Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
October 8, 2014
4 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: **Drug Utilization Review Board Members**

FROM: **Bethany Holderread, Pharm.D.**

SUBJECT: **Packet Contents for Board Meeting – October 8, 2014**

DATE: **September 29, 2014**

NOTE: **The DUR Board will meet at 4:00 p.m. The meeting will be held at 4345 N Lincoln Blvd.**

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

Action Item – Vote to Prior Authorize Versacloz™ (Clozapine Oral Suspension) – See Appendix C

Action Item – Vote to Prior Authorize Grastek® (Timothy Grass Pollen Allergen Extract) and Ragwitek™ (Short Ragweed Pollen Allergen Extract) – See Appendix D

30-Day Notice to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin) – See Appendix E

Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine) – See Appendix F

Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Plaque Psoriasis, and Ankylosing Spondylitis and 30-Day Notice to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab) – See Appendix G

Action Item – Annual Review of Bladder Control Medications – See Appendix H

FDA and DEA Updates – See Appendix I

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board

(DUR Board)

Meeting – October 8, 2014 @ 4:00 p.m.

Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

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 10, 2014 DUR Minutes – Vote
   B. September 10, 2014 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/FDA Safety Alerts – See Appendix B**
   A. Medication Coverage Activity for September 2014
   B. Pharmacy Help Desk Activity for September 2014
   C. Overview of Safety Alerts

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

5. **Action Item – Vote to Prior Authorize Versacloz™ (Clozapine Oral Suspension) – See Appendix C**
   A. COP Recommendations

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

6. **Action Item – Vote to Prior Authorize Grastek® (Timothy Grass Pollen Allergen Extract) and Ragwitek™ (Short Ragweed Pollen Allergen Extract) – See Appendix D**
   A. COP Recommendations

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

7. **30-Day Notice to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin) – See Appendix E**
   A. Introduction
   B. Product Summaries
   C. COP Recommendations

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

8. Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine) – See Appendix F

A. Current Prior Authorization Criteria
B. Utilization of Antidepressants
C. Prior Authorization of Antidepressants
D. Market News and Updates
E. Product Summaries
F. COP Recommendations
G. Utilization Details of Antidepressants

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

9. Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Plaque Psoriasis, and Ankylosing Spondylitis and 30-Day Notice to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab) – See Appendix G

A. Current Prior Authorization Criteria
B. Utilization of Biologic Products
C. Prior Authorization of Biologic Products
D. Market News and Updates
E. Product Summaries
F. COP Recommendations
G. Utilization Details of Biologic Products

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

10. Action Item – Annual Review of Bladder Control Medications – See Appendix H

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

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

11. FDA and DEA Updates – See Appendix I

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

12. Future Business

A. Annual Reviews
B. New Product Reviews

Items to be presented by Dr. Muchmore, Chairman:

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF SEPTEMBER 10, 2014

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

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

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

OTHERS PRESENT:		
Dr. Fran Kaiser, Merck	Mark DeClerk, Lilly	Michael Mason, Alcon
Tarolyn Carlton, OAPI	Warren Tayes, Merck	Jim Fowler, Astra Zeneca
Sam Smothers , Medimmune	Roger Grotzinger, BMS	Jon Maguire, GSK
Mai Duong, Novartis	Brian Maves, Pfizer	Lance Burchan, Medimmune
Audrey Rattan, OAPI	Toby Thompson, Alcon	Chris Lewis, Lundbeck
Cheri Ritchie, Otsuka	John Omick, Lunbeck	Richard Uhles, Forest
Bob Gustafson, Lundbeck	Don Kempin, Novo Novadisk	Tiffany York, US BIO Services
Charlene Kaiser, Amgen	Ron Schnare, Shire	Sharon Jackson, GSK
Richard Ponder, J & J		

PRESENT FOR PUBLIC COMMENT:	
Fran E. Kaiser MD	Merck
Kim Lonergan	Otsuka
Dr. Robert Welliver	OUHSC
Jeremy Franklin	Medimmune

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**

FRAN E. KAISER **AGENDA NO. 6 AND 10**
KIM LONGERAN **AGENDA NO. 8**
DR. ROBERT WELLIVER **AGENDA NO. 7**
JEREMY FRANKLIN **AGENDA NO. 7**

ACTION: NONE REQUIRED

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

3A: JULY 9, 2014 DUR MINUTES – VOTE

3B: JULY 9, 2014 DUR RECOMMENDATIONS MEMORANDUM

Dr. Cothran stated that *"Kelli Brodersen was marked absent last meeting and she should have been marked present."*

Dr. Winegardener moved to approve with corrections; seconded by Ms. Bruna Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/DRUG UTILIZATION REVIEW OF PRENATAL VITAMINS

4A: MEDICATION COVERAGE ACTIVITY FOR AUGUST 2014

4B: PHARMACY HELP DESK ACTIVITY FOR AUGUST 2014

4C: DRUG UTILIZATION REVIEW OF PRENATAL VITAMINS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE ZOHYDRO™ ER (HYDROCODONE BITARTRATE) AND XARTEMIS™ XR (OXYCODONE/ACETAMINOPHEN)**

5A: COP RECOMMENDATIONS

*Dr. Preslar moved to accept with the change of Xartemis™ XR (oxycodone/acetaminophen) Approval Criteria No. 1 to read: An **acute** pain requiring around the clock opioid treatment…*

Materials included in agenda packet; presented by Dr. Holderread

Dr. Preslar moved to approve; seconded by Ms. Bruna Varalli-Claypool

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE ZONTIVITY™ (VORAPAXAR)**

6A: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Anderson

Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF SYNAGIS® (PALIVIZUMAB)**

7A: CURRENT PRIOR AUTHORIZATION CRITERIA

7B: UTILIZATION OF SYNAGIS®

7C: PRIOR AUTHORIZATION OF SYNAGIS®

7D: MARKET NEWS AND UPDATES

7E: COP RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Anderson

Ms. Bruna Varalli-Claypool recommends "*a motion to keep current Synagis criteria with no changes"*

Ms. Bruna Varalli-Claypool to approve; seconded by Dr. Preslar.

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF ATYPICAL ANTIPSYCHOTICS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VERSACLOZ™ (CLOZAPINE ORAL SUSPENSION)**

8A: CURRENT TIER STRUCTURE

8B: UTILIZATION OF ATYPICAL ANTIPSYCHOTICS

8C: PRIOR AUTHORIZATION OF ATYPICAL ANTISYCHOTICS

8D: ATYPICAL ANTIPSYCHOTIC UTILIZATION TREND

8E MARKET NEWS AND UPDATES

8F: COP RECOMMENDATIONS

8G: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF ADHD AND NARCOLEPSY MEDICATIONS**

9A: CURRENT AUTHORIZATION CRITERIA

9B: UTILIZATION OF ADHD & NARCOLEPSY MEDICATIONS

9C: PRIOR AUTHORIZATION OF ADHD & NARCOLEPSY MEDICATIONS

9D: MARKET NEWS AND UPDATES

9E: COP RECOMMENDATIONS

9F: UTILIZATION DETAILS

Materials included in agenda packet; presented by Dr. Adams

Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **30-DAY NOTICE TO PRIOR AUTHORIZE GRASTEK® (TIMOTHY GRASS POLLEN ALLERGEN EXTRACT) AND RAGWITEK™ (SHORT RAGWEED POLLEN ALLERGEN EXTRACT)**

10A: INTRODUCTION

10B: PRODUCT SUMMARIES

10C: COP RECOMMENDATIONS

Dr. Muchmore recommends *"Montelukast should be used with an antihistamine in the previous season" "If they have done the 30 days of Montelukast and an antihistamine then they meet the criteria."*

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **FDA AND DEA UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **FUTURE BUSINESS**

12A: ANNUAL REVIEWS

12B: NEW PRODUCT REVIEWS

Materials included in agenda packet; submitted by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ADJOURNMENT**

The meeting was adjourned at 5:15 pm.

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

Memorandum

Date: September 11, 2014

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

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

Subject: DUR Board Recommendations From Meeting of September 10, 2014

Recommendation 1: Vote to Prior Authorize Zohydro™ ER (Hydrocodone Bitartrate) and Xartemis™ XR (Oxycodone/Acetaminophen)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Zohydro™ ER (hydrocodone bitartrate) and Xartemis™ XR (oxycodone/acetaminophen) to the Special PA category of the Opioid Analgesics Product Based Prior Authorization category with the following criteria:

Zohydro™ ER (Hydrocodone Bitartrate) Extended-Release Capsules Approval Criteria:

1. A chronic pain condition requiring daily, around-the-clock, long-term opioid treatment; and
2. A patient-specific, clinically significant reason why the member cannot use all other available long-acting Tier-2 and Tier-3 medications.
3. Tier structure rules still apply.

Xartemis™ XR (Oxycodone/APAP) Extended-Release Tablets Approval Criteria:

1. An acute pain condition requiring around-the-clock opioid treatment; and
2. A patient-specific, clinically significant reason for the following:
    a. Why the member cannot use any other opioid medication for treatment of acute pain; and

b. Why the member requires a long-acting medication for an acute pain condition; and
c. Why the member cannot use Oxycontin® (oxycodone ER) and OTC acetaminophen individual products in place of this combination product.

3. A quantity limit of 4 tablets per day will apply with a maximum approval duration of 10 days; and
4. The member must not exceed 3,250mg of acetaminophen per day from all sources.
5. Tier structure rules still apply.

Recommendation 2: Vote to Prior Authorize Zontivity™ (Vorapaxar) and Update the Anticoagulant Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Zontivity™ (vorapaxar) with the following criteria:

Zontivity™ (Vorapaxar) Approval Criteria:

1. An FDA approved diagnosis of one of the following: history of myocardial infarction (MI) or peripheral arterial disease (PAD); and
2. Zontivity™ must be used in combination with aspirin and/or clopidogrel (not monotherapy); and
3. Zontivity™ will not be approved for members with the following situations: history of transient ischemic attack (TIA), stroke, or intracranial hemorrhage (ICH), or active pathological bleeding; and
4. A quantity limit of 30 tablets per 30 days will apply.

