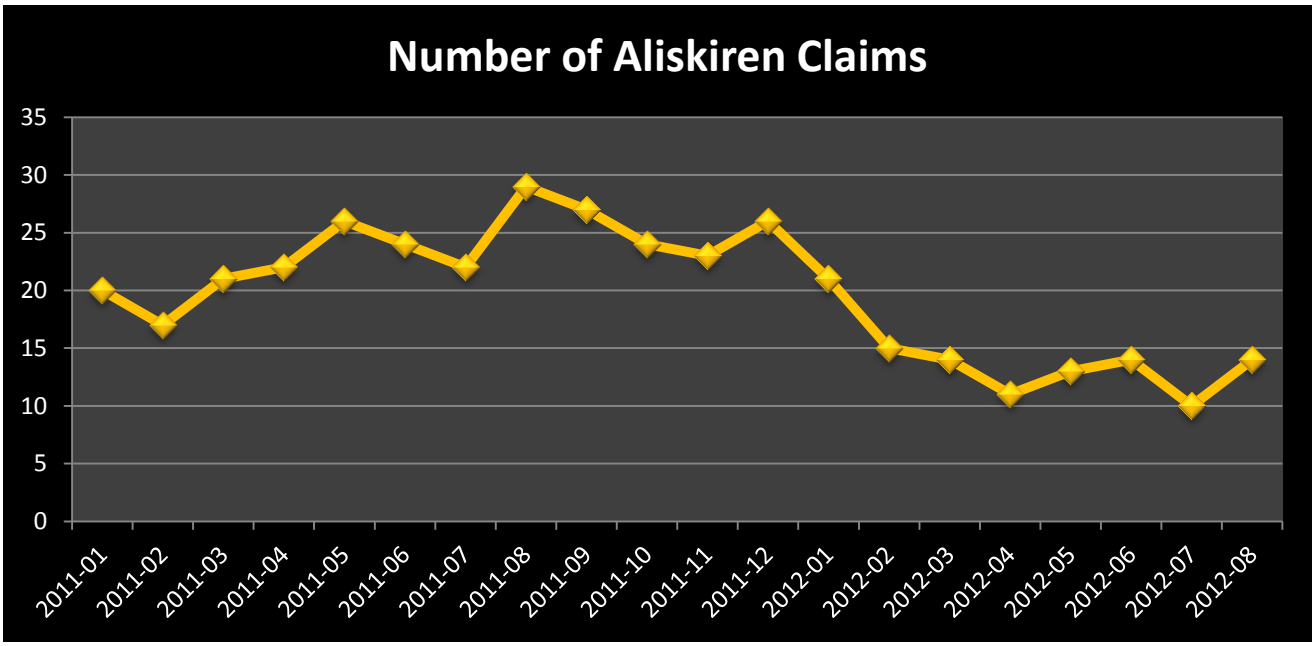
Intervention and Results

Utilization data was analyzed in the SoonerCare population to reveal members with a diagnosis code of Diabetes Type II on concomitant therapy of aliskiren and either an ACE inhibitor and/or an ARB from July through December 2011. Letters were sent to the prescribers of these members notifying them of the warnings in March of 2012. The letter and the response page are included as Attachment A. The results are as follows:

Total Members on Aliskiren	Diabetic Members on Aliskiren and ACEI/ARB	Letters Sent Prescribers	Diabetic Members Currently* on Aliskiren and ACEI/ARB
48 members	18 members	18 letters	2 members

*checked on 9/25/2012

The following trend shows the overall utilization of aliskiren products (Tekturna®, Tekturna HCT®, Tekamlo®, and Amturnide®) over the past 20 months.



Aliskiren utilization in the total SoonerCare population was re-evaluted in September 2012. For the first half of 2012, there were 16 diabetic members on aliskiren; however, only two are taking aliskiren concomitantly with an ACEI or ARB. They are the same members whose doctor has already received a letter in March of 2012.

Recommendations

The College of Pharmacy recommends no further action at this time. The data indicates good prescriber response to the College's initial intervention letter. Overall utilization of these medications has decreased in the SoonerCare population most likely due to the manufacturer warning, the College's intervention letter, and the FDA safety alert.

2. Sildenafil Utilization in Pediatric Members

Oklahoma Health Care Authority
October 2012

Background

On August 30, 2012, the FDA recommended that Revatio® (sildenafil) not be prescribed to children ages 1 through 17 for pulmonary arterial hypertension[3]. This recommendation is based on a recent long-term clinical pediatric trial showing that:

1. Children taking a high dose of Revatio® had a higher risk of death than children taking a low dose.
2. Low doses of Revatio are not effective in improving exercise ability.

Most deaths were caused by pulmonary hypertension and heart failure, which are the most common causes of death in children with PAH. The following new information is being added to the Revatio® drug label:

1. A new warning stating the use of Revatio® is not recommended in pediatric patients.
2. Results of the Revatio® trial in pediatric patients.

Evaluation of Sildenafil Utilization

Utilization of sildenafil (Revatio® and Viagra®) in the SoonerCare population in the past three months showed the following results:

Total Members	Members age 0-17 yrs	Members with Chronic Pulmonary Heart Disease*
104 members	83 members	74 members (20 adults, 54 pediatric)

*Coded on at least one medical claim in the past 2 years.

The data shows 80% of the use for these medications in the SoonerCare population is in the pediatric population 0-17 years of age. Clinical evidence was further reviewed to determine the appropriateness of this off-labeled use. The American College of Chest Physicians (ACCP)[4] recommends use of sildenafil as a first line option in functional class II and either sildenafil or bosentan as first line options in functional class III pulmonary hypertension. In the United States, there are no agents currently approved for pediatric use in the treatment of pulmonary arterial hypertension. It is the consensus of professionals in this field that adult treatment guidelines can be applied to the treatment of pediatrics[5]. The ACCP treatment guidelines are included as Attachment B. It is important to note the clinical trial that served as the basis for the FDA safety alert had no placebo arm for the extended results. It is unknown what the death rate would have been without treatment compared with sildenafil or if the patients were treated with another agent. The REVEAL Study[6], a prospective observational study, evaluated

the survival rates of newly or previously diagnosed patients (aged ≥ 3 months at diagnosis) with PAH enrolled from March 2006 to December 2009 at 55 US centers. The results are as follows:

Type of PAH	Survival Rates (2,635 Total Patients Evaluated)			
	1 year	3 year	5 year	7 year
PAH	85%	68%	57%	49%
Idiopathic/Familial PAH	91% ± 2%	74% ± 2%	65% ± 3%	59% ± 3%

According to the data presented in the FDA safety alert, the mortality rate of the patients on high dose sildenafil was approximately 10% at 3 years and 20-25% at 5 years. Another prospective cohort study conducted in the United Kingdom[7] following pediatric patients with idiopathic PAH showed survival rates of 89%, 84% and 75% at 1, 3, and 5 years respectively. These rates cannot be compared across trials; however this information adds perspective to the data being considered.

Pediatric Cardiologists Opinion

The College reached out to 6 pediatric cardiologists and received one response. Dr. Overholt, currently practicing at the University of Oklahoma's Children's Hospital advised further discussion before SoonerCare makes the decision to restrict this medication for pediatric members. He is in the process of organizing a response to our proposed criteria and advised against restricting the use of sildenafil for pediatric members as it may increase overall costs and risks of complications.

Conclusions

1. The majority of sildenafil use for PAH in the SoonerCare population is in members 0-17 years of age.
2. There are currently no agents approved for the pediatric population in the treatment of PAH.
3. There are few options available in the armamentarium of treatments, and sildenafil is currently recommended as one of the first line options.
4. Clinical evidence behind the FDA safety warning warrants further evaluation.

Recommendations

The College of Pharmacy recommends the following:

1. Maintain coverage of sildenafil products for pediatric members.
2. Send letters to current prescribers of sildenafil products in pediatric members notifying them of the FDA safety alert. The letter is included as attachment C for the DUR Board's review.

3. Overview of FDA Safety Alerts

Oklahoma Health Care Authority
October 2012

Introduction

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
9/19/2012	**Mirapex® (pramipexole)**	**Possible Risk of Heart Failure**
Issue Details: Results of recent studies suggest a potential risk of heart failure that needs further review of available data. Because of the study limitations, FDA is not able to determine whether Mirapex increases the risk of heart failure. **FDA Recommendations:** FDA has not concluded that Mirapex® increases the risk of heart failure. Continue to follow the recommendations in the drug label when prescribing Mirapex®. Patients should continue as directed.		

Date	Drug	Issue
8/15/2012	**Codeine Use in Certain Children After Tonsillectomy/Adenoidectomy**	**Risk of Rare, But Life-Threatening Adverse Events or Death**
Issue Details: The FDA is reviewing reports. Children developed serious adverse effects or died after taking codeine for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. These children (ages 2-5) had evidence of an inherited (genetic) ability to convert codeine into life-threatening or fatal amounts of morphine in the body. **FDA Recommendations:** Health care professionals should be aware, If prescribing codeine-containing drugs, the lowest effective dose for the shortest period of time should be used on an as needed basis.		

Date	Drug	Issue
7/23/2012	**Ampyra® (dalfampridine)**	**Seizure Risk for Multiple Sclerosis Patients**
Issue Details: Seizures are a known side effect of Ampyra. Ampyra is eliminated from the body through the kidneys. Patients with kidney impairment may develop higher blood levels of the drug, increasing seizure risk. Seizures happened within days to weeks after starting the recommended dose and occurred in patients having no history of seizures. **FDA Recommendations:** Patients and caregivers are advised to not change the Revatio® dose or stop taking Revatio® without talking to a health care professional.		

Date	Drug	Issue
5/14/2012	**Gilenya® (fingolimod)**	**Safety Review of a Reported Death After the First Dose**
Issue Details: FDA has received a report of a patient with MS who died within 24 hours of taking the first dose of Gilenya®. FDA could not definitively conclude that Gilenya® was related to any of the deaths. However, based on data, FDA remains concerned about the cardiovascular effects of Gilenya® after the first dose. Maximum heart rate lowering usually occurs within 6 hours of the first dose, but may occur as late as 20 hours post 1st dose. **FDA Recommendations:** Gilenya® is now contraindicated in **patients** with certain pre-existing or recent (within last 6 months) heart conditions or stroke, or who are taking certain antiarrhythmic medications. FDA also recommend cardiovascular monitoring is extended past 6 hours in patients who are at higher risk or who may not tolerate bradycardia. Extended monitoring should include continuous ECG monitoring overnight.		

Date	Drug	Issue
5/7/2012	**Revlimid® (lenalidomide)**	**Increased Risk of Developing New Malignancies**
Issue Details: Newly-diagnosed patients treated with Revlimid® had an increased risk of developing second primary malignancies compared to similar patients who received a placebo. Trials showed there was an increased risk of developing acute myelogenous leukemia, myelodysplastic syndromes, and Hodgkin lymphoma. **FDA Recommendations:** Healthcare professionals should consider both the potential benefit of Revlimid® and the risk of second primary malignancies when deciding to treat patients with this drug, and monitor patients for this risk.		

Date	Drug	Issue
4/26/2012	**Victrelis® (boceprevir) and Ritonavir-Boosted Human Immunodeficiency Virus (HIV) Protease Inhibitor Drugs**	**Drug Interactions**
Issue Details: Co-administration of Victrelis® (boceprevir), along with certain ritonavir-boosted HIV protease inhibitors, is not recommended. The findings of a drug-drug interaction study and clinical trial showed that co-administration increased the possibility of reducing the effectiveness of the medicines, permitting the amount of HCV or HIV virus in the blood to increase. Ritonavir-boosted HIV protease inhibitors include: Reyataz®, Prezista®, and Kaletra®. **FDA Recommendations:** drug label has been revised.		

[1] http://www.pharma.us.novartis.com/assets/pdf/Tekturna_Quo_Site_for_Professionals.pdf
[2] http://www.fda.gov/Drugs/DrugSafety/ucm300889.htm#data
[3] http://www.fda.gov/Drugs/DrugSafety/ucm317123.htm
[4] David B. Badesch, MD, FCCP; Steven H. Abman, MD; Gerald Simonneau, MD; Lewis J. Rubin, MD, FCCP; Vallerie V. McLaughlin, MD,FCCP. Medical Therapy for Pulmonary Arterial Hypertension*: Updated ACCP Evidence-Based Clinical Practice Guidelines. *CHEST*.June 2007; 131(6):1917-1928. doi:10.1378/chest.06-2674. Available Online at: http://journal.publications.chestnet.org/article.aspx?articleid=1085181#t1
[5] Galiè N, Hoeper MM, Humbert M, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension: The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009; 30: 2493–2537.
[6] Raymond L. Benza, MD; Dave P. Miller, MS; Robyn J. Barst, MD, FCCP; David B. Badesch, MD, FCCP; Adaani E. Frost, MD, FCCP; Michael D. McGoon, MD, FCCP. An Evaluation of Long-term Survival From Time of Diagnosis in Pulmonary Arterial Hypertension From the REVEAL Registry. *CHEST*.August 2012;142(2):448-456. doi: 10.1378/chest.11-1460. Available online at: http://journal.publications.chestnet.org/article.aspx?articleid=1262338
[7] S Moledina, A A Hislop, H Foster, I Schulze-Neick, S G Haworth. Childhood idiopathic pulmonary arterial hypertension: a national cohort study. *Heart* 2010;96:1401-1406 doi:10.1136/hrt.2009.182378. Available online at: http://heart.bmj.com/content/96/17/1401.abstract?ijkey=a4ddf96e30151c41dedc9340c808e917666ef1d9&keytype2=tf_ipsecsha

Attachment A

SoonerCare
Pharmacy Services

Dear Prescriber,

A review of SoonerCare pharmacy claims indicates that you have at least one diabetic patient on the combination of aliskiren (Tekturna®) and either an angiotensin-converting enzyme (ACE) inhibitor OR angiotensin receptor blocker (ARB).

A recent study shows that these combinations **increase incidence of hyperkalemia, hypotension, non-fatal strokes, and renal complications** in type 2 diabetic patients.