The College of Pharmacy also recommends updating the prior authorization criteria for the following medications to reflect new FDA approved indications:

Pradaxa® (Dabigatran) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
   a. Non-valvular atrial fibrillation; or
   b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) after treatment with parenteral anticoagulant for 5 to 10 days; or
   c. To reduce the risk of recurrent DVT or PE in patients who have been previously treated.

Eliquis® (Apixaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
   a. Non-valvular atrial fibrillation; or

b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and PE following initial therapy; or
c. PE or DVT prophylaxis in patients who have had hip or knee replacement surgery.

Recommendation 3: Fiscal Year 2014 Annual Review of Synagis® (Palivizumab)

MOTION CARRIED. Approval was not unanimous.

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection: *Members must be included in one of the following age groups at the beginning of the RSV season:
   1. Infants and children less than 24 months old with Chronic Lung Disease (CLD) (formerly bronchopulmonary dysplasia) who have required medical treatment (O2, bronchodilator, corticosteroid, or diuretic therapy) for CLD in the 6 months prior to RSV season
   2. Infants up to 24 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure
   3. Infants less than 12 months of age, born at 28 weeks gestation or earlier
   4. Infants less than 6 months of age, born at 29 to 31 weeks gestation
   5. Infants less than 12 months of age, with congenital abnormalities of the airway
   6. Infants less than 12 months of age, with severe neuromuscular disease
   7. Infants up to 3 months old at the start of RSV season, born at 32 to 34 weeks gestation, who have one of the following risk factors (up to three doses only):
      a. Child care attendance
      b. Siblings younger than 5 years of age

   *Treatment is authorized for the entire RSV season (as indicated) except for members meeting criteria #7, in which case, a maximum of 3 doses will be authorized. Prescribers may request special consideration for additional doses (up to the end of the RSV season as indicated) on an individual patient basis for members meeting criteria #7.

B. Length of treatment: Synagis® is approved for use only during RSV season. Approval dates will be November 1 through March 31.

C. Units authorized: The maximum duration of therapy is five doses, with a dose to be administered no more often than every 30 days. Infants born at 32-34 weeks gestation will receive a maximum of three doses. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses

administered prior to the member's discharge from a hospital will be counted as one of the approved total.

D. Dose-pooling: To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

Recommendation 4: Fiscal Year 2014 Annual Review of Atypical Antipsychotics and 30-Day Notice to Prior Authorize Versacloz™ (Clozapine Oral Suspension)

NO ACTION REQUIRED.

Recommendation 5: Fiscal Year 2014 Annual Review of ADHD & Narcolepsy Medications

MOTION CARRIED by unanimous approval.

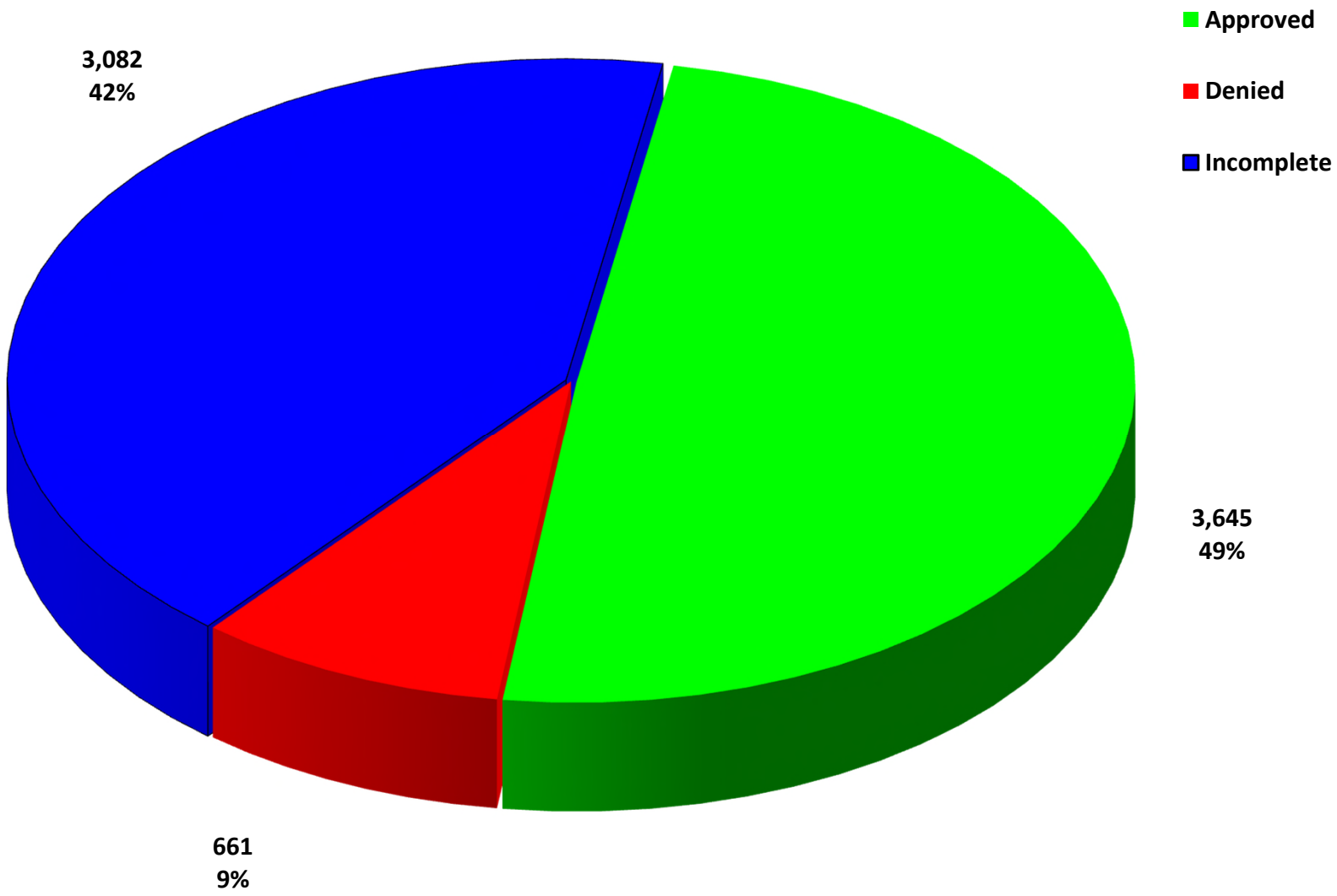
The College of Pharmacy recommends moving Quillivant XR® and Daytrana™ to Tier-3 of the ADHD & Narcolepsy Medications Product Based Prior Authorization category to promote supplemental rebate participation. If no supplemental rebate participation, these products will remain in the Special PA category. The existing criteria for this category will apply. Additionally, the College of Pharmacy recommends moving products to lower tiers when appropriate and cost effective, based on State Maximum Allowable Cost (SMAC).

Recommendation 6: 30-Day Notice to Prior Authorize Grastek® (Timothy Grass Pollen Allergen Extract) and Ragwitek™ (Short Ragweed Pollen Allergen Extract)

NO ACTION REQUIRED.

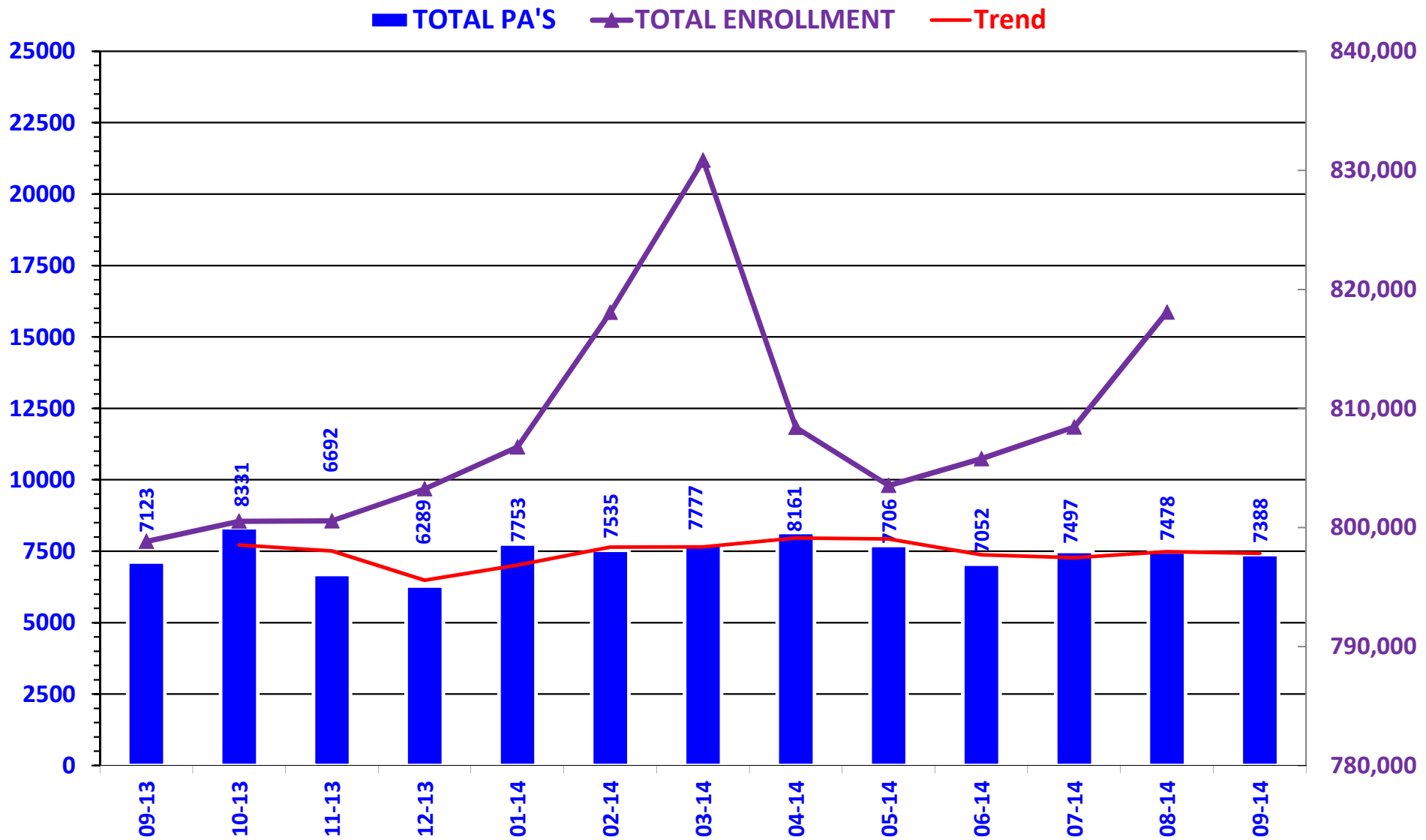
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: SEPTEMBER



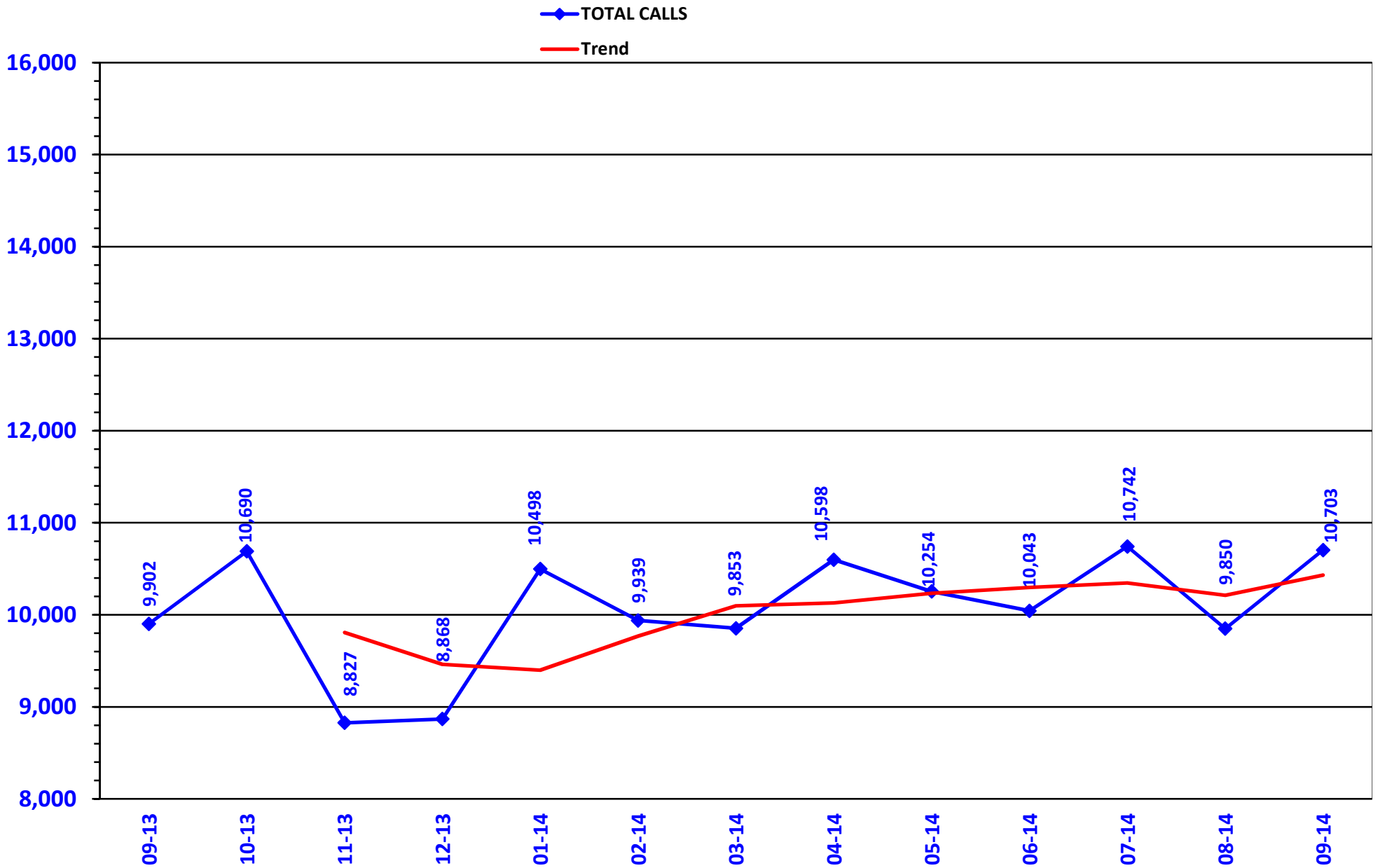
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: SEPTEMBER 2013 - SEPTEMBER 2014



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
SEPTEMBER 2013 – SEPTEMBER 2014



Prior Authorization Activity
9/1/2014 Through 9/30/2014

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	319	143	8	168	350
Analgesic - NonNarcotic	15	0	3	12	0
Analgesic, Narcotic	378	196	28	154	197
Angiotensin Receptor Antagonist	34	4	8	22	221
Antiasthma	175	63	19	93	341
Antibiotic	20	3	1	16	299
Anticoagulant	90	70	1	19	285
Anticonvulsant	84	42	5	37	313
Antidepressant	267	55	39	173	345
Antidiabetic	139	73	7	59	349
Antigout	11	6	0	5	252
Antihistamine	213	172	2	39	354
Antimigraine	47	9	4	34	245
Antiplatelet	19	14	1	4	335
Antiulcers	227	61	54	112	164
Anxiolytic	92	59	7	26	230
Atypical Antipsychotics	387	226	14	147	326
Biologics	42	22	1	19	296
Bladder Control	49	8	5	36	357
Botox	20	17	0	3	358
Cardiovascular	24	20	0	4	321
Cephalosporins	25	7	2	16	7
Chronic Obstructive Pulmonary Disease	20	6	2	12	303
Dermatological	108	13	58	37	85
Endocrine & Metabolic Drugs	70	45	2	23	132
Erythropoietin Stimulating Agents	31	20	1	10	121
Fibromyalgia	120	35	19	66	349
Fish Oils	29	7	8	14	357
Gastrointestinal Agents	58	8	20	30	172
Genitourinary Agents	15	4	1	10	20
Growth Hormones	59	48	2	9	164
Hematopoietic Agents	10	6	0	4	130
Hepatitis C	63	42	4	17	8
HFA Rescue Inhalers	50	22	3	25	345
Insomnia	42	8	2	32	210
Linzess, Amitiza, and Relistor	52	10	7	35	207
Multiple Sclerosis	32	19	1	12	204
Muscle Relaxant	80	21	20	39	57
Nasal Allergy	112	6	39	67	227
Neurological Agents	73	59	3	11	349
Nsaids	156	22	15	119	319
Ocular Allergy	37	9	0	28	194
Ophthalmic Anti-infectives	26	2	2	22	16
Osteoporosis	31	7	4	20	332
Other*	168	37	41	90	240
Otic Antibiotic	45	13	5	27	8
Pediculicide	72	24	3	45	19
Prenatal Vitamins	13	0	0	13	0
Statins	48	16	4	28	353
Stimulant	1,213	562	54	597	339
Suboxone/Subutex	208	161	7	40	80
Synagis	12	0	0	12	0
Testosterone	64	28	11	25	346

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Antibiotic	12	1	1	10	3
Topical Antifungal	43	1	6	36	25
Topical Corticosteroids	82	2	23	57	269
Vitamin	51	22	21	8	347
Pharmacotherapy	60	53	2	5	192
Emergency PAs	1	1	0	0	
Total	**6,043**	**2,610**	**600**	**2,833**	
Overrides					
Brand	46	37	0	9	318
Cumulative Early Refill	7	7	0	0	180
Dosage Change	388	338	4	46	7
High Dose	5	5	0	0	237
Ingredient Duplication	51	42	0	9	4
Lost/Broken Rx	67	60	1	6	6
NDC vs Age	55	54	1	0	261
Nursing Home Issue	33	32	1	0	4
Other*	40	29	4	7	16
Prescriber Temp Unlock	1	0	1	0	0
Quantity vs. Days Supply	597	401	38	158	252
STBS/STBSM	10	10	0	0	50
Stolen	7	4	2	1	3
Temporary Unlock	19	13	6	0	20
Third Brand Request	27	10	4	13	16
Overrides Total	**1,345**	**1,035**	**61**	**249**	
Total Regular PAs + Overrides	**7,388**	**3,645**	**661**	**3,082**	

Denial Reasons	
Unable to verify required trials.	2,560
Does not meet established criteria.	648
Lack required information to process request.	519

Other PA Activity	
Duplicate Requests	472
Letters	3,254
No Process	27
Changes to existing PAs	521
Helpdesk Initiated Prior Authorizations	900
PAs Missing Information	76

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

Overview of Safety Alerts

Overview of Safety Alerts

Oklahoma Health Care Authority
October 2014

Introduction[1,2,3,4,5,6]

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

Date	Drug	Issue
04/16/2014	**Extended release – Long Acting (ER/LA) Opioid Analgesics (morphine, fentanyl, buprenorphine, methadone, hydromorphone, oxymorphone, tapentadol, oxycodone)**	**Addiction, Abuse, Misuse**
Issue Details: Based on safety concerns regarding serious risks with ER and LA opioid analgesics, including addiction, abuse, misuse, overdose, and death, the FDA sent letters to manufacturers of these medications outlining new safety information requirements for the drug product labels. The label requirements stress the importance of selecting the correct patient population for use of ER/LA opioid analgesics. The FDA emphasized that ER/LA opioid analgesics should only be used for the management of pain severe enough to require around-the-clock, long term analgesia for which alternative treatment options with non-opioid analgesics or immediate-release opioids has been inadequate. **FDA Recommendations:** Required label changes include a stronger boxed warning as well as updates to the Indications, Dosing and Administration, and Warnings and Precautions sections of the label. These changes are specifically related to the abuse potential, modification to the dosage and administration, and required enhancement of the REMS for each drug. Educational materials will be made available for patients and health care professionals. The REMS requires manufacturers to make available continuing education courses for health care professionals. **Update - 8/19/14**: Notification to manufacturers from the FDA regarding approval of amendments to REMS, as recommended. **SoonerCare Action:** A post card detailing the FDA requirements and label updates to ER/LA opioid analgesics went out to the top 200 prescribers of these medications.		