According to the *Dear Healthcare Provider Letter* from Novartis, prescribers are encouraged to review treatment at a patient's next routine visit. Aliskiren (Tekturna®) or aliskiren-containing fixed combination products should not be used in combination with ACE inhibitors or ARBs in patients with diabetes, therefore:

- Stop aliskiren-containing treatment in patients who are diabetic and also taking an ACE inhibitor or an ARB. Alternative antihypertensive treatment should be considered as necessary.
- Stop the use of Valturna® (aliskiren and valsartan) in patients who are diabetic, as this product contains aliskiren and an ARB. Alternative antihypertensive treatment should be considered as necessary.
- Aliskiren-containing products should not be initiated in diabetic patients who are also taking either an ACE inhibitor or an ARB.
- Patients should NOT stop any treatment before discussing with a healthcare professional.

To view more of the *Dear Healthcare Provider Letter* regarding these recent findings go to: http://www.pharma.us.novartis.com/assets/pdf/TKT-1118923%20Dear_HCP_Letter_email_with%20Tek-Val%20PIs_vf.pdf

Please remember that you are receiving this letter based upon the information available in the SoonerCare claims database at the time of review. Recent changes to therapy may not be reflected.

We value your response to this information regarding the member's current anti-hypertension therapy. Please note any comments on the attached provider response form and return the form in the enclosed envelope. This helps us ensure a high standard of quality of care for our SoonerCare members. Thank you for your time and assistance in this process.

Sincerely,

Oklahoma Health Care Authority

SoonerCare Pharmacy Services
Pharmacy Management Consultants
PO Box 26901; ORI W-4403
Oklahoma City, Oklahoma 73190
Phone: (800) 522-0114, option 4

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

Provider #: XXXXXX Provider Name: XXXXXX

Prescriber NPI: XXXXXXX

Patient Id: XXXXXXX Screening Date:

This information is communicated strictly in confidence to the provider for evaluation and response:

- ☐ Not my patient.
- ☐ No longer my patient.
- ☐ Medication has been changed prior to date of review letter.
- ☐ I was unaware of this situation and will consider making appropriate changes in therapy.
- ☐ I am aware of this situation and will plan to continue monitoring this therapy.
- ☐ Other, comments:

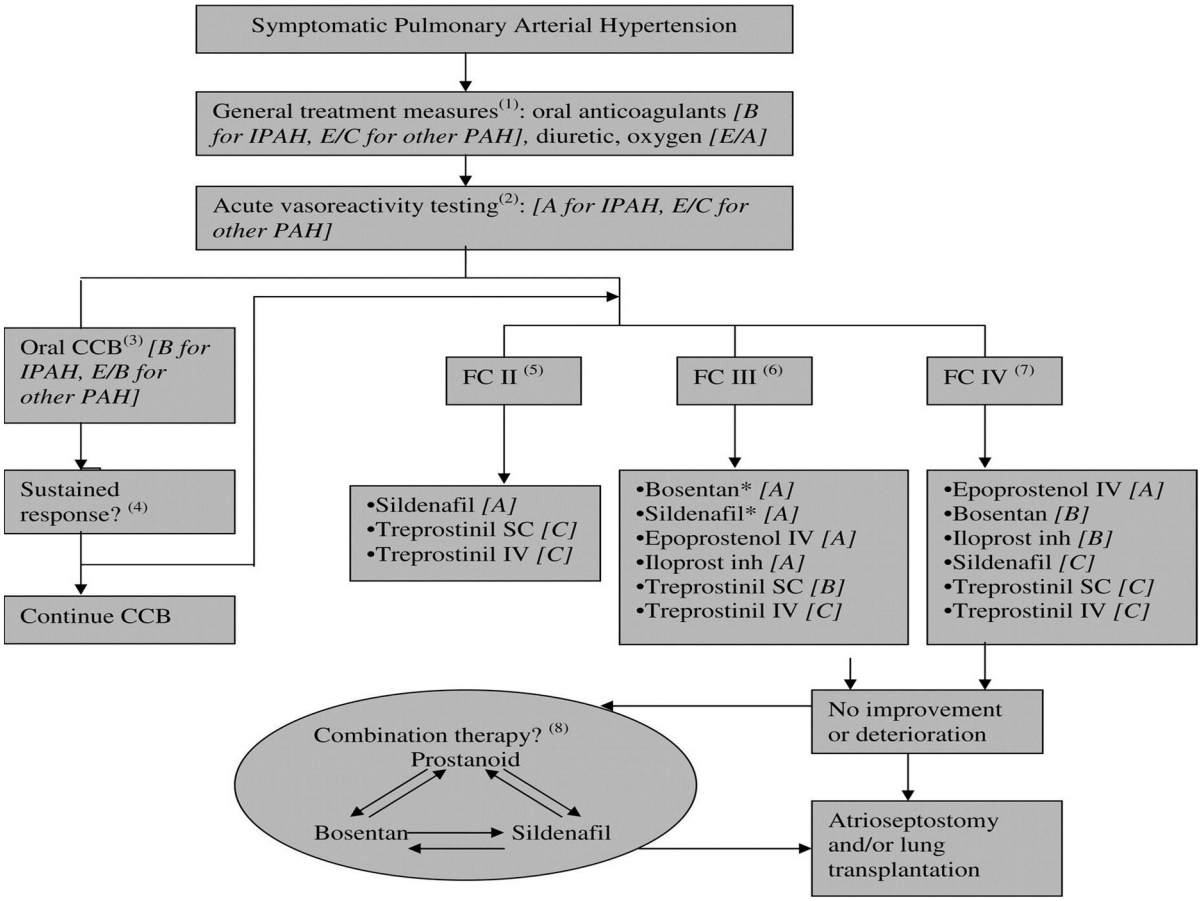
Name (please print) Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-6002 or (866) 335-3331

SoonerCare Pharmacy Services
Pharmacy Management Consultants
PO Box 26901; ORI W-4403
Oklahoma City, Oklahoma 73190
Phone: (800) 522-0114, option 4

Attachment B



* Not in order of preference.

Treatment algorithm for PAH. (1) Anticoagulation should be considered for patients with IPAH, and patients with an indwelling catheter for the administration of an IV prostanoid, in the absence of contraindications. Diuretics and oxygen should be added as necessary. (2) A positive acute vasodilator response is defined as a fall in PAPm ≥ 10 mm Hg to ≤ 40 mm Hg, with an unchanged or increased cardiac output when challenged with inhaled nitric oxide, IV epoprostenol, or IV adenosine. (3) Consideration should be given to using a PAH-specific medication such as a phosphodiesterase 5 inhibitor, endothelin receptor antagonist, or prostanoid as first-line treatment instead of a CCB in patients with PAH that is not IPAH or PAH associated with anorexigen use, or in those in an advanced functional class (FC) given the exceedingly low long-term response rate to CCB monotherapy in the former and poor prognosis in the latter. (4) Sustained response to CCB therapy is defined as being in functional class I or II with normal or near-normal hemodynamics after several months of treatment. (5) The risks and benefits of treatment in early PAH should be considered. (6) First-line therapy for functional class III includes bosentan, sildenafil, epoprostenol, inhaled (inh) iloprost, and treprostinil (see text for details). (7) Most experts recommend IV epoprostenol as first-line treatment for unstable patients in functional class IV. (8) RCTs studying add-on combination treatment regimens are underway.

Strength of Recommendation:
A = Strong recommendation, B = Moderate recommendation, C = Weak recommendation, D = Negative recommendation, I = No recommendation possible (inconclusive), E/A = Strong recommendation based on expert opinion only, E/B = Moderate recommendation based on expert opinion only, E/C = Weak recommendation based on expert opinion only, E/D = Negative recommendation based on expert opinion only

Attachment C

SoonerCare
Pharmacy Services

Dear Prescriber,

A review of SoonerCare pharmacy claims indicates that you have at least one pediatric patient on sildenafil (Revatio® or Viagra®). On August 30, 2012, the FDA recommended that (sildenafil) not be prescribed to children ages 1 through 17 for pulmonary arterial hypertension. This recommendation is based on a recent long-term clinical pediatric trial showing that:

1. Children taking a high dose of Revatio® had a higher risk of death than children taking a low dose.
2. Low doses of Revatio® are not effective in improving exercise ability.

Most deaths were caused by pulmonary hypertension and heart failure, which are the most common causes of death in children with PAH. The following new information is being added to the Revatio® drug label:

1. A new warning stating the use of Revatio® is not recommended in pediatric patients.
2. Results of the Revatio® trial in pediatric patients.

Additional Information for Healthcare Professionals

- Use of Revatio®, particularly chronic use, is not recommended in children. An unexpectedly higher risk of mortality was found in pediatric patients taking a high dose of Revatio® when compared to pediatric patients taking a low dose.
- The maximum recommended dose of Revatio® for adult patients with PAH is 20mg three times a day.
- Report adverse events involving sildenafil to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

To view more of the FDA safety alert go to: http://www.fda.gov/Drugs/DrugSafety/ucm317123.htm

Please remember that you are receiving this letter based upon the information available in the SoonerCare claims database at the time of review. Recent changes to therapy may not be reflected.

We value your response to this information regarding the member's current anti-hypertension therapy. Please note any comments on the attached provider response form and return the form in the enclosed envelope. This helps us ensure a high standard of quality of care for our SoonerCare members. Thank you for your time and assistance in this process.

Sincerely,

Oklahoma Health Care Authority

SoonerCare Pharmacy Services
Pharmacy Management Consultants
PO Box 26901; ORI W-4403
Oklahoma City, Oklahoma 73190
Phone: (800) 522-0114, option 4

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

Provider #: XXXXXX Provider Name: XXXXXX

Prescriber NPI: XXXXXXX

Patient Id: XXXXXXX Screening Date:

This information is communicated strictly in confidence to the provider for evaluation and response:

- ☐ Not my patient.
- ☐ No longer my patient.
- ☐ Medication has been changed prior to date of review letter.
- ☐ I was unaware of this situation and will consider making appropriate changes in therapy.
- ☐ I am aware of this situation and will plan to continue monitoring this therapy.
- ☐ Other, comments:

Name (please print) _____ Signature _____

Please Return This Page Only

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SoonerCare Pharmacy Services
Pharmacy Management Consultants
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Phone: (800) 522-0114, option 4

Appendix C

Vote to Prior Authorize Cialis® (tadalafil)

Oklahoma HealthCare Authority

October 2012

Recommendations

The College of Pharmacy recommends the addition of a Tier 3 and placement of Cialis® (tadalafil) into Tier 3 of the Benign Prostatic Hyperplasia PBPA category with the following criteria:

Tier 2 Prior Authorization Criteria:

1. FDA approved diagnosis.
2. A 4-week trial of two Tier 1 medications from different pharmacological classes within 90 days.
3. Documented adverse effect, drug interaction, or contraindication to all available Tier 1 products.

Tier 3 Prior Authorization Criteria:

1. FDA approved diagnosis of BPH.
2. Trial of at least two Tier 1 medications from different pharmacological classes.
3. A 4-week trial of each Tier 2 medication within the past 5 months.
4. Documented adverse effect, drug interaction, or contraindication to all available Tier 2 products.
5. Authorizations for Cialis® (tadalafil) will be granted for 5mg tablets only.

Tier 1	Tier 2	Tier 3
Uroxatral® (Alfuzosin)	Rapaflo® (Silodosin)	**Cialis® (tadalafil) 5mg**
Hytrin® (Terazosin)	Cardura XL® (Doxazosin)	
Cardura® (Doxazosin)	Avodart® (Dutasteride)	
Flomax® (Tamsulosin)	Jalyn® (Dutasteride/Tamsulosin)	
Proscar® (Finasteride)		

Appendix D

Vote to Prior Authorize Neupro® (Rotigotine Transdermal System)

Oklahoma Health Care Authority
October 2012

Recommendations:

The College of Pharmacy recommends the prior authorization of Neupro® (rotigotine transdermal system) with the following criteria:

Parkinson's Disease:

1. FDA approved indication for the treatment of signs and symptoms of Parkinson's Disease.
2. Must be 18 years old or older.
3. Prior use of or clinically significant reason why member cannot use oral dopamine agonists.

Restless Leg Syndrome:

1. FDA approved indication of Restless Leg Syndrome.
2. Must be 18 years or older.
3. Must provide documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
    a. carbidopo/levodopa
    b. pramipexole
    c. ropinirole

Appendix E

Fiscal Year 2012Annual Review of Bladder Control Medications And 30 Day Notice to Prior Authorize Myrbetriq™ (Mirabegron)

Oklahoma HealthCare Authority
October 2012

Current Prior Authorization Criteria

Tier 2 Authorization Criteria:

1. Trial of one Tier 1 medication that yielded inadequate clinical response or adverse effects, or
2. A unique indication which the Tier 1 drugs lack.

Tier 3 Authorization Criteria:

1. Trial of all Tier 2 medications that yielded inadequate clinical response or adverse effects, or
2. A unique indication which the Tier 2 drugs lack.

This category will be grandfathered.