Date	Drug	Issue
05/06/2014	**Aspirin**	**No benefits for patients who have not had previous cardiovascular events**
Issue Details: The FDA issued a report regarding the use of daily aspirin for primary prevention of cardiovascular events. Available data shows that patients who have had a myocardial infarction, stroke, or who have coronary artery disease will have lower risk of recurrence by taking a daily aspirin. However, a daily aspirin provides no benefit for patients who have not had any of these events, but does increase the risk for gastrointestinal (GI) bleeding or cerebral hemorrhage. **FDA Recommendations**: News items were published recommending that patients discuss the risks and benefits with their healthcare provider prior to starting a daily aspirin regimen.		

Date	Drug	Issue
05/22/2014	**Linagliptin (Tradjenta® & Jentadueto®)**	**Risk of serious hypersensitivity reactions of anaphylaxis, angioedema, and exfoliative skin conditions**
Issue Details: Post marketing reports of serious hypersensitivity reactions, including anaphylaxis, angioedema, and exfoliative skin conditions in patients treated with linagliptin. Reactions occur within the first three months of treatment. **FDA Recommendations:** The product label has been modified to include the contraindication, warning, and precautions regarding these hypersensitivity reactions. **Evaluation:** From January 1, 2014 to July 31, 2014, 256 SoonerCare members were on one of these medications. No known hypersensitivity reactions with these medications were reported to SoonerCare. Claims analysis regarding these reactions is under further review.		

Date	Drug	Issue
06/26/2014	**Oral Viscous Lidocaine**	**Risk of serious adverse events when used for teething pain in infants and children**
Issue Details: The FDA issued a Drug Safety Communication regarding the use of oral viscous lidocaine 2% solution for teething pain in infants and children. Serious adverse events, including seizure, severe brain injury, heart problems, and death have occurred due to overdose, and accidental swallowing of lidocaine. **FDA Recommendations:** A Black Box Warning has been added to the product label. Parents and caregivers are encouraged not to use over-the-counter (OTC) topical medications for teething pain, but to follow the American Academy of Pediatric' s (AAP) recommendations to use a chilled teething ring or gentle rubbing of the gums with a finger. **SoonerCare action:** Educational information regarding this warning will be included in the SoonerCare member newsletter and the SoonerCare Text for Baby Program.		

Date	Drug	Issue
07/2014	**Linaclotide (Linzess®)**	**Increased possibility of dehydration and death in young children**
Issue Details: In nonclinical studies, a single, clinically relevant adult dose of linaclotide caused death from dehydration in juvenile mice due to increased fluid secretion as a consequence of guanylate cyclase-C (GC-C) agonism; death occurred within 24 hours after administration. The safety and efficacy for use in children under 18 years of age has not been established. The expression of GC-C is increased in children less than 6 years of age compared to older children and adults; therefore this medication is determined to be contraindicated for use in children under the age of 6 years. **FDA Recommendations:** A Black Box Warning has been added to the product label contraindicating the use of linaclotide in children younger than 6 years of age. **Evaluation:** Evaluation of SoonerCare claims for members utilizing linaclotide did not reveal any utilization in members under the age of 10 years. SoonerCare criteria restricts use of this medication to members 18 years and older.		

Date	Drug	Issue
8/14/2014	**Growth Hormone**	**Increased risk of stroke in adults**
Issue Details: A research article published by French scientists in *Neurology* suggests that use of growth hormone is associated with an increased risk of hemorrhagic stroke (standardized incidence ratio from 3.5 to 7.0), particularly subarachnoid hemorrhage (standardized incidence ratio from 5.7 to 9.3). Growth hormone has mitogenic and proliferative properties suggesting an increased risk of cardiac and cerebrovascular mortality noted in a preliminary study. Further investigation reveals a high incidence of stroke in the study population, occurring at an average age of 24.2 years. Studied growth hormone treatment studied was started at a mean age of 11 years and continued for an average of 3.9 years. Researchers felt that this is a "strong relationship" and that patients using growth hormone not only for growth hormone deficiency, but also for performance enhancement should be informed of the risk. **FDA Recommendations:** The FDA has not acted on this information yet. Further study is recommended. **Evaluation:** During fiscal year 2014, there were 242 SoonerCare members utilizing growth hormone.		

[1] FDA Drug Safety Information and Adverse Event Reporting Program (opioids) available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm396503.htm Last revised 5/18/2013. Last accessed 9/29/2014

[2] Preidt, Robert, "Daily Aspirin Regimen Not Safe for Everyone: FDA." WebMD, Available online at: http://www.webmd.com/heart-disease/news/20140506/daily-aspirin-regimen-not-safe-for-everyone-fda-warns. Last revised 05/06/2014. Last accessed 09/29/2014.

[3] FDA Drug Safety Communication (linagliptin) available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm360497.htm. Last revised 6/13/2014. Last accessed 9/29/2014.

[4] FDA Drug Safety Communication (viscous lidocaine) available online at http://www.fda.gov/Drugs/DrugSafety/ucm402240.htm Last revised 6/26/2014. Last accessed 9/29/2014.

[5] FDA Drug Safety Communication (linaclotide) available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm409253.htm Last revised 8/15/2014. Last accessed 9/29/2014.

[6] Poidvin A et al."Use of Growth Hormone in Children Linked to Stroke in Adults." The Pharmaceutical Journal. Available online at: http://www.pharmaceutical-journal.com/news-and-analysis/news/use-of-growth-hormone-in-children-linked-to-stroke-in-adults/20066165.article. Last revised 08/14/2014. Last accessed 09/29/14

Appendix C

Vote to Prior Authorize Versacloz™ (Clozapine Oral Suspension)

Oklahoma Health Care Authority
October 2014

Recommendations

The College of Pharmacy recommends the addition of Versacloz™ (clozapine oral suspension) to Tier-3 of the Atypical Antipsychotics Product Based Prior Authorization category with the following criteria:

Atypical Antipsychotics*		
Tier-1	**Tier-2**	**Tier-3+**
clozapine (Clozaril®)¥	Supplemental Rebated Products	aripiprazole (Abilify®)
olanzapine (Zyprexa®)		aripiprazole (Abilify Maintena®)
quetiapine (Seroquel®)		asenapine (Saphris®)
risperidone (Risperdal®)		clozapine (Fazaclo®)
risperidone (Risperdal Consta®)		clozapine oral suspension (Versacloz™)
ziprasidone (Geodon®)		iloperidone (Fanapt™)
		lurasidone (Latuda®)
		olanzapine/fluoxetine (Symbyax®)
		paliperidone (Invega®)
		paliperidone (Invega Sustenna®)
		quetiapine ER (Seroquel XR®)

*Mandatory Generic Plan Applies
+ May be rebated to Tier-2 status only
¥ Does not count toward a Tier-1 trial
ER = extended-release

Atypical Antipsychotic Tier-2 Approval Criteria:

1. A trial of two Tier-1 products (not including clozapine), at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
2. Clozapine is available without prior authorization, but does not count towards a Tier-1 trial.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. A trial of two Tier-1 products (not including clozapine), at least 14 days in duration, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
2. A trial of two Tier-2 medications, at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
3. A manual prior authorization may be submitted for consideration of a Tier-3 product when the member has had at least four trials of Tier-1 and Tier-2 products (two trials must be

from Tier-1) that did not yield an adequate response or resulted in intolerable adverse effects.
4. Use of Versacloz™ (clozapine oral suspension) and Fazaclo® (clozapine orally disintegrating tablet) requires a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Atypical Antipsychotic for Adjunctive Treatment for Depression Approval Criteria:
1. Use of Abilify® (aripiprazole), Seroquel XR® (quetiapine extended release), or Symbyax® (olanzapine/fluoxetine) for a diagnosis of depression requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and a dual acting antidepressant) that did not yield an adequate response.
2. Tier structure rules still apply.

Current Users or Inpatient Discharge Approval Criteria:
1. Members currently stabilized on a higher tiered medication defined by paid claim(s) for the higher tiered medication in the past 90 days will be approved.
2. Members being released from a hospital and stabilized on a higher tiered medication will be approved.

Clinical Exceptions:
1. Approvals will be granted for members with clinical conditions for which lower tiered drugs are contraindicated.
2. Approvals will be granted for members whose current regimen includes drugs known to adversely interact with all lowered tiered drugs.
3. Lurasidone (Latuda®) may be approved for pregnant women with appropriate diagnosis.

Second Opinion Process for Children 0 - 4 Years of Age:
1. Children less than 5 years of age will require a “second opinion” prior authorization to be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted child psychiatrist.

Appendix D

Vote to Prior Authorize Grastek® (Timothy Grass Pollen Allergen Extract) and Ragwitek™ (Short Ragweed Pollen Allergen Extract)

Oklahoma Health Care Authority
October 2014

Recommendations

The College of Pharmacy recommends the prior authorization of Grastek® and Ragwitek™ with the following criteria:

Grastek® (Timothy Grass Pollen Allergen Extract) Approval Criteria:

1. Member must be 5 years of age or older; and
2. Member must have a positive skin test or in vitro testing for pollen specific IgE antibodies for Timothy grass or cross-reactive grass pollen (cool season grasses); and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trails must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids:** Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of the grass pollen season and continue throughout the season; and
7. The first dose must be given in the physician's office and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home.
12. Prescriber must be an allergist, immunologist or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Ragwitek™ (Short Ragweed Pollen Allergen Extract) Approval Criteria:

1. Member must be 18 years of age or older; and
2. Member must have a positive skin test or in vitro testing for pollen specific IgE antibodies to short ragweed pollen; and
3. Member must not have severe uncontrolled asthma; and
4. Member must have failed conservative attempts to control allergic rhinitis symptoms; and
5. Member must have failed pharmacological agents used to control allergies including the following (dates and duration of trails must be indicated on the prior authorization request):
    a. **Antihistamines:** Trials of two different products for 14 days each during a previous season; and
    b. **Montelukast:** One 14-day trial during a previous season in combination with an antihistamine; and
    c. **Nasal steroids**: Trials of two different products for 21 days each during a previous season; and
6. Treatment must begin greater than or equal to 12 weeks prior to the start of ragweed pollen season and continue throughout the season; and
7. The first dose must be given in the physician's office and the member must be observed for at least 30 minutes post dose; and
8. A quantity limit of one tablet daily will apply; and
9. Initial approvals will be for the duration of six months of therapy to include 12 weeks prior to the season and continue throughout the season; and
10. Member must not be allergic to other allergens for which they are receiving treatment via subcutaneous immunotherapy also known as "allergy shots"; and
11. Member or family member must be trained in the use of an auto-injectable epinephrine device and have such a device available for use at home.
12. Prescriber must be an allergist, immunologist or be an advanced care practitioner with a supervising physician that is an allergist or immunologist.

Appendix E

30-Day Notice to Prior Authorize Sivextro™ (Tedizolid), Dalvance™ (Dalbavancin), and Orbactiv™ (Oritavancin)

Oklahoma Health Care Authority
October 2014

Introduction[1,2,3]

In recent years there has been a dramatic rise in the frequency and severity of infections and the emergence of resistance to many of the antimicrobial agents commonly used to treat skin and soft tissue infections (SSTI). From 2000 to 2004, there was a 29% increase in total hospital admissions for SSTIs. Additionally, 6.3 million physician's office visits per year are attributable to SSTIs. Annual emergency department visits for SSTIs have increased to 3.4 million in 2005 compared to 1.2 million in 1993. These increased rates may be related to the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA).

The Food and Drug Administration (FDA) defines acute bacterial skin and skin structure infections (ABSSSI) to include cellulitis/erysipelas, wound infection, and major cutaneous abscess that have a minimum lesion surface area of approximately 75 cm^2. Common bacterial pathogens known to cause ABSSSI are *Streptococcus pyogenes* and *Staphylococcus aureus* including MRSA. Less common causes of ABSSI include other *Streptococcus* species, *Enterococcus faecalis*, or Gram-negative bacteria.

Current guidelines by the Infectious Diseases Society of America (IDSA) were released June 2014 for the diagnosis and management of SSTI. IDSA guidance recommends treatment of severe, purulent infections empirically with intravenous vancomycin, daptomycin, ceftaroline, telavancin, or linezolid. Sivextro™, Dalvance™, and Orbactiv™ were under investigation at the time these guidelines were proposed and were not included. The guidance does note the newer agents to be effective in SSTI including those caused by MRSA, but do not discuss a specific place in therapy.

Sivextro™ (Tedizolid Phosphate) Summary[3,4]

Indications: Sivextro™ (tedizolid phosphate) is an oxazolidinone-class antibacterial drug indicated in adults for the treatment of ABSSSI caused by susceptible isolates of the following gram-positive microorganisms: *Staphylococcus aureus* MRSA and methicillin-susceptible (MSSA) isolates, *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus* Group (including *Streptococcus anginosus, Streptococcus intermedius*, and *Streptococcus constellatus*), and *Enterococcus faecalis.*

- **Dosing:**
  - Sivextro™ is available in the following dosage forms:
    - 200mg oral tablet, and
    - 200mg sterile lyophilized powder in single-use vial for reconstitution for intravenous (IV) infusion.
  - The recommended regimen is:
    - 200mg tablet orally once daily for six days, or
    - 200mg via IV infusion over one hour once daily for six days.

- **Mechanism of Action:** Sivextro™ (tedizolid phosphate) is the prodrug of tedizolid. Tedizolid binds to the 50S subunit of the bacterial ribosome resulting in inhibition of protein synthesis. Based on its mechanism of action, tedizolid is unlikely to exhibit cross-resistance to non-oxazolidinone antibacterials.

- **Contraindications:** None.

- **Warnings and Precautions:**
  - **Neutropenia:** The safety and efficacy of Sivextro™ in patients with neutropenia (neutrophil counts <1000 cells/mm^3) have not been adequately evaluated. In an animal model of infection, the antibacterial activity of Sivextro™ was reduced in the absence of granulocytes. Consider alternative therapies in neutropenic patients.
  - ***Clostridium difficile*-associated diarrhea:** Evaluate if diarrhea occurs.

- **Efficacy:**
  - The efficacy of Sivextro™ in the treatment of ABSSSI was investigated in two double-blind, non-inferiority clinical trials, ESTABLISH-1 and ESTABLISH-2. Both trials compared Sivextro™ to Zyvox®, the other currently available oxazolidinone antibiotic for the treatment of ABSSI suspected or documented to be caused by a gram-positive pathogen.
  - ESTABLISH-1 randomized patients 18 years or older to receive Sivextro™ 200mg orally once daily for six days or Zyvox® 600mg orally every twelve hours for ten days. The primary efficacy outcome was early clinical response at the 48 to 72 hour assessment with no increase in lesion surface area and oral temperature $\leq$ 37.6°C. Results found 79.5% of patients treated with Sivextro™ and 79.4% treated with Zyvox® met the outcome demonstrating non-inferiority.
- ESTABLISH-2 randomized patients 12 years of age and older to receive IV Sivextro™ or Zyvox® for a minimum of one day (two doses) before patients were permitted to step-down to oral therapy. The primary outcome was early clinical response rate defined as 20% or greater reduction in area of the primary lesion at 48 to 72 hours. Results found 85% of patients randomized to Sivextro™ and 83% receiving Zyvox® met the primary outcome demonstrating non-inferiority.

Dalvance™ (Dalbavancin) Summary[5,6]

Indications: Dalvance™ (dalbavancin) is a semisynthetic lipoglycopeptide indicated for ABSSSI caused by designated susceptible strains of Gram-positive microorganisms.

- **Dosing:**
  - Dalvance™ is available as 500mg of lyophilized powder in a single-use vial for reconstitution for injection.
  - Recommended regimen of Dalvance™ is a two-dose regimen consisting of 1000mg followed one week later by 500mg. The dose should be administered by IV infusion over 30 minutes.
  - Dosage adjustment for patients with creatinine clearance less than 30mL/min and not receiving regularly scheduled hemodialysis: 750mg followed one week later by 375mg

- **Mechanism of Action:** Dalvance™ interferes with cell wall synthesis by binding to the D-alanyl-D-alanine terminus of the stem pentapeptide in nascent cell wall peptidoglycan, thus preventing cross-linking. Dalvance™ is bactericidal *in vitro* against *Staphylococcus aureus* and *Streptococcus pyogenes* when dosed according to the recommended dosage regimen.

- **Contraindications:** Hypersensitivity to Dalvance™.

- **Warnings and Precautions:**
  - Serious hypersensitivity (anaphylactic) and skin reactions have been reported with glycopeptide antibacterial agents, including Dalvance™; exercise caution in patients with known hypersensitivity to glycopeptides.
  - Rapid IV infusion of glycopeptide antibacterial agents can cause reactions.
  - Alanine Aminotransferase (ALT) elevations with Dalvance™ treatment were reported in clinical trials.
  - *Clostridium difficile*-associated diarrhea (CDAD) has been reported with nearly all systemic antibacterial agents, including Dalvance™. Evaluate if diarrhea occurs.

- **Efficacy:**
  - The efficacy of Dalvance™ for the treatment of ABSSSI was investigated in two double-blind, non-inferiority clinical trials, DISCOVER-1 and DISCOVER-2. Both trials compared Dalvance™ to IV vancomycin followed by oral linezolid (Zyvox®).
  - Patients were randomized to receive Dalvance™ 1000mg once on day one followed by 500mg once on day eight or vancomycin 1 gram or 15 mg/kg every 12 hours for at least three days, after which they could be switched to oral linezolid to complete a 10-to-14 day course of treatment.
  - The primary endpoint in both studies was the clinical response rate defined as patients who had no increase from baseline in lesion area 48-72 hours after initiation of therapy, and had a temperature consistently at or below 37.6°C.

Study	Drug	Cessation of Lesion Spread	Reduction in Lesion Area
DISCOVER-1 (n=573)	Dalvance™	83.3% (240/288)	89.9% (259/288)
	Vancomycin/linezolid	81.8% (233/285)	90.9% (259/285)
DISCOVER-2 (n=739)	Dalvance™	76.8% (285/371)	87.6% (325/371)
	Vancomycin/linezolid	78.3% (288/368)	85.9% (316/368)

Orbactiv™ (Oritavancin) Summary[7]

Indications: Orbactiv™ (oritavancin) is a lipoglycopeptide antibacterial drug indicated for the treatment of adult patients with ABSSSI caused or suspected to be caused by susceptible isolates of designated Gram-positive microorganisms.

- **Dosing:**
  - Orbactiv™ is available as 400mg of lyophilized powder in a single-use vial for reconstitution for injection.
  - The recommended regimen is 1200mg in a single dose administered by IV infusion over three hours.

- **Mechanism of Action:** Orbactiv™ has three mechanisms of action:
  - Inhibition of the transglycosylation (polymerization) step of cell wall biosynthesis by binding to the stem peptide of peptidoglycan precursors; and
  - Inhibition of the transpeptidation (crosslinking) step of cell wall biosynthesis by binding to the peptide bridging segments of the cell wall; and
  - Disruption of bacterial membrane integrity, leading to depolarization, permeabilization, and cell death.
  - These multiple mechanisms contribute to the concentration-dependent bactericidal activity of Orbactiv™.

- **Contraindications:**
  - Use of IV unfractionated heparin sodium is contraindicated for 48 hours after Orbactiv™ administration.
  - Known hypersensitivity to Orbactiv™.

- **Warnings and Precautions:**
  - **Concomitant warfarin use:** Co-administration of Orbactiv™ and warfarin may result in higher exposure of warfarin, which may increase the risk of bleeding. Use Orbactiv™ in patients on chronic warfarin therapy only when the benefits can be expected to outweigh the risk of bleeding.
  - **Coagulation test interference:** Orbactiv™ has been shown to artificially prolong activated partial thromboplastin time (aPTT) for up to 48 hours, and may prolong PT and INR for up to 24 hours.
  - Hypersensitivity reactions have been reported with the use of antibacterial agents including Orbactiv™. Discontinue infusion if signs of acute hypersensitivity occur. Monitor patients closely with known hypersensitivity to glycopeptides.
  - Infusion-related reactions have been reported. Slow the rate or interrupt infusion if infusion reaction develops.
  - ***Clostridium difficile*-associated colitis:** Evaluate patients if diarrhea occurs.
  - **Osteomyelitis:** Institute appropriate alternate antibacterial therapy in patients with confirmed or suspected osteomyelitis.