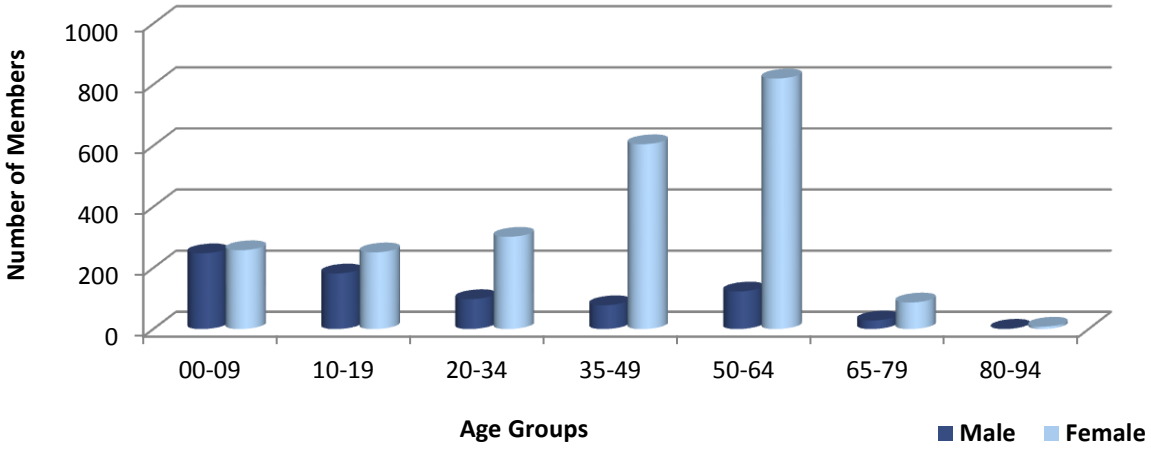
Bladder Control Medications		
Tier-1	**Tier-2**	**Tier-3**
Flavoxate **(Urispas®)** Oxybutynin **(Ditropan®)**	Oxybutynin ER Tabs **(Ditropan XL®)** Tolterodine **(Detrol®)**	Oxybutynin Patch **(Oxytrol®)** Oxybutynin Gel **(Gelnique™)** Tolterodine ER Tabs **(Detrol LA®)** Fesoterodine **(Toviaz™)** Solifenacin **(VESIcare®)** Darifenacin **(Enablex®)** Trospium **(Sanctura™)** Trospium ER **(Sanctura XR™)**

Utilization of Bladder Control Medications

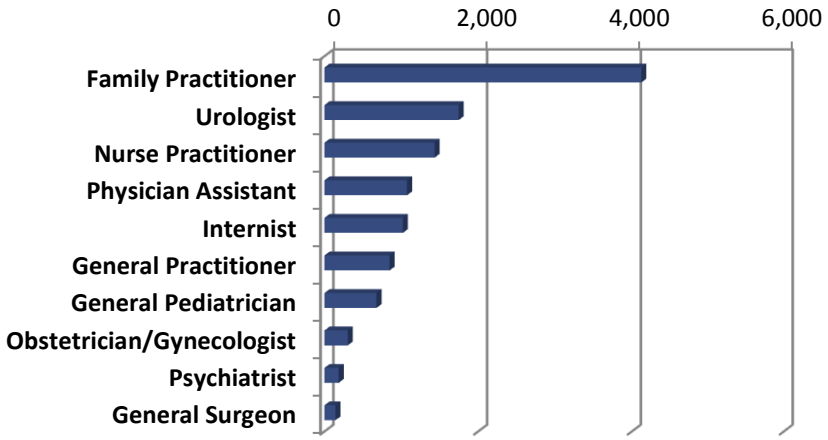
Comparison of Fiscal Years

Fiscal Year	Total Members	Total Claims	Total Cost	Cost per Claim	Per-Diem Cost	Total Units	Total Days
2011	**2,970**	**11,775**	**$888,710.92**	**$75.47**	**$2.38**	**883,555**	**373,054**
2012	**3,089**	**12,948**	**$1,001,324.63**	**$77.33**	**$2.46**	**981,022**	**407,621**
% Change	**4.0%**	**10.0%**	**12.7%**	**2.5%**	**3.4%**	**11.0%**	**9.3%**
Change	**119**	**1,173**	**$112,613.71**	**$1.86**	**$0.08**	**97,467**	**34,567**

Demographics of Members Utilizing Bladder Control Medications: FY 2012



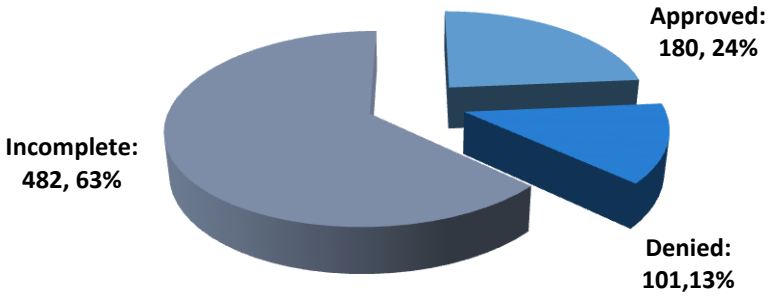
Prescribers of Bladder Control Medications by Number of Claims: FY 2012



Prior Authorization of Bladder Control Medications

There were a total of 765 petitions submitted for this PBPA category during fiscal year 2012. The following chart shows the status of the submitted petitions.

Status of Petitions for Bladder Control Medications: FY 2012



Market News and Updates

Upcoming Patent Expirations :

- **Enablex® (darifenacin)**- August 2016

Label Changes :

- **Detrol® (tolterodine) and Detrol LA® (tolterodine LA)**
  - September 2011- Warning adding of the potential to cause anaphylaxis and angioedema requiring hospitalization and emergency treatment with the first or subsequent doses.
- **Toviaz™ (fesoterodine)**
  - February 2011- Warning added that angioedema of the face, lips, tongue and/or larynx has been reported, in some cases after the first dose.
  - December 2011- Adverse reaction of pruritis and urticaria added.

Myrbetriq™ (Mirabegron) [(1)]

- Myrbetriq™ (Mirabegron) was FDA approved June 2012. It is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.
- Myrbetriq™ (Mirabegron) is available in 25 MG and 50 MG extended-release tablets. The recommended starting dose is 25 MG once daily and can be taken with or without food. If within 8 weeks the patient finds the 25 MG dose tolerable and effective, the dose may be increased to 50 MG once daily.
- Myrbetriq™ (Mirabegron) can cause an increase in blood pressure and periodically blood pressure should be monitored, especially in hypertensive patients. However, Myrbetriq™ is not recommended in severe uncontrolled hypertensive patients. Myrbetriq™ (Mirabegron) should be administered with caution in patients with urinary retention with bladder outlet obstruction and in patients taking anti-muscarinic drugs for OAB because of risk of urinary retention.

Cost

Myrbetriq™ (Mirabegron) comes in the following strengths:

Dose	Estimated Acquisition Cost (EAC)+	Est. 30 Day Cost*
25 MG tablet	$7.34	$220.20
50 MG tablet	$7.34	$220.20

+not including $4.02 dispensing fee

*once daily dosing

Recommendations

The College of Pharmacy recommends the placement of Myrbetriq™ (mirabegron) within Tier 3 of the Bladder Control Medications with the existing criteria:

This category will be grandfathered.

Bladder Control Medications		
Tier-1	**Tier-2**	**Tier-3**
Flavoxate **(Urispas®)** Oxybutynin **(Ditropan®)**	Oxybutynin ER Tabs **(Ditropan XL®)** Tolterodine **(Detrol®)**	Oxybutynin Patch **(Oxytrol®)** Oxybutynin Gel **(Gelnique™)** Tolterodine ER Tabs **(Detrol LA®)** Fesoterodine **(Toviaz™)** Solifenacin **(VESIcare®)** Darifenacin **(Enablex®)** Trospium **(Sanctura™)** Trospium ER **(Sanctura XR™)** **Mirabegron (Myrbetriq™)**

Utilization Details of Bladder Control Medications: Fiscal Year 2012

MEDICATION	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
SANCTURA TAB 20MG	1	60	30	1	$142.72	2	1.00	$4.76	0.01%
OXYTROL DIS 3.9MG/24	10	128	406	2	$3,349.84	0.32	5.00	$8.25	0.33%
TOVIAZ TAB 4MG	30	875	875	6	$4,210.28	1	5.00	$4.81	0.42%
TROSPIUM CL TAB 20MG	32	1,900	950	7	$4,439.54	2	4.57	$4.67	0.44%
ENABLEX TAB 7.5MG	107	3,917	3,647	26	$19,770.85	1.07	4.12	$5.42	1.98%
DETROL LA CAP 2MG	127	4,698	4,515	20	$24,991.37	1.04	6.35	$5.54	2.50%
FLAVOXATE TAB 100MG	135	7,843	2,758	84	$7,336.20	2.84	1.61	$2.66	0.73%
TOVIAZ TAB 8MG	141	4,230	4,230	20	$20,137.95	1	7.05	$4.76	2.01%
OXYBUTYNIN TAB 5MG ER	144	6,169	4,916	44	$8,142.90	1.25	3.27	$1.66	0.81%
ENABLEX TAB 15 MG	188	8,140	7,120	29	$40,836.88	1.14	6.48	$5.74	4.08%
VESICARE TAB 10MG	196	6,600	6,540	34	$37,406.45	1.01	5.76	$5.72	3.74%
DETROL TAB 1MG	198	11,438	6,094	76	$35,303.93	1.88	2.61	$5.79	3.53%
OXYBUTYNIN TAB 15MG ER	209	9,581	7,431	42	$15,289.49	1.29	4.98	$2.06	1.53%
VESICARE TAB 5MG	268	11,156	9,956	44	$61,511.15	1.12	6.09	$6.18	6.15%
SANCTURA XR CAP 60MG	451	17,147	15,308	89	$90,511.26	1.12	5.07	$5.91	9.04%
OXYBUTYNIN TAB 10MG ER	461	19,651	15,841	99	$24,378.32	1.24	4.66	$1.54	2.44%
DETROL LA CAP 4MG	986	38,864	37,008	148	$204,135.46	1.05	6.66	$5.52	20.39%
OXYBUTYNIN SYP 5MG/5ML	1,105	285,125	31,032	344	$11,425.46	9.19	3.21	$0.37	1.14%
DETROL TAB 2MG	1,684	99,616	52,404	439	$313,824.81	1.9	3.84	$5.99	31.35%
OXYBUTYNIN TAB 5MG	6,467	443,464	196,320	1,905	$73,788.15	2.26	3.39	$0.38	7.37%
TOTALS:	**12,940**	**980,602**	**407,381**	**3,089***	**$1,000,933.01**	**2.41**	**4.19**	**$2.46**	**100%**

Total number of unduplicated members

Product Information of Myrbetriq™ (mirabegron)[1]

INDICATIONS: Myrbetriq™ is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

DOSAGE FORM: Extended-release tablets: 25 MG and 50 MG.

ADMINISTRATION:

- Recommended starting dose is 25 MG once daily, with or without food.
- 25 MG is effective within 8 weeks. Based on individual efficacy and tolerability, may increase dose to 50 MG once daily.
- Swallow whole with water, do not chew, divide or crush.
- Patients with Severe Renal Impairment or Patients with Moderate Hepatic Impairment: Maximum dose is 25 MG once daily.
- Patients with End Stage Renal Disease (ESRD) or Patients with Severe Hepatic Impairment: Not recommended.

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS:

- Increases in Blood Pressure: Myrbetriq™ can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Myrbetriq™ is not recommended for use in severe uncontrolled hypertensive patients.
- Urinary Retention in Patients with Bladder Outlet Obstruction and in Patients Taking Antimuscarinic Drugs for Overactive Bladder: Administer with caution in these patients because of risk of urinary retention.

SPECIAL POPULATIONS:

- **Pregnancy Category C**: Use only if the benefit to the mother outweighs the potential risk to the fetus.
- **Nursing Mothers**: Myrbetriq™ is predicted to be excreted in human milk and is not recommended for use by nursing mothers.
- **Pediatric Use**: The safety and effectiveness of Myrbetriq™ in pediatric patients have not been established.
- **Geriatric Use**: No dose adjustment is recommended for elderly patients.

ADVERSE REACTIONS: (> 2% and > placebo)

- Hypertension
- Urinary tract infections
- Nasopharyngitis
- Headache

DRUG INTERACTIONS:

- Drugs Metabolized by CYP2D6 (e.g. Metoprolol and Desipramine): Mirabegron is CYP2D6 inhibitor and when used concomitantly with drugs metabolized by CYP2D6, especially narrow therapeutic index drugs, appropriate monitoring and possible dose adjustment of those drugs may be necessary.
- Digoxin: When initiating a combination of Myrbetriq™ and digoxin, prescribe the lowest dose of digoxin; monitor serum digoxin concentrations to titrate digoxin dose to desired clinical effect.

1. "MYBETRIQ HIGHLIGHTS OF PRESCRIBING INFORMATION.". N.p., 2012. Web. 23 Aug 2012. http://myrbetriq.com/Content/pdfs/11G054-MIR-WPI.pdf.

Appendix F

Fiscal Year 2012 Annual Review of Antidepressants PBPA Category *and* 30 Day Notice to Prior Authorize Forfivo XL® (Bupropion Extended Release) and Fluoxetine 60mg Tablets

Oklahoma Health Care Authority
October 2012

Prior Authorization of Antidepressants

Tier 2 Authorization Criteria

1. A documented, recent (within 6 months) trial of a Tier 1 medication at least 4 weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier 1 selection can be from any classification.
2. Prior stabilization on the Tier 2 medication documented within the last 100 days. A past history of success on the Tier 2 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by Tier 1 products or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Tier 3 Authorization Criteria

1. A documented, recent (within 6 months) trial with a Tier 1 and a Tier 2 medication at least 4 weeks in duration and titrated to recommended dose, that did not provide an adequate response. Tier 1 and Tier 2 selection can be from any classification.
2. Prior stabilization on the Tier 3 medication documented within the last 100 days. A past history of success on the Tier 3 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

SSRIs (Selective Serotonin Reuptake Inhibitors)		
Tier 1	**Tier 2**	**Tier 3**
citalopram (Celexa®)	escitalopram (Lexapro®)	
fluoxetine (Prozac®, Sarafem®)	fluoxetine (Prozac Weekly™)	
fluvoxamine (Luvox®)	fluvoxamine (Luvox CR®)	
paroxetine (Paxil®, Paxil CR®)	paroxetine (Pexeva®)	
sertraline (Zoloft®)		
Dual Acting Antidepressants		
Tier 1	**Tier 2**	**Tier 3**
venlafaxine (Effexor®, Effexor XR® Caps)	duloxetine (Cymbalta®)	Venlafaxine ER Tabs®
mirtazapine (Remeron® Tabs & SolTab®)		desvenlafaxine (Pristiq®)
trazodone (Desyrel®)		nefazodone (Serzone®)
bupropion (Wellbutrin®, Wellbutrin SR® & XL®)		bupropion ER (Aplenzin®)
		trazodone ER (Oleptro®)
		vilazodone (Viibryd®)
Monoamine Oxidase Inhibitors		
Tier 1	**Tier 2**	**Tier 3**
		selegiline transderm patch (Emsam®)
		tranylcypromine (Parnate®)
		phenelzine (Nardil®)
		selegiline (Zelapar®)

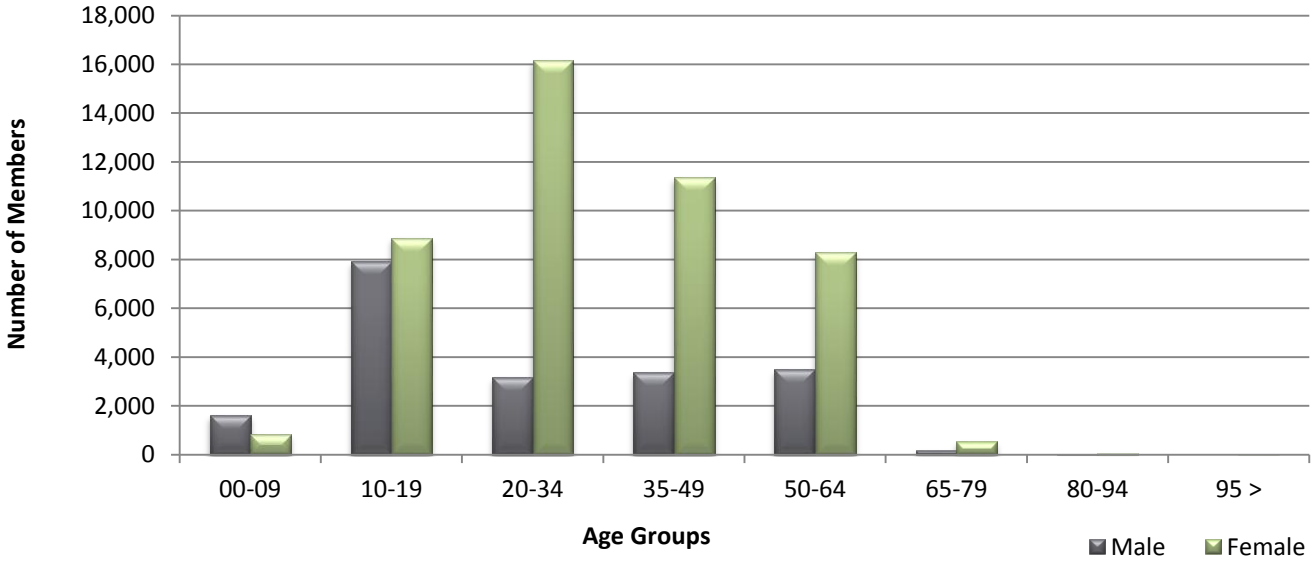
Mandatory generic plan applies, Tiers based on FY2012 Supplemental Rebate participation

Utilization of Antidepressant Medications

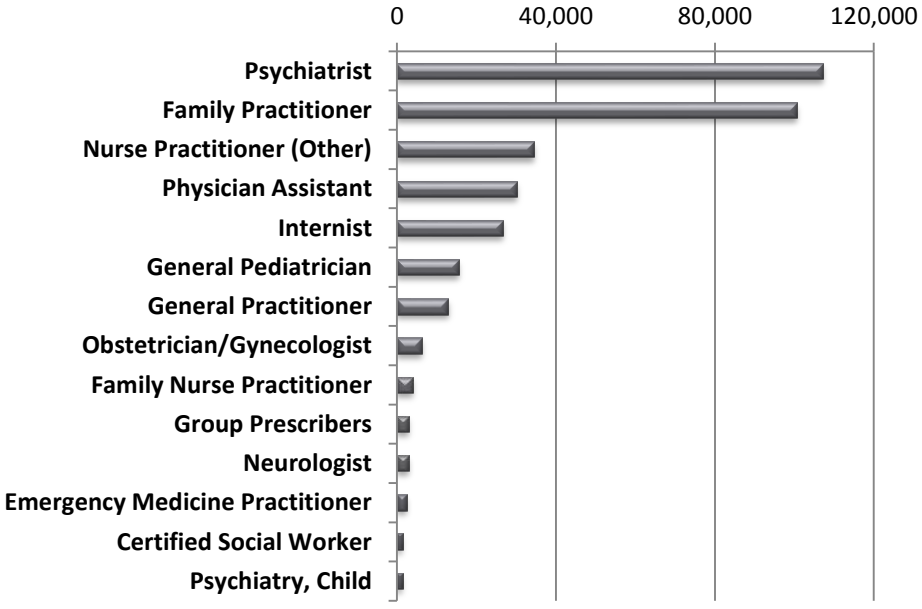
Fiscal Year Comparison

Fiscal Year	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2011	60,089	317,755	$8,277,972.89	$26.05	$0.80	12,519,672	10,379,732
2012	65,898	356,617	$9,399,603.68	$26.36	$0.80	13,991,850	11,683,256
% Change	**9.70%**	**12.20%**	**13.50%**	**1.20%**	**0.00%**	**11.80%**	**12.60%**
Change	**5,809**	**38,862**	**$1,121,630.79**	**$0.31**	**$0.00**	**1,472,178**	**1,303,524**

Demographics of Members: FY 2012



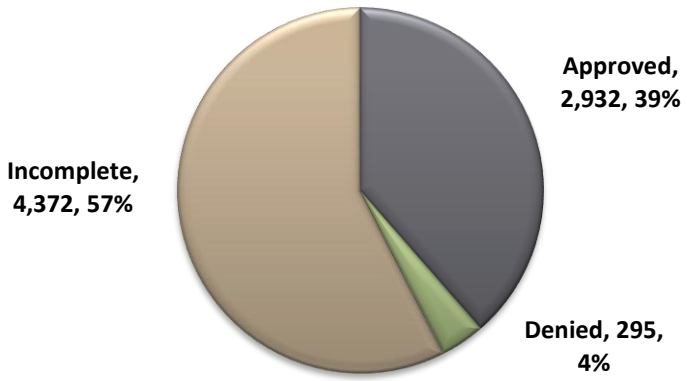
Top Prescriber Specialties: FY 2012



Prior Authorization of Antidepressant Medications

There were a total of 7,599 petitions submitted for this category during fiscal year 2012. Computer edits are in place to detect tier-1 medications in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.

Status of Petitions for Antidepressant Medications: FY 2012



Market News and Update

Patent Expirations:

- Lexapro® – generic became available in May of 2012 and has been placed on Tier 1
- Cymbalta® – anticipated patent expiration in 2013

Fluoxetine 60mg tablets became available late 2011. The price has increased in 2012 to $2.51 per tablet. Fluoxetine 20mg caps are currently 17 cents a capsule and fluoxetine 40mg caps are 23 cents a capsule. There are no known advantages of the 60mg tablets over the other doses available, except the convenience of taking one tablet as opposed to three 20mg capsules if the desired daily dose is 60mg per day.

Forfivo XL™ was approved by the FDA in late 2011 and was recently marketed in September of 2012 for the treatment of major depressive disorder. It is an extended release formulation of bupropion available as 450mg tablets indicated to be dosed once daily. Forfivo XL™ is bioequivalent to three 150mg tablets of Wellbutrin XL®. Forfivo XL™ is not to be used for dose titration. It can be used in patients who are receiving 300 mg/day of another bupropion formulation for at least 2 weeks, and require a dosage increase to 450 mg/day. Patients who are currently being treated with other bupropion products at 450 mg/day can be switched to equivalent dose of Forfivo XL™ once daily. The safety and efficacy profile of Forfivo XL™ is similar to Wellbutrin XL®. The following is a cost comparison of available bupropion products:

Bupropion Extended Release Products*	SMAC	EAC
Wellbutrin XL® 150mg	$0.73	
Wellbutrin XL® 300mg	$0.83	
Wellbutrin SR® 150mg	$0.38	
Wellbutrin SR® 200mg	$0.59	
Aplenzin® 348mg		$8.41
Aplenzin® 522mg		$19.15
Forfivo XL™ 450mg		$4.75

*Only top highest strengths listed for comparison. SMAC = state maximum allowable cost pricing for generic products. EAC = estimated acquisition cost pricing for branded products.

Recommendations

The College of Pharmacy recommends the following changes to the Antidepressant PBPA category:

1. Add Forfivo XL™ (bupropion extended release) to Tier 3
2. Revise the antidepressants PBPA category prior authorization criteria as shown below:

Tier 2 Authorization Criteria

1. A documented, recent (within 6 months) trial of two Tier 1 medications at least 4 weeks in duration and titrated to recommended dosing, that did not provide an adequate response. Tier 1 selection must include at least one medication from the SSRI category and one medication from the dual acting category.
2. Prior stabilization on the Tier 2 medication documented within the last 100 days. A past history of success on the Tier 2 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by Tier 1 products or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Tier 3 Authorization Criteria

1. A documented, recent (within 6 months) trial with two Tier 1 medications (one from each category) and a Tier 2 medication at least 4 weeks in duration and titrated to recommended dose, that did not provide an adequate response.
2. Prior stabilization on the Tier 3 medication documented within the last 100 days. A past history of success on the Tier 3 medication will also be considered with adequate documentation.
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class.
4. A petition may be submitted for consideration whenever a unique member specific situation exists.

Special Criteria:

1. Use of fluoxetine 60mg tablets requires clinically significant reason why member cannot take three fluoxetine 20mg capsules.

Utilization Details of Antidepressant Medications

BRAND NAME	CLAIMS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
CITALOPRAM SOL 10MG/5ML	121	39	$5,643.75	7.25	3.10	$1.63	0.06%
CITALOPRAM TAB 10MG	8,890	3,213	$68,857.21	1.03	2.77	$0.25	0.73%
CITALOPRAM TAB 20MG	37,011	13,169	$277,380.64	1.07	2.81	$0.22	2.95%
CITALOPRAM TAB 40MG	25,425	7,015	$196,017.19	1.05	3.62	$0.23	2.09%
CELEXA TAB 40MG	18	2	$2,914.77	1.33	9.00	$5.40	0.03%
Subtotals	71,465		$550,813.56	1.06	4.26	$0.23	5.86%
SERTRALINE CON 20MG/ML	261	63	$14,047.08	3.33	4.14	$1.79	0.15%
SERTRALINE TAB 100MG	28,377	6,722	$254,724.08	1.29	4.22	$0.27	2.71%
ZOLOFT TAB 100MG	24	4	$5,016.44	1.15	6.00	$4.92	0.05%
SERTRALINE TAB 25MG	7,763	2,755	$60,890.75	1.04	2.82	$0.25	0.65%
SERTRALINE TAB 50MG	23,745	8,664	$190,668.31	1.07	2.74	$0.25	2.03%
ZOLOFT TAB 50MG	6	1	$787.57	1.00	6.00	$4.38	0.01%
Subtotals	60,176		$526,134.23	1.18	4.32	$0.27	5.60%
TRAZODONE TAB 100MG	21,117	5,915	$171,911.06	1.34	3.57	$0.26	1.83%
TRAZODONE TAB 150MG	12,131	3,380	$134,367.94	1.28	3.59	$0.34	1.43%
TRAZODONE TAB 300MG	513	167	$58,130.74	1.06	3.07	$3.07	0.62%
TRAZODONE TAB 50MG	24,818	7,905	$160,471.58	1.24	3.14	$0.21	1.71%
OLEPTRO TAB 24HR150	4	2	$407.60	1.00	2.00	$3.40	0.00%
Subtotals	58,583		$525,288.92	1.28		$0.28	5.59%
FLUOXETINE CAP 10MG	8,698	3,029	$64,786.94	1.18	2.87	$0.24	0.69%
FLUOXETINE CAP 20MG	29,289	9,023	$242,951.20	1.39	3.25	$0.25	2.58%
PROZAC CAP 20MG	28	3	$12,700.42	1.94	9.33	$13.23	0.14%
FLUOXETINE CAP 40MG	9,652	2,833	$149,524.38	1.04	3.41	$0.44	1.59%
FLUOXETINE CAP 90MG DR	69	9	$5,787.08	0.16	7.67	$2.96	0.06%
PROZAC WEEKL CAP 90MG	9	1	$1,282.14	0.14	9.00	$5.09	0.01%
FLUOXETINE SOL 20MG/5ML	909	181	$13,320.25	3.47	5.02	$0.50	0.14%
FLUOXETINE TAB 10MG	1,767	714	$13,337.39	0.96	2.47	$0.24	0.14%
FLUOXETINE TAB 20MG	532	257	$6,181.71	1.12	2.07	$0.36	0.07%
Subtotals	50,953		$509,871.51	1.30	5.01	$0.30	5.42%
APLENZIN TAB 348MG	4	1	$778.88	1.00	4.00	$6.49	0.01%
APLENZIN TAB 522MG	6	2	$2,628.76	1.00	3.00	$14.60	0.03%
BUPROPION TAB 100MG	1,763	700	$51,847.86	1.93	2.52	$0.96	0.55%
BUPROPION TAB 75MG	1,539	549	$36,463.23	1.70	2.80	$0.78	0.39%
BUPROPION TAB 100MG SR	1,550	614	$30,888.30	1.49	2.52	$0.66	0.33%
BUDEPRION TAB 100MG SR	65	29	$1,200.63	1.40	2.24	$0.62	0.01%
BUPROPION TAB 100MG ER	57	17	$1,145.54	1.47	3.35	$0.67	0.01%
BUPROPION TAB 150MG SR	8,375	2,833	$208,835.06	1.70	2.96	$0.80	2.22%
BUDEPRION TAB 150MG SR	158	79	$3,861.31	1.70	2.00	$0.76	0.04%
BUPROPION TAB 200MG SR	1,048	256	$37,455.00	1.69	4.09	$1.14	0.40%
BUPROPION TAB 200MG ER	3	3	$122.28	1.50	1.00	$1.02	0.00%
BUPROPN HCL TAB 150MG XL	5,709	2,115	$166,835.28	1.04	2.70	$0.88	1.77%
BUDEPRION XL TAB 150MG	180	88	$5,459.04	1.15	2.05	$0.95	0.06%
WELLBUTRIN TAB XL 150MG	19	2	$9,221.12	2.26	9.50	$16.18	0.10%
BUPROPN HCL TAB 300MG XL	5,721	1,440	$187,471.40	1.00	3.97	$0.95	1.99%
BUDEPRION XL TAB 300MG	301	74	$9,729.74	1.00	4.07	$1.01	0.10%
WELLBUTRIN TAB XL 300MG	2	1	$585.86	1.00	2.00	$9.76	0.01%
Subtotals	26,500		$754,529.29	1.38	3.22	$0.88	8.02%
PAXIL SUS 10MG/5ML	35	11	$6,692.94	8.04	3.18	$6.52	0.07%
PAROXETINE SUS 10MG/5ML	1	1	$111.79	8.00	1.00	$4.47	0.00%
PAROXETINE TAB 10MG	2,518	1,007	$24,753.77	0.99	2.50	$0.30	0.26%
PAXIL TAB 10MG	9	1	$1,075.93	1.00	9.00	$3.98	0.01%
PAROXETINE TAB 20MG	8,190	3,131	$85,023.08	1.00	2.62	$0.30	0.90%
PAROXETINE TAB 30MG	1,982	475	$25,189.27	1.21	4.17	$0.39	0.27%
PAXIL TAB 30MG	1	1	$40.60	2.00	1.00	$8.12	0.00%