- **Efficacy:**
  - The efficacy of Orbactiv™ for the treatment of ABSSSI was investigated in two double-blind, non-inferiority clinical trials. Both trials compared Orbactiv™ 1000mg IV to IV vancomycin dosed 1 gram or 15 mg/kg every twelve hours for 7 to 10 days. The primary endpoint in both trials was early clinical response defined as cessation of spread or reduction in size of baseline lesion, absence of fever, and no rescue antibacterial drug at 48 to 72 hours after initiation of therapy.

Study	Drug	Clinical Response Rate
Trial-1 (n=954)	Orbactiv™	82.3% (391/475)
	Vancomycin	78.9% (378/479)
Trial-2 (n=1005)	Orbactiv™	80.1% (403/503)
	Vancomycin	82.9% (416/502)

Cost Comparison

Medication	Regimen	Cost per Unit	Cost of Therapy
Sivextro™ 200mg Tablets	200mg once daily for 6 days	$311.52[+]	$1,869.12
Sivextro™ 200mg Vial	200mg once daily for 6 days	$248.16[+]	$1,488.96
Dalvance™ 500mg Vial	1000mg Day 1 then 500mg Day 8	$1,573.44[+]	$4,720.32
Orbactiv™ 400mg Vial	1200mg Day 1	$1,020.80[+]	$3,062.40
Zyvox® 600mg Tablets[∞]	600 mg every 12 hours for 10 days[*]	$143.17[+]	$2,863.40
Zyvox® 100mg/5mL Suspension[∞]	600 mg every 12 hours for 10 days[*]	$4.77[+]	$600.00
Zyvox® 600mg/300mL IV Soln	600 mg every 12 hours for 10 days[*]	$0.45[**]	$2,700.00
Vancomycin 500mg Vial	1000mg every 12 hours for 7-10 days	$3.00[**]	$84.00 to $120.00

+Estimated acquisition cost (EAC)
*FDA approved regimen: 600mg every 12 hours for 10 to 14 days. Sivextro™ noninferiority study dosed Zyvox® for 10 days.
**SMAC= State maximum allowable cost.
∞ Zyvox® rebate not shown.

Recommendations

The College of Pharmacy recommends the prior authorization of Sivextro™, Dalvance™, and Orbactiv™ with the following criteria:

Sivextro™ (Tedizolid Phosphate) Tablet Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent; and
2. A patient-specific, clinically significant reason why the member cannot use Zyvox® (linezolid) or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of six tablets per six days will apply.

Dalvance™ (Dalbavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid) or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of two vials per seven days will apply.

Orbactiv™ (Oritavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid) or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of three vials per 30 days will apply.

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[1] FDA Guidance for Industry. Acute Bacterial Skin and Skin Structure Infections: Developing Drugs for Treatment. October 2013. Available online at: http://www.fda.gov/downloads/Drugs/.../Guidances/ucm071185.pdf. Last accessed 09/2014.

[2] Stevens DL, Bisno AL, Chambers HF, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10-52. Available online at: http://cid.oxfordjournals.org/content/early/2014/06/14/cid.ciu296.full.pdf+html. Last accessed: 09/2014.

[3] "RxCounselor." *Your Guide to Newly Approved Brand Drugs* 9.32 (July 2014). Available online at: <http://www.catamaranrx.com/>. Last accessed 09/2014.

[4] Sivextro™ Product Information. Cubist Pharmaceuticals. Available online at: http://www.merck.com/product/usa/pi_circulars/r/ http://sivextro.com/pdf/PrescribingInformation.pdf. Last revised 06/2014. Last accessed 09/2014.

[5] Dalvance™ Product Information. Durata Therapeutics. Available online at: http://content.stockpr.com/duratatherapeutics/files/docs/Dalvance+APPROVED+USPI.PDF. Last revised on 05/2014. Last accessed 09/2014.

[6] "The Medical Letter on Drugs and Therapeutics." *Two New Drugs for Skin and Skin Structure Infections* 56.1449 (2014).

[7] Orbactiv™ Product Information. The Medicines Company. Available online at: http://www.themedicinescompany.com/app/webroot/img/orbactiv-prescribing-information.pdf. Last revised on 09/2014. Last accessed 09/2014.

Appendix F

Fiscal Year 2014 Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Fetzima® (Levomilnacipran), Khedezla® (Desvenlafaxine), and Brintellix® (Vortioxetine)

Oklahoma Health Care Authority
October 2014

Current Prior Authorization Criteria

Antidepressants		
Tier-1	**Tier-2**	**Tier-3**
Selective Serotonin Reuptake Inhibitors (SSRIs)		
citalopram (Celexa®) escitalopram (Lexapro®) fluoxetine (Prozac®, Sarafem®) fluvoxamine (Luvox®) paroxetine (Paxil®, Paxil CR®) sertraline (Zoloft®)	fluoxetine (Prozac® Weekly™) fluvoxamine CR (Luvox CR®) paroxetine (Pexeva®)	fluoxetine 60mg tablets*
Dual Acting Antidepressants		
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®) mirtazapine (Remeron®, Remeron® SolTab™) trazodone (Desyrel®) venlafaxine (Effexor®, Effexor XR® capsules)	duloxetine (Cymbalta®) venlafaxine ER tablets (Effexor XR® tablets)	bupropion (Aplenzin®) bupropion (Forfivo XL®) desvenlafaxine (Pristiq®) nefazodone (Serzone®) trazodone ER (Oleptro®) vilazodone (Viibryd®)
Monoamine Oxidase Inhibitors (MAOIs)		
		phenelzine (Nardil®) selegiline (Emsam®) tranylcypromine (Parnate®)

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

Antidepressant Tier-2 Approval Criteria:

1. A documented, recent (within six months) trial of two Tier-1 medications at least four 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; or
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; or
3. A unique FDA-approved indication not covered by Tier-1 products or other products from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique member-specific situation exists.

Antidepressant Tier-3 Approval Criteria:

1. A documented, recent (within six months) trial with two Tier-1 medications (one from each category), and a Tier-2 medication at least four weeks in duration and titrated to recommended dose, that did not provide an adequate response; or
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; or
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique member-specific situation exists.

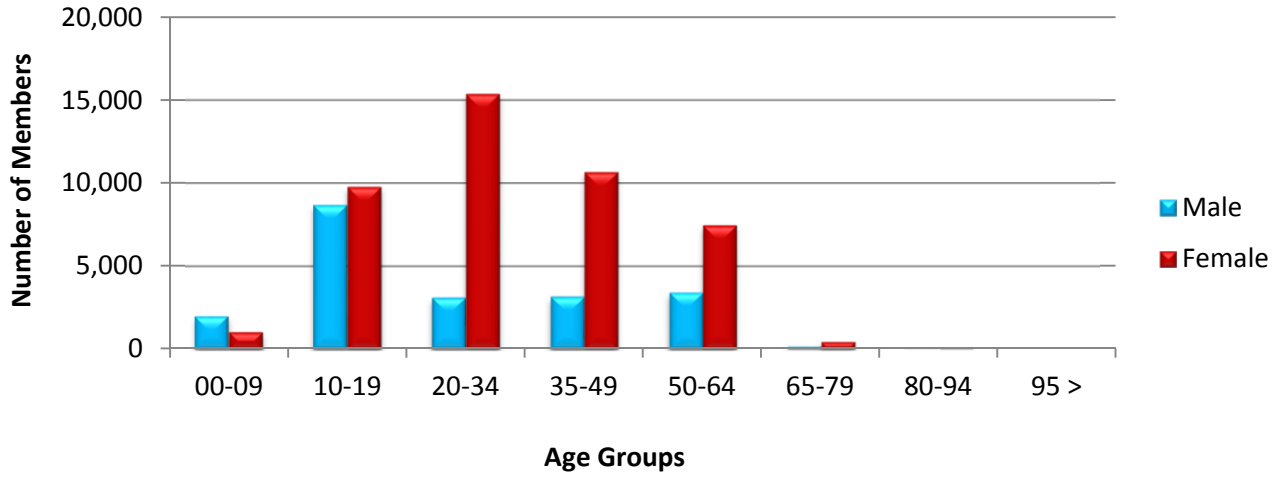
Utilization of Antidepressants

Comparison of Fiscal Years

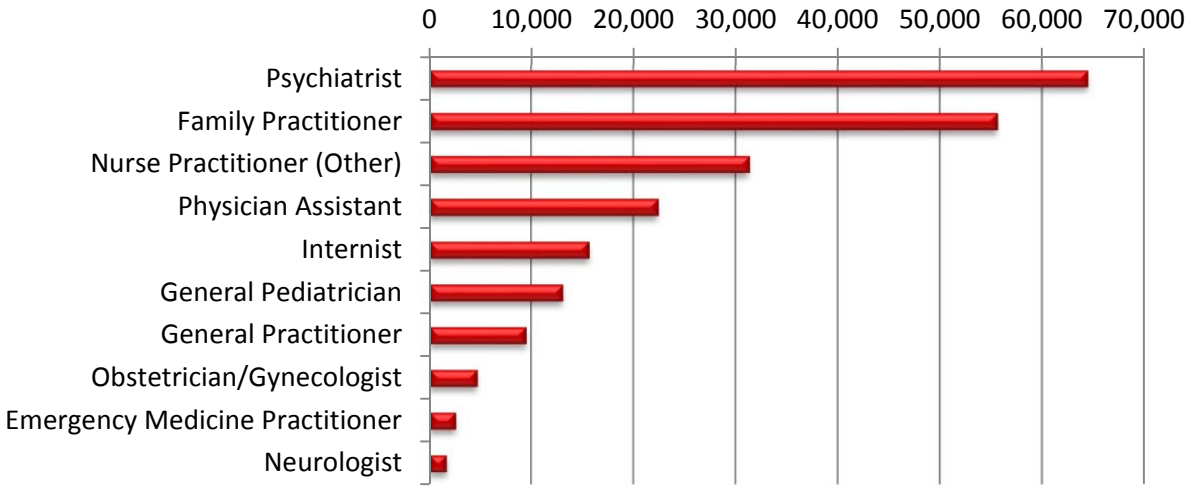
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	67,994	364,188	$9,275,845.72	$25.47	$0.78	14,081,181	11,962,241
2014	69,663	378,393	$8,927,947.01	$23.59	$0.72	14,544,725	12,411,558
% Change	**2.50%**	**3.90%**	**-3.80%**	**-7.40%**	**-7.70%**	**3.30%**	**3.80%**
Change	**1,669**	**14,205**	**-$347,898.71**	**-$1.88**	**-$0.06**	**463,544**	**449,317**

*Total number of unduplicated members.