PAROXETINE TAB 40MG	5,993	1,455	$75,882.13	1.06	4.12	$0.36	0.81%
PAXIL TAB 40MG	4	1	$1,762.45	1.00	4.00	$4.52	0.02%
PAROXETIN ER TAB 12.5MG	211	84	$21,529.38	1.00	2.51	$3.01	0.23%
PAXIL CR TAB 12.5MG	7	4	$1,290.40	1.00	1.75	$3.91	0.01%
PAROXETINE TAB 25MG ER	704	177	$74,580.29	1.08	3.98	$3.05	0.79%
PAXIL CR TAB 25MG	9	5	$1,109.67	1.00	1.80	$4.11	0.01%
PAROXETIN ER TAB 37.5MG	370	76	$41,645.94	1.05	4.87	$3.18	0.44%
PAXIL CR TAB 37.5MG	7	1	$888.74	1.00	7.00	$4.23	0.01%
PEXEVA TAB 20MG	10	4	$2,061.05	1.00	2.50	$5.73	0.02%
PEXEVA TAB 40MG	14	2	$2,641.61	1.00	7.00	$4.89	0.03%
Subtotals	20,065		$366,279.04	1.05	3.71	$0.53	3.88%
VENLAFAXI ER CAP 37.5MG	496	315	$5,491.04	1.01	1.57	$0.39	0.06%
VENLAFAXINE CAP 150MG ER	5,703	1,338	$100,993.45	1.26	4.26	$0.53	1.07%
EFFEXOR XR CAP 150MG	190	43	$54,412.75	1.34	4.42	$7.52	0.58%
VENLAFAXINE CAP 37.5MG	453	258	$4,810.78	1.02	1.76	$0.36	0.05%
EFFEXOR XR CAP 37.5MG	19	6	$4,073.41	1.00	3.17	$4.79	0.04%
VENLAFAXINE CAP 75MG ER	3,714	1,389	$51,557.45	1.06	2.67	$0.41	0.55%
EFFEXOR XR CAP 75MG	83	23	$18,981.97	1.03	3.61	$5.43	0.20%
VENLAFAXINE TAB 100MG	970	250	$35,222.90	2.01	3.88	$1.20	0.37%
VENLAFAXINE TAB 25MG	67	30	$2,191.22	1.78	2.23	$1.07	0.02%
VENLAFAXINE TAB 37.5MG	1,535	629	$34,236.49	1.75	2.44	$0.73	0.36%
VENLAFAXINE TAB 50MG	333	114	$9,973.90	1.77	2.92	$0.95	0.11%
VENLAFAXINE TAB 75MG	4,353	1,287	$105,394.62	1.88	3.38	$0.78	1.12%
VENLAFAXINE TAB 150MG ER	295	83	$34,420.77	1.24	3.55	$3.72	0.37%
VENLAFAXINE TAB 225MG ER	437	91	$118,013.04	1.03	4.80	$7.53	1.26%
VENLAFAXINE TAB 37.5 ER	52	17	$4,164.70	0.96	3.06	$2.50	0.04%
VENLAFAXINE TAB 75MG ER	119	39	$11,195.78	1.00	3.05	$3.02	0.12%
Subtotals	18,819		$595,134.27	1.42		$0.97	6.32%
MIRTAZAPINE TAB 15MG ODT	161	67	$4,765.54	0.97	2.40	$0.92	0.05%
MIRTAZAPINE TAB 30MG ODT	190	54	$7,126.26	1.05	3.52	$1.08	0.08%
REMERON SLTB TAB 30MG	1	1	$29.58	1.00	1.00	$0.99	0.00%
MIRTAZAPINE TAB 45MG ODT	72	24	$3,089.23	1.00	3.00	$1.19	0.03%
MIRTAZAPINE TAB 15MG	7,682	2,499	$72,659.02	0.94	3.07	$0.30	0.77%
MIRTAZAPINE TAB 30MG	6,325	1,789	$62,620.70	1.00	3.54	$0.31	0.67%
MIRTAZAPINE TAB 45MG	2,316	526	$30,898.00	1.01	4.40	$0.40	0.33%
MIRTAZAPINE TAB 7.5MG	286	81	$2,358.47	0.99	3.53	$0.28	0.03%
Subtotals	17,033		$183,546.80	0.97	3.06	$0.34	1.96%
CYMBALTA CAP 20MG	535	170	$102,742.35	1.34	3.15	$6.49	1.09%
CYMBALTA CAP 30MG	4,002	1,288	$898,942.66	1.25	3.11	$6.96	9.56%
CYMBALTA CAP 60MG	11,363	2,542	$2,367,492.65	1.10	4.47	$6.13	25.19%
Subtotals	15,900		$3,369,177.66	1.14	3.58	$6.34	35.84%
LEXAPRO SOL 5MG/5ML	49	6	$8,538.85	11.25	8.17	$7.49	0.09%
ESCITALOPRAM SOL 5MG/5ML	13	7	$2,865.88	13.08	1.86	$8.53	0.03%
LEXAPRO TAB 10MG	3,453	946	$429,363.14	1.02	3.65	$3.82	4.57%
ESCITALOPRAM TAB 10MG	1,234	601	$146,296.06	1.02	2.05	$3.59	1.56%
LEXAPRO TAB 20MG	5,816	1,372	$810,851.16	1.04	4.24	$4.09	8.63%
ESCITALOPRAM TAB 20MG	2,041	933	$262,483.53	1.04	2.19	$3.77	2.79%
LEXAPRO TAB 5MG	134	39	$14,824.87	1.03	3.44	$3.61	0.16%
ESCITALOPRAM TAB 5MG	36	16	$3,438.31	1.06	2.25	$3.75	0.04%
Subtotals	12,776		$1,678,661.80	1.07	3.48	$3.93	17.87%
LUVOX CR CAP 100MG	85	25	$28,781.30	1.62	3.40	$11.03	0.31%
LUVOX CR CAP 150MG	135	22	$48,550.30	1.61	6.14	$12.22	0.52%
FLUVOXAMINE TAB 100MG	1,501	257	$30,229.77	1.87	5.84	$0.64	0.32%
FLUVOXAMINE TAB 25MG	285	69	$4,043.00	1.10	4.13	$0.46	0.04%
FLUVOXAMINE TAB 50MG	851	196	$14,499.75	1.36	4.34	$0.57	0.15%
Subtotals	2,857		$126,104.12	1.63		$1.44	1.34%
PRISTIQ TAB 100MG	575	141	$90,314.97	1.03	4.08	$4.71	0.96%
PRISTIQ TAB 50MG	638	172	$97,742.77	1.00	3.71	$4.54	1.04%
Subtotals	1,213		$188,057.74	1.02	3.90	$4.62	2.00%

VIIBRYD TAB 10MG	8	5	$828.49	1.00	1.60	$3.89	0.01%
VIIBRYD TAB 20MG	47	20	$5,878.17	1.00	2.35	$4.17	0.06%
VIIBRYD TAB 40MG	134	47	$16,198.71	1.00	2.85	$4.06	0.17%
Subtotals	189		$22,905.37	1.00	2.27	$4.08	0.24%
NEFAZODONE TAB 100MG	14	2	$426.96	2.14	7.00	$1.02	0.00%
NEFAZODONE TAB 150MG	17	4	$651.21	2.09	4.25	$1.10	0.01%
NEFAZODONE TAB 200MG	34	5	$1,155.66	1.81	6.80	$0.97	0.01%
NEFAZODONE TAB 250MG	14	2	$520.17	1.76	7.00	$1.05	0.01%
NEFAZODONE TAB 50MG	9	2	$345.37	2.67	4.50	$1.27	0.00%
Subtotals	88		$3,099.37	1.99	5.91	$1.04	0.03%
Totals	356,617	65,898*	$9,399,603.68	1.20	5.41	$0.80	100.00%

***Total number of unduplicated members.**

PRODUCT DETAILS OF FORFIVO XL™ (Bupropion extended release)

FDA-APPROVED IN NOVEMBER 2011

INDICATIONS: Treatment of major depressive disorder.

DOSAGE FORMS: Forfivo XL™ is supplied as an extended-released tablet of 450mg.

ADMINISTRATION:

- Use one tablet (450 mg) once daily without regard to food.
- Swallow the tablet whole. Do not chew, divide, or crush.
- Do not initiate treatment with Forfivo XL™. Use another bupropion formulation for initial dose titration.
- Can be used in patients who are receiving 300 mg/day of another bupropion formulation for at least 2 weeks, and require a dosage of 450 mg/day.
- Patients who are currently being treated with other bupropion products at 450 mg/day can be switched to equivalent dose of Forfivo XL™ once daily.

CONTRAINDICATIONS:

- Seizure disorder.
- Current use of other bupropion products.
- Current or prior diagnosis of bulimia or anorexia nervosa.
- Abrupt discontinuation of alcohol or sedatives.
- Use with monoamine oxidase (MAO) inhibitor: stop at least 2 weeks prior to bupropion use.
- Known hypersensitivity to bupropion or other ingredients of Forfivo XL™.

SPECIAL POPULATIONS:

- **Pregnancy:** Pregnancy Category C. One study has been conducted in pregnant women. This retrospective, managed-care database study assessed the risk of congenital malformations overall, and cardiovascular malformations specifically, following exposure to bupropion in the first trimester compared to the risk of these malformations following exposure to other antidepressants in the first trimester and bupropion outside of the first trimester. This study included 7,005 infants with antidepressant exposure during pregnancy, 1,213 of whom were exposed to bupropion in the first trimester. The study showed no greater risk for congenital malformations overall, or cardiovascular malformations specifically, following first trimester bupropion exposure compared to exposure to all other antidepressants in the first trimester, or bupropion outside of the first trimester. The results of this study have not been corroborated. Forfivo XL™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Nursing Mothers:** Like many other drugs, bupropion and its metabolites are secreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Forfivo XL™ tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- **Pediatrics**: Safety and effectiveness in pediatric patients have not been established. Anyone considering the use of Forfivo XL™ in a child or adolescent must balance the potential risks with the clinical need.
- **Geriatrics:** Reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. A single-dose pharmacokinetic study demonstrated that the disposition of bupropion and its metabolites in elderly subjects was similar to that of younger subjects; however, another pharmacokinetic study, single and multiple doses, has suggested that the elderly are at increased risk for accumulation of bupropion and its metabolites.

WARNINGS AND PRECAUTIONS:

- **Clinical Worsening and Suicide Risk in Treating Psychiatric Disorder:** Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical

worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

- **Neuropsychiatric Symptoms and Suicide Risk in Smoking Cessation Treatment:** Forfivo XL™ is not approved for smoking cessation treatment, but bupropion under the name Zyban® is approved for this use. Serious neuropsychiatric symptoms have been reported in patients taking bupropion for smoking cessation. These have included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, hostility, agitation, aggression, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide.
- **Activation of Mania/Hypomania:** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. It should be noted that Forfivo XL™ is not approved for use in treating bipolar depression.
- **Seizures:** Bupropion is associated with a dose-related risk of seizures. Forfivo XL™ should be discontinued and not restarted in patients who experience a seizure while on treatment.
- **Psychosis and Other Neuropsychiatric Events:** Depressed patients treated with bupropion have been reported to show a variety of neuropsychiatric signs and symptoms, including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment. It is recommended stopping bupropion when the symptoms occurred.
- **Severe Hypertension:** In clinical practice, hypertension, in some cases severe, requiring acute treatment, has been reported in patients receiving bupropion alone and in combination with nicotine replacement therapy. These reactions have been observed in both patients with and without evidence of preexisting hypertension. There is no clinical experience establishing the safety of Forfivo XL™ tablets in patients with a recent history of myocardial infarction or unstable heart disease. Therefore, care should be exercised if it is used in these groups. Bupropion was well tolerated in depressed patients who had previously developed orthostatic hypotension while receiving tricyclic antidepressants, and was also generally well tolerated in a group of 36 depressed inpatients with stable congestive heart failure (CHF). However, bupropion was associated with a rise in supine blood pressure in the study of patients with CHF, resulting in discontinuation of treatment in 2 patients for exacerbation of baseline hypertension.
- **Agitation and Insomnia:** Increased restlessness, agitation, anxiety, and insomnia, especially shortly after initiation of treatment, have been associated with treatment with bupropion.
- **Altered Appetite and Weight:** In placebo-controlled short-term studies of major depressive disorder using the sustained-release formulation of bupropion hydrochloride, patients experienced weight gain 2% to 3% and weight loss 14% to 19%.
- **Hypersensitivity Reactions:** Anaphylactoid/anaphylactic reactions characterized by symptoms such as pruritus, urticaria, angioedema, and dyspnea requiring medical treatment have been reported in clinical trials with bupropion. In addition, there have been rare spontaneous postmarketing reports of erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock associated with bupropion. A patient should stop taking Forfivo XL™ and consult a doctor if experiencing allergic or anaphylactoid/anaphylactic reactions (e.g., skin rash, pruritus, hives, chest pain, edema, and shortness of breath) during treatment. Arthralgia, myalgia, and fever with rash and other symptoms suggestive of delayed hypersensitivity have been reported in association with bupropion. These symptoms may resemble serum sickness.

ADVERSE REACTIONS:

- **Common adverse reactions:** Most common adverse reactions are (incidence ≥ 5%; ≥ 2 times placebo rate): Dry mouth, nausea, insomnia, dizziness, pharyngitis, abdominal pain, agitation, anxiety, tremor, palpitation, sweating, tinnitus, myalgia, anorexia, urinary frequency, rash.
  Reactions resulting in discontinuation, in addition to those listed above for the sustained-release formulation of bupropion hydrochloride, include vomiting, seizures, and sleep disturbances.

DRUG INTERACTIONS:

- Ticlopidine or clopidogrel: May increase bupropion exposure. Coadministration of FORFIVO XL with ticlopidine or clopidogrel is not recommended.
- Drugs metabolized by CYP2D6 (e.g., desipramine, paroxetine, fluoxetine, sertraline, venlafaxine): Consider dose reduction when using with bupropion. Bupropion & hydroxybupropion inhibit CYP2D6.
- Nicotine transdermal system: Monitor for severe hypertension.
- Drug laboratory test interactions: May cause false-positive urine immunoassay screening test results for amphetamines.