Demographics of Members Utilizing Antidepressants



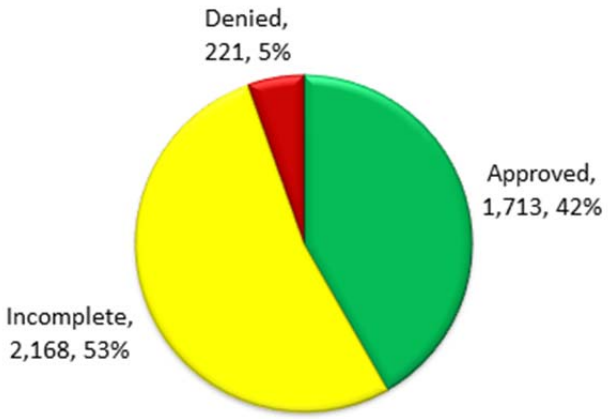
Top Prescriber Specialties of Antidepressants by Number of Claims



Prior Authorization of Antidepressants

There was a total of 4,102 petitions submitted for the antidepressant category during fiscal year 2014. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,2,3]

Anticipated Patent Expirations:

- Emsam® (selegiline transdermal patches)- 6/2018
- Viibryd® (vilazodone tablets)- 6/2022
- Pexeva® (paroxetine mesylate tablets)- 2/2023
- Aplenzin® (bupropion hydrobromide ER tablets)- 6/2026
- Pristiq® (desvenlafaxine ER tablets)- 7/2027
- Oleptro® (trazodone ER tablets)- 3/2029

New FDA Approvals:

- In July 2013, the FDA approved two new antidepressants, Khedezla® (desvenlafaxine ER tablets) and Fetzima® (levomilnacipran ER capsules), both of which are selective serotonin and norepinephrine reuptake inhibitors (SNRIs).
- In September 2013, the FDA approved Brintellix® (vortioxetine tablets), which has a unique mechanism of action different from other currently available antidepressants.

Khedezla® (Desvenlafaxine Extended-Release Tablets) Summary[4,5]

- **Indications:** Khedezla® (desvenlafaxine) is indicated for the treatment of major depressive disorder. Khedezla® is approved for use in adult patients.

- **Dosing:**
  - Khedezla® is available as 50mg and 100mg oral, extended-release tablets.
  - The recommended dose for Khedezla® is 50mg once daily, with or without food.
  - The maximum recommended dose in patients with moderate renal impairment or moderate to severe hepatic impairment is 50mg per day. The maximum recommended dose in patients with severe renal impairment or end stage renal disease is 50mg every other day.
  - Khedezla® should be taken at approximately the same time each day, and tablets must be swallowed whole with fluid and not divided, crushed, chewed, or dissolved.
  - When discontinuing therapy, gradual dose reduction is recommended whenever possible to minimize discontinuation symptoms.

- **Mechanism of Action:** Khedezla® (desvenlafaxine) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI). Desvenlafaxine is the major active metabolite of the antidepressant venlafaxine.

- **Contraindications:**
  - The concurrent use of MAOIs with Khedezla®, use of an MAOI within seven days of stopping treatment of Khedezla®, or use of Khedezla® within fourteen days of stopping an MAOI
  - Starting Khedezla® in a patient who is being treated with an MAOI, including linezolid or intravenous methylene blue
  - Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride, or to any of the excipients contained in Khedezla®

- **Efficacy:**
  - The efficacy of Khedezla® as a treatment for depression was established in four 8-week, randomized, double-blind, placebo-controlled, fixed-dose studies (at doses of 50mg to 400mg per day) in adult outpatients who met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive disorder.
  - Khedezla® showed superiority over placebo as measured by improvement in the 17-item Hamilton Rating Scale for Depression (HAM-D_{17}) total score in four studies and overall improvement, as measurement by the Clinical Global Impressions Scale – Improvement (CGI-I), in three of the four studies.

- In clinical studies, doses of 50mg to 400mg per day were shown to be effective, although no additional benefit was demonstrated at doses greater than 50mg per day and adverse reactions and discontinuations were more frequent at higher doses.

- **Safety:**
  - Khedezla® has a black box warning for an increased risk of suicidal thoughts and behaviors.
  - Khedezla® has a risk of potentially life-threatening serotonin syndrome, when taken alone or concomitantly with other serotonergic drugs and with drugs that impair the metabolism of serotonin.
  - Cases of seizure have been reported in pre-marketing clinical studies with Khedezla®. Patients with a history of seizures were excluded from pre-marketing studies. Khedezla® should be prescribed with caution in patients with a seizure disorder.
  - The most common adverse reactions leading to discontinuation of Khedezla® were nausea, vomiting, dizziness, and headache. Other common adverse reactions include insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders.

Fetzima® (Levomilnacipran Extended-Release Capsules) Summary[6,7]

- **Indications:** Fetzima® (levomilnacipran) is indicated for the treatment of major depressive disorder. Fetzima® is approved for use in adult patients.

- **Dosing:**
  - Fetzima® is available as 20mg, 40mg, 80mg, and 120mg oral, extended-release capsules.
  - The recommended dose range for Fetzima® is 40mg to 120mg once daily, with or without food.
  - Fetzima® should be initiated at 20mg once daily for two days then increased to 40mg once daily. Based on efficacy and tolerability, Fetzima® may then be increased in increments of 40mg at intervals of two or more days. The maximum recommended dose is 120mg once daily.
  - For patients with moderate renal impairment, the maintenance dose should not exceed 80mg once daily. For patients with severe renal impairment, the maintenance dose should not exceed 40mg once daily. Fetzima® is not recommended for patients with end stage renal disease.
  - Fetzima® should be taken at approximately the same time each day and should be swallowed whole. Do not open, chew, or crush the capsule.
  - When discontinuing therapy, gradual dose reduction is recommended whenever possible to minimize discontinuation symptoms.

- **Mechanism of Action:** Fetzima® (levomilnacipran) is a selective serotonin and norepinephrine reuptake inhibitor (SNRI). Levomilnacipran is the 1S,2R-enantiomer of Savella® (milnacipran), which is indicated for the treatment of fibromyalgia. Fetzima® is not indicated for the treatment of fibromyalgia.

- **Contraindications:**
  - The concurrent use of MAOIs with Fetzima®, use of an MAOI within seven days of stopping treatment of Fetzima®, or use of Fetzima® within fourteen days of stopping an MAOI
  - Starting Fetzima® in a patient who is being treated with an MAOI, including linezolid or intravenous methylene blue
  - Hypersensitivity to levomilnacipran, milnacipran hydrochloride, or to any of the excipients contained in Fetzima®

- **Efficacy:**
  - The efficacy of Fetzima® for the treatment of major depressive disorder was established in three 8-week randomized, double-blind, placebo-controlled studies (at doses of 40mg to 120mg once daily) in adult outpatients who met the DMV-IV criteria for major depressive disorder.
  - In all three studies, Fetzima® demonstrated superiority over placebo in the improvement of depression symptoms as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) total score. Fetzima® also demonstrated superiority over placebo as measured by improvement in the Sheehan Disability Scale (SDS) functional impairment total score.

- **Safety:**
  - Fetzima® has a black box warning for an increased risk of suicidal thoughts and behaviors.
  - Fetzima® has a risk of potentially life-threatening serotonin syndrome, when taken alone or concomitantly with other serotonergic drugs and with drugs that impair the metabolism of serotonin.
  - The most common adverse reaction leading to discontinuation of Fetzima® was nausea. Other common adverse reactions include constipation, hyperhidrosis, increased heart rate, erectile dysfunction, tachycardia, vomiting, and palpitations.

Brintellix® (Vortioxetine Tablets) Summary[8,9]

- **Indications:** Brintellix® (vortioxetine) is indicated for the treatment of major depressive disorder. Brintellix® is approved for use in adult patients.

- **Dosing:**
  - Brintellix® is available as 5mg, 10mg, 15mg, and 20mg oral, immediate-release, film-coated tablets.
  - The recommended starting dose for Brintellix® is 10mg once daily, without regard to meals. Dosage should then be increased to 20mg per day, as tolerated.
  - No dose adjustment of Brintellix® on the basis of renal function is necessary. No dose adjustment of Brintellix® in patients with mild to moderate hepatic impairment is necessary; however, Brintellix® has not been studied and is therefore not recommended in patients with severe hepatic impairment.
  - When discontinuing therapy, gradual dose reduction is recommended whenever possible to minimize discontinuation symptoms.

- **Mechanism of Action:** The mechanism of action of Brintellix® is not fully understood, but is thought to be related to its enhancement of serotonergic activity in the CNS through inhibition of the reuptake of serotonin (5-HT).