PATIENT COUNSELING INFORMATION:

- Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Forfivo XL™ and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and Other Serious Mental Illnesses, and Suicidal Thoughts or Actions", "Quitting Smoking, Quit-Smoking Medication, Changes in Thinking and Behavior, Depression, and Suicidal Thoughts or Actions" and "What Other Important Information Should I Know about Forfivo XL™" is available for Forfivo XL™.
- Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.
- Patients should be made aware that Forfivo XL™ contains the same active ingredient (bupropion) found in Zyban®, which is used as an aid to smoking cessation treatment, and that FORFIVO XL should not be used in combination with Zyban® or any other medications that contain bupropion hydrochloride (such as Wellbutrin XL®, Wellbutrin SR®, the immediate-release formulation Wellbutrin®, or Aplenzin® extended release tablet.
- Patients should be told that Forfivo XL™ should be discontinued and not restarted if they experience a seizure while on treatment.
- Patients should be told that any CNS-active drug like Forfivo XL™ tablets may impair their ability to perform tasks requiring judgment or motor and cognitive skills. Consequently, until they are reasonably certain that Forfivo XL™ tablets do not adversely affect their performance they should refrain from driving an automobile, or operating complex, hazardous machinery.
- Patients should be told that the excessive use or abrupt discontinuation of alcohol or sedatives (including benzodiazepines) may alter the seizure threshold. Some patients have reported lower alcohol tolerance during treatment with bupropion. Patients should be advised that the consumption of alcohol should be minimized or avoided.
- Patients should be advised to notify their physicians if they are taking or plan to take any prescription or over-the-counter drugs.
- Patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during therapy.
- Patients should be advised to swallow Forfivo XL™ tablets whole so that the release rate is not altered. Do not chew, divide, or crush tablets, as this may lead to an increased risk of adverse effects, including seizures.

REFERENCES:

1. Forfivo XL™ Prescribing Information. Pillar5 Pharma Inc. Available on line at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022497s000lbl.pdf. Last revised: November 2011.

Appendix G

Fiscal Year 2012 Annual Review of Alzheimer's Medications

Oklahoma HealthCare Authority
October 2012

Current Prior Authorization Criteria of Alzheimer's Medications

In April of 2011, an age restricion for members aged 0-50 years was applied for the following products in this category:

- Aricept ODT® (donepezil) and 23mg tablets
- Exelon® (rivastigmine) solution and patch
- Namenda® (memantine) solution and tablets
- Razadyne® (galantamine) solution and extended release capsules

Approval Criteria:

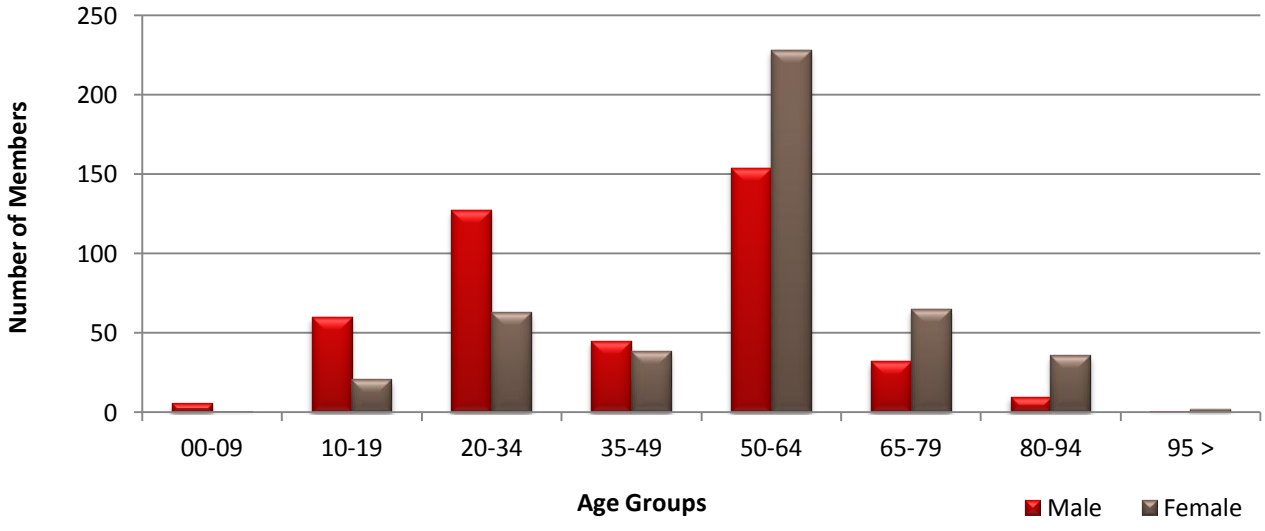
a. FDA approved diagnosis
b. Member must have a documented reason why the special formulation is clinically necessary over the regular formulation

Utilization of Alzheimer's Medications

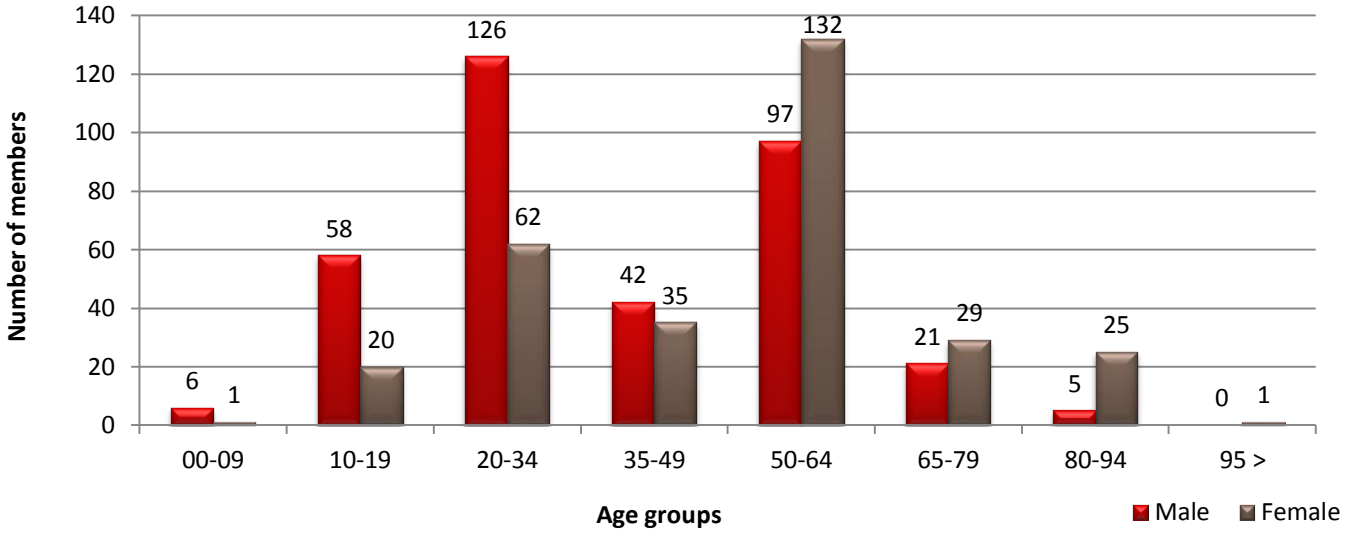
Comparison of Fiscal Years

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2011	844	6,731	$1,271,377.48	$188.88	$6.21	329,622	204,702
2012	890	8,125	$1,231,196.43	$151.53	$5.02	409,184	245,458
Percent Change	**5.50%**	**20.70%**	**-3.20%**	**-19.80%**	**-19.20%**	**24.10%**	**19.90%**
Change	**46**	**1,394**	**-$40,181.05**	**-$37.35**	**-$1.19**	**79,562**	**40,756**

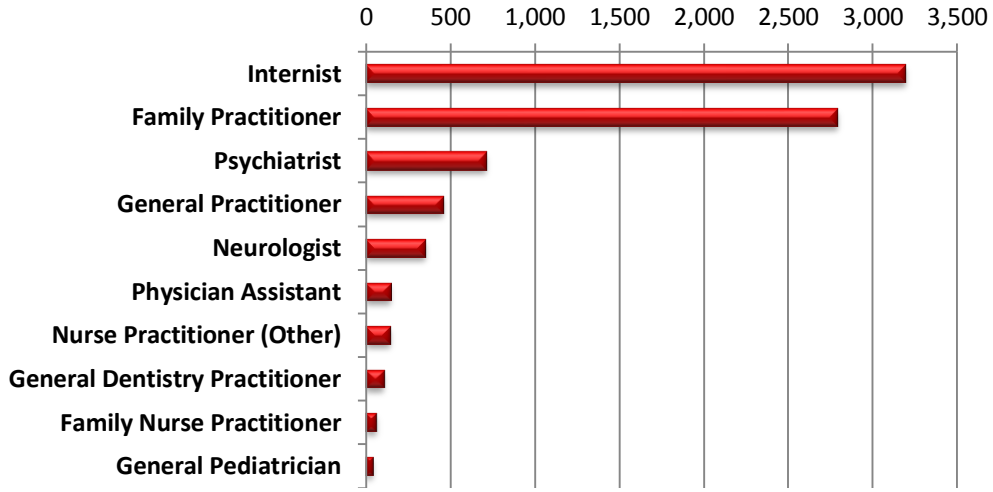
Demographics of All Members Utilizing Alzheimer's Medications: FY 2012



Demographics of All Members Utilizing Namenda®: FY 2012



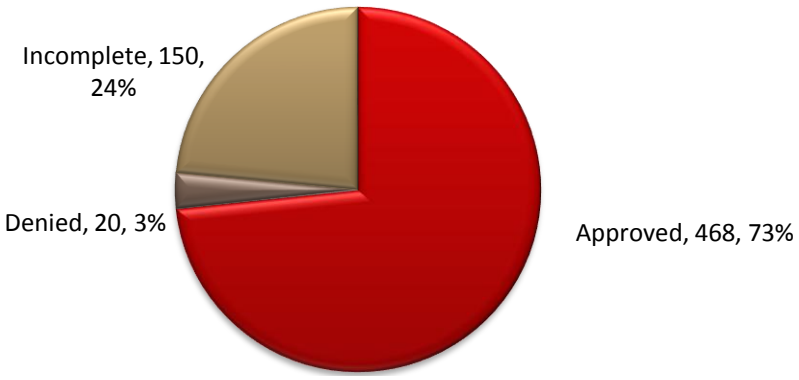
Top 10 Prescribers of Alzheimer's Medications by Number of Claims: FY 2012



Prior Authorization of Alzheimer's Medications

There were a total of 630 petitions submitted for this category during fiscal year 2012. The following chart shows the status of the submitted petitions.

Status of Petitions for Alzheimer's Medications: FY 2012



Market News and Updates

Upcoming Patent Expirations:

- Namenda® - April 2015

Conclusion and Recommendations

The College of Pharmacy recommends no changes to this category at this time.

Utilization Details of Alzheimer's Medications: Fiscal Year 2012

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	UNITS/ DAY	CLAIMS/ MEMBER	COST/ DAY	% COST
NAMENDA TAB 10MG	5,094	296,542	151,113	598	$1,064,666.12	1.96	8.52	$7.05	86.47%
DONEPEZIL TAB 10MG	1,724	56,621	53,922	245	$15,484.11	1.05	7.04	$0.29	1.26%
DONEPEZIL TAB 5MG	556	18,499	17,675	139	$5,461.20	1.05	4	$0.31	0.44%
NAMENDA TAB 5MG	470	25,883	14,283	82	$93,729.25	1.81	5.73	$6.56	7.61%
EXELON DIS 9.5MG/24	99	2,930	2,930	13	$24,553.27	1	7.62	$8.38	1.99%
RIVASTIGMINE CAP 3MG	45	2,550	1,410	7	$7,481.31	1.81	6.43	$5.31	0.61%
RIVASTIGMINE CAP 1.5MG	28	1,570	860	6	$4,419.79	1.83	4.67	$5.14	0.36%
EXELON DIS 4.6MG/24	27	787	787	6	$5,211.07	1	4.5	$6.62	0.42%
RIVASTIGMINE CAP 4.5MG	23	1,140	690	3	$3,272.44	1.65	7.67	$4.74	0.27%
GALANTAMINE TAB 8MG	17	610	530	4	$1,169.69	1.15	4.25	$2.21	0.10%
GALANTAMINE TAB 4MG	15	540	450	2	$1,025.55	1.2	7.5	$2.28	0.08%
GALANTAMINE CAP 8MG ER	8	240	240	2	$548.86	1	4	$2.29	0.04%
ARICEPT TAB 23MG	8	240	240	2	$2,073.74	1	4	$8.64	0.17%
RIVASTIGMINE CAP 6MG	5	300	150	1	$878.16	2	5	$5.85	0.07%
NAMENDA SOL 10MG/5ML	3	585	90	1	$702.49	6.5	3	$7.81	0.06%
NAMENDA TAB 5-10MG	3	147	88	2	$519.38	1.67	1.5	$5.90	0.04%
TOTALS:	**8,125**	**409,184**	**245,458**	**890***	**$1,231,196.43**	**1.67**	**9.13**	**$5.02**	**100%**

Total number of unduplicated members

Appendix H

30 Day Notice to Prior Authorize Miscellaneous Butalbital-Acetaminophen-Caffeine Products (Dolgic Plus®, Phrenilin Forte®, Esgic-Plus®, Orbivan®, Orbivan® CF)

Oklahoma Health Care Authority
October, 2012

Introduction[1, 2]

The International Headache Society has developed guidelines for diagnosis and treatment of headaches. Tension-type headaches (TTH) were previously known by some of the following terms: tension, muscle contraction, psychomyogenic, stress, idiopathic, and psychogenic.

Tension-type headache is the most common type of primary headache with prevalence in the general population of 30-78%. It is characterized by generalized pressure or a sensation of tightness in the head. The discomfort level is usually mild to moderate and does not worsen with activity. Although nausea and photophobia or phonophobia can occur, they generally are not prominent features. Tension-type headache is classified as episodic (<15 days a month) or chronic (>15 days a month).

Some patients with tension-type headache exhibit evidence of increased muscle tension, with prominent scalp tenderness, muscle tenderness in the temporomandibular joint muscles, or tight, tender cervical and trapezius muscles. Poor posture is often evident, which can play a role in causing tension-type headache. If there is no evidence of increased pericranial or cervical muscle tightness (no tenderness or limitation of motion in the neck) found during clinical examination, the pain likely originates centrally or is due to psychological factors.

The occasional tension-type headache can be alleviated by a hot shower, massage, sleep, and patient recognition and avoidance of stress factors. Episodic tension-type headache is usually well treated with analgesics such as aspirin, acetaminophen, and NSAIDs or combinations of these agents with caffeine or sedating medications.

Indications and Dosing Recommendations [3, 4, 5, 6]

Dolgic Plus® (butalbital-acetaminophen-caffeine, 50-750-40 mg) by Shionogi, Inc was FDA approved in December 2011 for the treatment of tension headache. The dose is 1 tablet every 4 hours, not to exceed 5 tablets per day. (3750 mg of APAP)

Phrenilin Forte® (butalbital-acetaminophen 50-650 mg) by Valeant Pharmaceuticals was approved in June 2006. It is approved for treatment of tension headache at a dose of one capsule every 4 hours, not to exceed 6 capsules per day. (3900 mg of APAP)

Orbivan® (butalbital-acetaminophen-caffeine 50-300-40 mg), was originally developed by Atley Pharmaceuticals and FDA approved in May 2010, but was acquired for marketing and distribution by ECR Pharmaceutical in March 2012. The dose is 1-2 caps every 4 hours as needed for relief of the symptom complex of tension (or muscle contraction) headache, but total daily dose should not exceed 6 capsules. (1800 mg of APAP)

Orbivan® CF (butalbital-acetaminophen 50-300 mg), caffeine-free product by ECR Pharmaceuticals was approved in March 2012 for tension (or muscle contraction) headache. The dose is 1-2 tablets every 4 hours, with a maximum of 6 tablets per day. (1800 mg of APAP)

Esgic-Plus® (butalbital-acetaminophen-caffeine 50-500-40 mg), manufactured by Mikart, Inc. and distributed by Forest Laboratories, has been approved since 1996. It is indicated for relief of the symptom complex of tension (or muscle contraction) headache. Approved dose is one capsule every 4 hours, not to exceed 6 capsules per day.

Cost Comparison

Medication	State Maximum Allowable Cost (SMAC)	Estimated Acquisition Cost (EAC)	Estimated Monthly Cost*
Butalbital-APAP-Caffeine tablet (50-325-40 mg)	$0.21		$41.82
Butalbital-APAP-Caffeine capsule (50-325-40 mg)	$0.46		$86.82
Butalbital-APAP-Caffeine tablet (50-500-40 mg)	$0.15		$31.02
Butalbital-APAP tablet (50-325 mg)	$0.37		$70.62
Butalbital-APAP tablet (50-650 mg)	$0.50		$94.02
Esgic-Plus® capsules (50-500-40 mg)	$1.63		$297.42
Dolgic Plus® tablet (50-750-40 mg)		$5.29	$797.52
Phrenilin Forte® capsule (50-650 mg)		$5.47	$988.62
Orbivan® capsule (50-300-40 mg)		$1.28	$349.62
Orbivan® CF tablet (50-300 mg)		$1.28	$349.62

*Dispensing fee of $4.02 is included

Recommendations

The College of Pharmacy recommends the prior authorization of these products with the following criteria:

1. FDA approved indication for the treatment of tension-type headache
2. Must be 12 years old or older.
3. A clinical reason why generic tablet formulation cannot be utilized.

Product Information

INDICATIONS: These products are indicated for the relief of the symptoms associated with complex of tension (or muscle contraction) headaches.

Evidence supporting the efficacy and safety of this combination product in the treatment of multiple recurrent headaches is unavailable. Caution in this regard is required as butalbital is habit-forming and potentially abusable.

DOSAGE FORMS:

- **Orbivan®** contains **50 mg butalbital, 300 mg acetaminophen, and 40 mg caffeine**. Available as hard gelatin capsules with a green cap, printed with AP, and a yellow body, printed with 661.
- **Orbivan® CF** contains **50 mg butalbital and 300 mg acetaminophen**. Available as yellowish round, unscored tablets with **BA 300 printed** on one side and plain on the other.
- **Phrenilin Forte® (butalbital 50 mg and acetaminophen 650 mg)** is available as amethyst, opaque capsules imprinted with VALEANT and PF 0844.
- **Dolgic Plus® (butalbital 50mg, acetaminophen 750mg and caffeine 40mg)** is available as oval shaped tablets with a convex face and are debossed "A 074" on one side.
- **Esgic-Plus® (butalbital 50mg, acetaminophen 500 mg and caffeine 40mg)** is available as red capsule, imprinted with FOREST 0372 and Esgic plus.
-

ADMINISTRATION:

- **Dolgic Plus®**: One tablet every 4 hours as needed. Total daily dosage should not exceed 5 tablets.
- **Phrenilin Forte®:** One tablet every 4 hours as needed. Total daily dosage should not exceed 6 capsules.
- **Orbivan®**: One to two capsules every 4 hours as needed. Total daily dosage should not exceed 6 capsules.
- **Orbivan® CF**: One to two tablets every 4 hours as needed. Total daily dosage should not exceed 6 tablets.
- **Esgic-Plus®:** One capsule every 4 hours as needed. Total daily dosage should not exceed 6 capsules.

Extended and repeated use is not recommended because of the potential for physical dependence.

CONTRAINDICATIONS:

- Hypersensitivity or intolerance to any component of this product
- Patients with porphyria.

SPECIAL POPULATIONS:

- **Pregnancy Category C: Teratogenic Effects**: Animal reproduction studies have not been conducted with this combination product. It is also not known whether butalbital and acetaminophen can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. This product should be given to a pregnant woman only when clearly needed.
- **Nonteratogenic Effects:** Withdrawal seizures were reported in a two-day-old male infant whose mother had taken a butalbital-containing drug during the last two months of pregnancy. Butalbital was found in the infant's serum. The infant was given phenobarbital 5 mg/kg, which was tapered without further seizure or other withdrawal symptoms.
- **Nursing Mothers:** Caffeine, barbiturates, and acetaminophen are excreted in breast milk in small amounts, but the significance of their effects on nursing infants is not known. Because of potential for serious adverse reactions in nursing infants from butalbital, acetaminophen, and caffeine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
- **Pediatric Use:** The safety and effectiveness in pediatric patients below the age of 12 have not been established.

- **Geriatric Use:** Clinical studies of butalbital, acetaminophen and caffeine capsules did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Butalbital is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

WARNINGS & PRECAUTIONS:

- **Drug dependency:** Prolonged use may produce drug tolerance and dependency (psychologic and physical).
- **Children:** Safety and efficacy in children under 12 years of age not established.
- **Elderly:** Per the Beers list, butalbital is highly addictive and causes more adverse effects than most sedative or hypnotic drugs in elderly patients.
- **Hepatotoxicity:** Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product. The excessive intake of acetaminophen may be intentional to cause self-harm or unintentional as patients attempt to obtain more pain relief or unknowingly take other acetaminophen-containing products. The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen. Instruct patients to look for acetaminophen or APAP on package labels and not to use more than one product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

ADVERSE REACTIONS:

Frequently Observed:

- drowsiness
- lightheadedness
- dizziness
- sedation
- shortness of breath
- nausea
- vomiting
- abdominal pain
- intoxicated feeling

Infrequently observed:

- **Central Nervous System:** headache, shaky feeling, tingling, agitation, fainting, fatigue, heavy eyelids, high energy, hot spells, numbness, sluggishness, seizure. Mental confusion, excitement, or depression can also occur due to intolerance, particularly in elderly or debilitated patients, or due to overdosage of butalbital.
- **Autonomic Nervous System:** dry mouth, hyperhidrosis.
- **Gastrointestinal:** difficulty swallowing, heartburn, flatulence, constipation.
- **Cardiovascular:** tachycardia.
- **Musculoskeletal:** leg pain, muscle fatigue.
- **Genitourinary:** diuresis.
- **Miscellaneous:** pruritus, fever, earache, nasal congestion, tinnitus, euphoria, allergic reactions.

Several cases of dermatological reactions, including toxic epidermal necrolysis and erythema multiforme, have been reported.

DRUG INTERACTIONS:

- Effects of these drugs may be decreased: Beta-blockers (eg, propranolol), corticosteroids, doxycycline, estrogens (including oral contraceptives), felodipine, griseofulvin, nifedipine, phenylbutazone, quinidine, theophylline, and warfarin.
- Carbamazepine, sulfinpyrazone: May increase risk of hepatotoxicity.
- MAO inhibitors**:** May increase CNS effects.
- Other CNS depressants (ethanol, narcotics, general anesthetics, tranquilizers, sedative-hypnotics): Increased drowsiness, dizziness and other CNS depressive effects may occur.
- Tricyclic antidepressants: Antidepressant effect may decrease.
- Drug / Lab test interactions: With Chemstrip bG and Dextrostix home blood glucose systems, may cause false decrease in mean glucose values; may give false-positive urinary 5-hydroxyindoleacetic acid test result.

PATIENT INFORMATION:

- Caution patient that dependency/tolerance may result from regular long-term use.
- Tell patient to take drug with full glass of water.
- Instruct patient not to discontinue drug abruptly after long-term regular use.
- Caution patient to avoid intake of alcoholic beverages and other CNS depressants without health care provider approval.
- Advise patient to avoid any hazardous activity (driving or smoking) if dizziness, drowsiness or a decrease in mental acuity occurs.
- Warn patient that orthostatic hypotension may occur. Instruct patient to change positions slowly and to sit or lie down if symptoms occur.
- Instruct patient not to take OTC or other medications unless directed by health care provider.
- Inform patient to report the following symptoms to health care provider: persistent or recurrent pain before next scheduled dose, difficulty breathing, increased drowsiness, vomiting or yellowing of skin or gums.

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Appendix I

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

FDA NEWS RELEASE

For Immediate Release: Sept. 12, 2012
FDA approves new multiple sclerosis treatment Aubagio

The U.S. Food and Drug Administration today approved Aubagio (teriflunomide), a once-a-day tablet for the treatment of adults with relapsing forms of multiple sclerosis (MS).
MS is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communication between the brain and other parts of the body. It is among the most common causes of neurological disability in young adults and occurs at least twice as frequently in women as in men. For most people with MS, episodes of worsening function (relapses) are initially followed by recovery periods (remissions). Over time, recovery periods may be incomplete, leading to progressive decline.
The most common side effects of Aubagio experienced by patients in clinical trials include diarrhea, abnormal liver tests, nausea, and hair loss.
The drug contains a Boxed Warning to alert prescribers and patients to the risk of liver problems, including death, and a risk of birth defects. Physicians should do blood tests to check liver function before a patient starts taking Aubagio and periodically during treatment.
Also included in the Boxed Warning is an alert noting that, based on animal studies, the drug may cause fetal harm. For this reason, Aubagio is labeled as Pregnancy Category X, which means women of childbearing age must have a negative pregnancy test before starting the drug and use effective birth control during treatment.
Aubagio will be dispensed with a patient Medication Guide that provides important instructions on its use and drug safety information.
Aubagio is made by Bridgewater, N.J.-based Sanofi Aventis.

Safety Announcements

Qualitest Hydrocodone Bitartrate and Acetaminophen Tablets 10 mg/500 mg: Recall - Potential for Oversized Tablets
[Posted 09/11/2012]

AUDIENCE: Consumer, Health Professional
ISSUE: Today, Qualitest, a subsidiary of Endo Health Solutions, issued a voluntary, nationwide retail level recall for one lot of Hydrocodone Bitartrate and Acetaminophen Tablets, USP 10 mg/500 mg. Bottles from the affected lot may contain tablets that have a higher dosage of acetaminophen, and as a result, it is possible that consumers could take more than the intended acetaminophen dose. Unintentional administration of tablets with increased acetaminophen content could result in liver toxicity, especially in patients on other acetaminophen containing medications, patients with liver dysfunction, or people who consume more than 3 alcoholic beverages a day.
BACKGROUND: Hydrocodone bitartrate and acetaminophen 10 mg/500 mg tablets are indicated for the relief of moderate to moderately severe pain. The affected lot, C1440512A, was distributed between May 14 and Aug. 3, 2012 to wholesale distributors and retail pharmacies nationwide. The lot number can be found on the

side of the manufacturer's bottle. Hydrocodone Bitartrate and Acetaminophen Tablets are approximately 16.51 mm in length, pink, capsule-shaped tablets, with "3600" debossed on one side of the tablet and "V" on the other.
RECOMMENDATION: Consumers who have lot C1440512A should contact Qualitest at 1-800-444-4011. Consumers who are unsure if they have the affected lot number should consult their pharmacy or health care professional. Pharmacists and wholesalers are asked to check their inventories for lot C1440512A, segregate any material from the lot, and to contact MedTurn at 1-800-967-5952 for instructions on product return.
Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm[1]
- Download form[2] or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

Safety Announcements

FDA Drug Safety Communication: Rare cases of serious burns with the use of over-the-counter topical muscle and joint pain relievers

Safety Announcement
[9-13-2012] The U.S. Food and Drug Administration (FDA) is alerting the public that certain over-the-counter (OTC) products that are applied to the skin for the relief of mild muscle and joint pain have been reported to cause rare cases of serious skin injuries, ranging from first- to third-degree chemical burns, where the products were applied. These OTC topical muscle and joint pain relievers are available as single- or combination-ingredient products that contain menthol, methyl salicylate, or capsaicin. The various formulations include creams, lotions, ointments, and patches.
When applied to the skin, the products produce a local sensation of warmth or coolness; they should not cause pain or skin damage. However, there have been rare cases of serious burns following their use (see Data Summary below). Some of the burns had serious complications requiring hospitalization. In many cases, the burns occurred after only one application of the OTC topical muscle and joint pain reliever, with severe burning or blistering occurring within 24 hours of the first application. Based on the reported cases, the majority of second- and third-degree burns occurred with the use of products containing menthol as the single active ingredient, and products containing both menthol and methyl salicylate, in concentrations greater than 3% menthol and 10% methyl salicylate. Few cases reported using a capsaicin-containing product.
Consumers using an OTC topical muscle and joint pain reliever who experience signs of skin injury where the product was applied, such as pain, swelling, or blistering of the skin, should stop using the product and seek medical attention immediately.

Additional Information for Health Care Professionals

- Rare cases of serious burns have been reported to occur on the skin where over-the-counter (OTC) topical muscle and joint pain relievers were applied. These products contain the active ingredients menthol, methyl salicylate, or capsaicin.
- Of the burns that have been reported, the majority of second- and third-degree burns occurred with the use of products containing menthol as the single active ingredient and products containing both menthol and methyl salicylate, in concentrations greater than 3% menthol and 10% methyl salicylate. Few cases reported using a capsaicin-containing product.
- When recommending OTC topical muscle and joint pain relievers to patients, counsel them about how to use the products appropriately and inform them about the risk of serious burns. The skin injuries

described were recently assessed by FDA. Existing Tentative Final Monograph does not at this time require labels of OTC topical muscle and joint topical pain relievers to carry a warning that use of the products could result in serious burns.

- If a patient experiences pain, swelling, or blistering of the skin where an OTC topical muscle and joint pain reliever was applied, advise the patient to discontinue using the product.
- Report adverse events involving OTC topical muscle and joint pain relievers to the FDA MedWatch program using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

A search of FDA's Adverse Event Reporting System (AERS) database (from 1969 through April 21, 2011), the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES) database (from 2004 to 2010), and the medical literature[1] identified 43 cases of burns on the application site associated with the use of over-the-counter (OTC) topical muscle and joint pain relievers containing the active ingredients menthol, methyl salicylate, or capsaicin. The products associated with these cases include patches, balms, and creams. All cases in this series include burns that were confirmed by a health care professional. In the case series, there were reports of burns ranging from first-degree to third-degree, but many cases did not specify the degree of the burn. Many cases occurred following one application of the OTC topical muscle and joint pain reliever, with severe burning or blistering occurring within 24 hours of the first application of the product. A majority of the second- and third-degree burns were reported with the use of products containing menthol as the single active ingredient or products containing both menthol and methyl salicylate, where the concentration of the ingredients was greater than 3% menthol and 10% methyl salicylate. Few cases reported using a capsaicin-containing product.

Safety Announcements

FDA Update: Budeprion XL 300 mg Not Therapeutically Equivalent to Wellbutrin XL 300 mg

October 3, 2012

The U.S. Food and Drug Administration (FDA) has reviewed new data that indicate Budeprion XL 300 mg (bupropion hydrochloride extended-release tablets), manufactured by Impax Laboratories, Inc., and marketed by Teva Pharmaceuticals USA, Inc., is not therapeutically equivalent to Wellbutrin XL 300 mg. FDA has changed the therapeutic equivalence rating for this product in the Agency's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book[1]) from AB to BX, signifying that Budeprion XL 300 mg fails to demonstrate therapeutic equivalence to Wellbutrin XL 300 mg. Impax has requested that the Agency withdraw approval of budeprion XL 300 mg extended-release tablets. Impax and Teva have stopped shipping the product and are issuing detailed information to their customers. This announcement relates only to Budeprion XL 300 mg manufactured by Impax and marketed by Teva. It does not affect the Impax/Teva Budeprion 150 mg product or generic bupropion products made by other manufacturers.

Background

FDA has approved five generic versions of Wellbutrin XL 300 mg. Each of these generics was approved based on bioequivalence studies comparing the 150 mg strength of the products to Wellbutrin XL 150 mg. Studies were not performed directly on the 300 mg strength of the products. Rather, the bioequivalence studies were performed using the 150 mg strength, and the results were extrapolated to establish bioequivalence of the 300 mg product. This methodology was based on FDA's guidance at the time the products were approved. FDA has determined that this approach is no longer appropriate to establish bioequivalence of 300 mg bupropion hydrochloride extended-release tablets to Wellbutrin XL 300 mg, and the Agency is revising its guidance to industry for how to conduct premarket bioequivalence studies in generic bupropion products. The Impax/Teva product, Budeprion XL 300 mg, was approved in December 2006. Soon after, FDA began to receive reports that patients who were switched from Wellbutrin XL 300 mg to its generic counterparts were

experiencing reduced efficacy. FDA analyzed those reports and concluded that the complaints appeared to be linked to the Impax/Teva product. FDA therefore asked Impax/Teva to conduct a study directly on its 300 mg extended-release product to compare its bioequivalence to Wellbutrin XL 300 mg. FDA asked that the study include patients who had reported lack of efficacy after switching from Wellbutrin XL 300 mg to Budeprion XL 300 mg. Impax/Teva began the study, but terminated it in late 2011, reporting that, despite efforts to enroll patients, Impax/Teva was unable to recruit a significant number of affected patients to generate the necessary data.

In 2010, in light of the public health interest in obtaining bioequivalence data, FDA decided to sponsor a bioequivalence study comparing Budeprion XL 300 mg to Wellbutrin XL 300 mg. This study was conducted in 24 healthy adult volunteers and was designed to measure both the rate and the extent of release of bupropion into the blood. The results of this study became available in August 2012, and show that Budeprion XL 300 mg tablets fail to release bupropion into the blood at the same rate and to the same extent as Wellbutrin XL 300 mg.

FDA has not identified any new safety information associated with Budeprion XL 300 mg; however, in some patients, the drug may not provide the desired efficacy (beneficial effect).

FDA did not conduct bioequivalence studies of the other four generic versions of Wellbutrin XL 300 mg. FDA did, however, recently ask each of the other manufacturers – Anchen, Actavis, Watson, and Mylan – to conduct their own studies to assess the bioequivalence of their 300 mg extended-release bupropion tablets to Wellbutrin XL 300 mg. FDA has asked these companies to submit the data from those studies no later than March 2013. FDA believes the study results may be unique to the Impax/Teva version of 300 mg bupropion hydrochloride. FDA does not currently have data indicating that the other four generic products are not bioequivalent to Wellbutrin XL 300 mg. The Agency will review the data from the additional bioequivalence studies when the data are received, and will provide additional updates at that time.

Conclusion

Budeprion XL 300 mg tablets manufactured by Impax and marketed by Teva are not therapeutically equivalent to Wellbutrin XL 300 mg and will be removed from the market by Impax/Teva. FDA's actions with respect to Budeprion XL 300 mg reflect FDA's ongoing role in monitoring drugs on the market to ensure their continued safety and efficacy. The role of patients and health care professionals in sharing their experiences with generic versions of Wellbutrin XL 300 mg contributed to further studies, which led to this action. FDA remains firmly committed to its science-based responsibilities and to making sure that generic drugs are safe and effective. This commitment is reflected in the results of the FDA-sponsored bioequivalence study described above. Patients taking Budeprion XL 300 mg as a substitute for Wellbutrin XL 300 mg should talk with their health care professionals if they have questions about taking this medication.

Current Drug Shortages Index (as of October 2, 2012):

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

Acetylcysteine Inhalation Solution
Alfentanil Injection (initial posting 1/23/2012) UPDATED 9/26/2012
Amikacin Injection UPDATED 9/20/2012
Amino Acid Products (initial posting 2/14/2012) UPDATED 9/24/2012
Ammonium Chloride Injection
Ammonul (sodium phenylacetate and sodium benzoate) Injection 10%/10% (initial posting 9/18/2008)
Amphetamine Mixed Salts, ER Capsules[7] (initial posting 10/31/2011)
Amphetamine Mixed Salts Immediate-Release Tablets (initial posting 1/12/2012) UPDATED 9/20/2012
Aquasol A

Atracurium besylate (initial posting 2/27/2012)
Atropine Sulfate Injection
Bacteriostatic 0.9% Sodium Chloride (initial posting 9/10/2012)
Boniva (ibandronate sodium) Injection (initial posting 6/6/2012)
Bumetanide Injection (initial posting 6/21/2012)
Bupivacaine Hydrochloride Injection
Buprenorphine Injection
Butorphanol Injection
Caffeine, anhydrous (125 mg/mL) and Sodium benzoate (125 mg/mL)
Caffeine and Ergotamine Tartrate Tablet (initial posting 3/8/2012)
Cardiolite, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection (initial posting 2/14/2012)
Cetrorelix Acetate for Injection (initial posting 9/20/2012) New!!
Chloroprocaine (Nesacaine) Injection (initial posting 3/28/2012)
Chromic Chloride Injection
Citric Acid; Gluconolactone; Magnesium Carbonate Solution; Irrigation (initial posting 6/30/2012)
Corticorelin Ovine Triflutate
Daunorubicin Hydrochloride Solution for Injection
Desmopressin Injection
Dexrazoxane Injection UPDATED 9/27/2012
Dextroamphetamine Tablets (initial posting 1/12/2012) UPDATED 9/20/2012
Dextrose Injection (initial posting 5/23/2012)
Diazepam Injection
Digoxin Injection
Dipyridamole Injection (initial posting 7/24/2012)
Doxorubicin (adriamycin) lyophilized powder (initial posting 12/2/2011)
Doxorubicin Liposomal (Doxil) Injection
Epinephrine Injection (initial posting 4/27/2012)
Epinephrine 1mg/mL (Preservative Free) (initial posting 6/21/2012) UPDATED 9/26/2012
Erythromycin Lactobionate Injection (initial posting 6/12/2012)
Esomeprazole (Nexium) For Delayed-Release Oral Suspension (initial posting 4/10/2012)
Ethiodol (ETHIODIZED OIL) ampules
Etomidate Injection (initial posting 2/9/2012) UPDATED 9/27/2012
Fentanyl Citrate Injection
Foscarnet Sodium Injection
Fosphenytoin Sodium Injection (initial posting 3/30/2012)
Fospropofol disodium (Lusedra) Injection (initial posting 6/18/2012)
Furosemide Injection (initial posting 6/20/2012)
Ganite (gallium nitrate injection) (initial posting 4/4/2012)
Helidac (bismuth subsalicylate/tetracycline hydrochloride/metronidazole) Therapy (initial posting 3/8/2012)
Heparin Sodium Premixes (initial posting 7/5/2012)
Hydromorphone Hydrochloride Injection (initial posting 3/7/2012) UPDATED 9/26/2012
Intravenous Fat Emulsion
Isoniazid Tablets UPDATED 9/20/2012
Ketorolac Injection
Leucovorin Calcium Lyophilized Powder for Injection
Leuprolide Acetate Injection
Lidocaine Hydrochloride Injection
Lidocaine HCL, 4% Topical Solution
Lorazepam Injection UPDATED 9/26/2012
Magnesium Sulfate Injection
Mannitol Injection

Methazolamide Tablets
Methotrexate Injection
Methyldopate Injection
Metoclopramide Injection
Midazolam Injection UPDATED 9/26/2012
Mitomycin Powder for Injection
Morphine Sulfate Injection
Morphine Sulfate Injection (Preservative Free)
Multi-Vitamin Infusion (Adult and pediatric) 9/18/2012
Mustargen (mechlorethamine HCl) injection UPDATED 9/26/2012
Nalbuphine HCl Injection (initial posting 5/15/2012)
Naloxone Injection (initial posting 2/22/2012)
Naltrexone Oral Tablets (initial posting 2/22/2012)
Nefazodone Tablets (initial posting 4/16/2012)
NeoProfen (ibuprofen lysine) Injection (initial posting 12/15/2011)
Neurolite, Kit for the Preparation of Technetium Tc99m Bicisate for Injection (initial posting 5/4/2012)
Norethindrone and Ethinyl Estradiol Tablets, USP (Ovcon 50 Tablets) (initial posting 4/16/2012)
Ondansetron Injection 2 mg/mL UPDATED 9/20/2012
Ondansetron Injection 32 mg/50 mL premixed bags
Ontak injection (initial posting 9/22/2011)
Oxsoralen (methoxsalen) 1% topical lotion (initial posting 7/6/2010)
Oxymorphone Hydrochloride Oral Tablet (initial posting 3/19/2012)
Pancuronium Bromide Injection
Pegasys (peginterferon alfa-2a) Injection - Prefilled Syringes (initial posting 3/26/2012) UPDATED 9/25/2012
Pentamidine isethionate inhalant (NebuPent) (initial posting 8/27/2012)
Pentamidine isethionate for injection (Pentam 300) (initial posting 8/27/2012)
Pentostatin for Injection (Nipent) (initial posting 3/21/2012)
Perflutren Lipid Microsphere (DEFINITY) Injection
Phentolamine Mesylate (initial posting 6/4/2012)
Phytonadione Injectable Emulsion (Vitamin K)
Pilocarpine HCL Opthalmic Gel 4% (Pilopine HS) (initial posting 6/1/2012)
Potassium Chloride Injection 2 mEq/mL (initial posting 5/15/2012) UPDATED 9/25/2012
Potassium Phosphate Injection
Procainamide HCL Injection
Prochlorperazine Injection (initial posting 1/30/2012)
Promethazine Injection (initial posting 2/10/2012)
Propofol Injection (initial posting 4/5/2012)
Protonix (pantoprazole) Injection (initial posting 2/23/2012)
Secretin Injection (ChiRhoStim) (initial posting 6/15/2012)
Selenium Injection
Sodium Acetate Injection (initial posting 3/20/2012)
Sodium Bicarbonate Injection (initial posting 4/4/2012)
Sodium Chloride 0.9% (5.8mL and 20mL) (initial posting 5/4/2012)
Sodium Chloride 23.4%
Sodium Lactate Injection (initial posting 5/17/2012)
Succinylcholine Injection (initial posting 8/17/2012)
Sufentanil Citrate Injection UPDATED 9/26/2012
Sulfamethoxazole 80mg/trimethoprim 16mg/ml injection (SMX/TMP)
Telavancin (Vibativ) Injection (initial posting 1/6/2012)
Tetracycline Capsules
Thiotepa for Injection (initial posting 12/2/2011)

Thyrogen (thyrotropin alfa) injection 1.1mg/vial (initial posting 11/22/2011)
Thyrolar Tablets (initial posting 12/31/2009
Ticarcillin disodium/Clavulanic Potassium Injection (Timentin) (initial posting 8/16/12)
Ticlopidine Tablets
Tobramycin Solution for Injection
Tromethamine Injection (initial posting 5/2/2012)
Viaspan Cold Storage Solution 1000 mL Bag (initial posting 4/16/2012)
Vinblastine Sulfate Injection (initial posting 1/31/2012)
Zinc Injection (initial posting 2/15/2012)