- **Contraindications:**
  - The concurrent use of MAOIs with Brintellix®, use of an MAOI within 21 days of stopping treatment of Brintellix®, or use of Brintellix® within 14 days of stopping an MAOI
  - Starting Brintellix® in a patient who is being treated with an MAOI, including linezolid or intravenous methylene blue
  - Hypersensitivity to vortioxetine or to any of the excipients contained in Brintellix®

- **Efficacy:**
  - The efficacy of Brintellix® as a treatment for major depressive disorder in patients aged 18 years to 75 years was demonstrated in five 6 to 8 week, randomized, double-blind, placebo-controlled, fixed-dose studies (at doses of 5mg to 20mg once daily) in adult inpatients and outpatients who met the DSM-IV criteria for major depressive disorder.
  - The efficacy of Brintellix® as a treatment for major depressive disorder in patients aged 64 years to 88 years was demonstrated in a randomized, double-blind, placebo-controlled, fixed-dose study in elderly patients with major depressive disorder. Patients meeting the diagnostic criteria for recurrent major depressive disorder with at least one previous major depressive episode before the age of 60 years and without comorbid cognitive impairment received Brintellix® 5mg or placebo.
  - The primary efficacy measures were the Hamilton Depression Scale (HAMD-24) total score in one study and the Montgomery-Asberg Depression Rating Scale (MADRS) total score in all other studies. In each of these studies, at least one dose group of Brintellix® was superior to placebo in improvement of depressive symptoms as measured by mean change from baseline to endpoint visit on the primary efficacy measurement. Two studies of the 5mg dose failed to show effectiveness.

- **Safety:**
  - Brintellix® has a black box warning for an increased risk of suicidal thoughts and behaviors, and for clinical worsening of depression.
  - Brintellix® has a risk of potentially life-threatening serotonin syndrome, when taken alone or concomitantly with other serotonergic drugs and with drugs that impair the metabolism of serotonin.
  - The most common adverse reaction leading to discontinuation of Brintellix® was nausea. Other common adverse reactions include constipation, vomiting, diarrhea, dry mouth, flatulence, dizziness, abnormal dreams, sexual dysfunction, and pruritus.

Cost Comparison

MEDICATION NAME	STRENGTH	COST/ UNIT	COST/ MONTH	COST/ YEAR
Khedezla® (desvenlafaxine)	50mg	$4.70-$11.70+	$141.00 - $351.00	$1,692.00 - $4,212.00
Fetzima® (levomilnacipran)	120mg	$7.13+	$213.90	$2,566.80
Brintellix® (vortioxetine)	20mg	$8.44+	$253.20	$3,038.40
sertraline	100mg	$0.11*	$3.30	$39.60
fluoxetine	20mg	$0.08*	$2.40	$28.80
bupropion XL	150mg	$1.15*	$34.50	$414.00
duloxetine	60mg	$1.33*	$39.90	$478.80

*State Maximum Allowable Cost (SMAC)
+Estimated Acquisition Cost (EAC)

Recommendations

The College of Pharmacy recommends the following changes and additions to the Antidepressants Product Based Prior Authorization (PBPA) category:

1. Place Khedezla®, Fetzima®, and Brintellix® into Tier-3.
2. Move duloxetine to Tier-1 based on generic availability and State Maximum Allowable Cost (SMAC).
3. Change the approval criteria for Tier-2 medications to include a required trial of duloxetine as one of the Tier-1 trials.
4. Create a Special PA category to include special dosage forms that are similar to currently available, cost-effective Tier-1 products. This category would include the following:
    a. fluoxetine 60mg tablets, Prozac Weekly®, Luvox CR®, Paxil CR®, Pexeva®, Aplenzin®, Forfivo XL®, Oleptro®, and venlafaxine ER tablets.
    b. Medications in the special PA category require a member-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications.
5. Tier-2 will include supplemental rebated products. If no products rebate to Tier-2, then Tier-2 will include the lowest cost Tier-3 product(s).

Antidepressants			
Tier-1	**Tier-2***	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			**fluoxetine 60mg tablets**
escitalopram (Lexapro®)			**fluoxetine DR (Prozac® Weekly™)**
fluoxetine (Prozac®, Sarafem®)			**fluvoxamine CR (Luvox CR®)**
fluvoxamine (Luvox®)			**paroxetine CR (Paxil CR®)**
paroxetine (Paxil®)			**paroxetine (Pexeva®)**
sertraline (Zoloft®)			
Dual Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)		**desvenlafaxine (Khedezla®)**	**bupropion ER (Aplenzin®)**
duloxetine (Cymbalta®)		desvenlafaxine (Pristiq®)	**bupropion ER (Forfivo XL®)**
mirtazapine (Remeron®, Remeron® SolTab™)		**levomilnacipran (Fetzima®)**	**trazodone ER (Oleptro®)**
trazodone (Desyrel®)		nefazodone (Serzone®)	**venlafaxine ER tablets**
venlafaxine (Effexor®, Effexor XR® capsules)		vilazodone (Viibryd®)	
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Brintellix®)	

*Tier-2 will include supplemental rebated products. If no products rebate to Tier-2, Tier-2 will include the lowest cost Tier-3 product(s).

Antidepressants Tier-2 Approval Criteria:

1. A documented, recent (within six months) trial of two Tier-1 medications at least four 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 (must include one trial with duloxetine); or
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; or
3. A unique FDA-approved indication not covered by Tier-1 products or other products from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique member-specific situation exists.

Antidepressants Tier-3 Approval Criteria:

1. A documented, recent (within six months) trial with two Tier-1 medications (one from each category, must include one trial with duloxetine) and a Tier-2 medication at least four weeks in duration and titrated to recommended dose, that did not provide an adequate response; or
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; or
3. A unique FDA-approved indication not covered by a lowered tiered product or other products from a different therapeutic class; or
4. A petition may be submitted for consideration whenever a unique member-specific situation exists.

Antidepressants Special PA Approval Criteria:

1. Use of any Special PA product will require a member-specific, clinically significant reason why the member cannot use other available generic Tier-1 products; or
2. A petition may be submitted for consideration whenever a unique member-specific situation exists.

Utilization Details of Antidepressants

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SERTRALINE PRODUCTS						
SERTRALINE TAB 100MG	30,780	7,125	$284,773.10	$0.28	$9.25	3.19%
SERTRALINE TAB 50MG	26,796	9,504	$216,176.31	$0.25	$8.07	2.42%
SERTRALINE TAB 25MG	10,730	3,912	$82,830.40	$0.25	$7.72	0.93%
SERTRALINE CON	379	111	$25,809.89	$2.19	$68.10	0.29%
ZOLOFT TAB 100MG	51	19	$5,425.33	$3.17	$106.38	0.06%
SUBTOTAL	**68,736**	**20,671**	**$615,015.03**	**$0.28**	**$8.95**	**6.89%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 20MG	30,253	9,611	$219,732.84	$0.22	$7.26	2.46%
FLUOXETINE CAP 40MG	13,145	3,600	$160,658.37	$0.35	$12.22	1.80%
FLUOXETINE CAP 10MG	10,353	3,648	$67,600.50	$0.21	$6.53	0.76%
FLUOXETINE TAB 10MG	2,966	1,062	$17,218.23	$0.19	$5.81	0.19%
FLUOXETINE SOL	1,030	247	$8,449.04	$0.28	$8.20	0.09%
FLUOXETINE TAB 20MG	1,007	474	$21,533.03	$0.68	$21.38	0.24%
PROZAC CAP 20MG	21	2	$11,327.33	$18.12	$539.40	0.13%
PROZAC CAP 40MG	12	1	$5,537.58	$15.38	$461.47	0.06%
SUBTOTAL	**58,787**	**18,645**	**$512,056.92**	**$0.27**	**$8.71**	**5.73%**
CITALOPRAM PRODUCTS						
CITALOPRAM TAB 20MG	28,883	10,003	$185,365.62	$0.19	$6.42	2.08%
CITALOPRAM TAB 40MG	18,887	5,036	$129,513.87	$0.19	$6.86	1.45%
CITALOPRAM TAB 10MG	9,164	3,082	$56,045.31	$0.19	$6.12	0.63%
CITALOPRAM SOL	241	60	$8,101.59	$1.18	$33.62	0.09%
CELEXA TAB 20MG	72	27	$502.92	$0.23	$6.99	0.01%
CELEXA TAB 40MG	12	1	$1,963.71	$5.45	$163.64	0.02%
CELEXA TAB 10MG	3	1	$435.03	$4.83	$145.01	0.00%
SUBTOTAL	**57,262**	**18,210**	**$381,928.05**	**$0.19**	**$6.67**	**4.28%**
TRAZODONE PRODUCTS						
TRAZODONE TAB 50MG	27,101	8,421	$173,115.33	$0.21	$6.39	1.94%
TRAZODONE TAB 100MG	21,468	5,971	$176,313.68	$0.26	$8.21	1.97%
TRAZODONE TAB 150MG	13,299	3,538	$135,348.44	$0.31	$10.18	1.52%
TRAZODONE TAB 300MG	709	181	$85,954.70	$3.43	$121.23	0.96%
SUBTOTAL	**62,577**	**18,111**	**$570,732.15**	**$0.29**	**$9.12**	**6.39%**
ESCITALOPRAM PRODUCTS						
ESCITALOPRAM TAB 20MG	11,990	2,986	$132,302.64	$0.33	$11.03	1.48%
ESCITALOPRAM TAB 10MG	10,889	3,852	$107,982.18	$0.30	$9.92	1.21%
ESCITALOPRAM TAB 5MG	620	254	$6,167.32	$0.31	$9.95	0.07%
ESCITALOPRAM SOL	97	23	$19,122.47	$6.85	$197.14	0.21%
LEXAPRO TAB 20MG	52	9	$11,484.69	$6.77	$220.86	0.13%
LEXAPRO TAB 10MG	26	7	$3,853.54	$4.94	$148.21	0.04%
LEXAPRO TAB 5MG	5	3	$352.67	$2.35	$70.53	0.00%
SUBTOTAL	**23,679**	**7,134**	**$281,265.51**	**$0.36**	**$11.88**	**3.15%**
MIRTAZAPINE PRODUCTS						
MIRTAZAPINE TAB 15MG	9,175	2,798	$94,443.77	$0.33	$10.29	1.06%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
MIRTAZAPINE TAB 30MG	6,926	2,063	$79,394.18	$0.36	$11.46	0.89%
MIRTAZAPINE TAB 45MG	2,583	616	$38,186.71	$0.44	$14.78	0.43%
MIRTAZAPINE TAB 7.5MG	256	92	$4,245.94	$0.58	$16.59	0.05%
MIRTAZAPINE TAB 15MG	225	85	$7,746.25	$1.13	$34.43	0.09%
MIRTAZAPINE TAB 30MG	184	55	$6,180.48	$1.03	$33.59	0.07%
MIRTAZAPINE TAB 45MG	48	16	$1,715.93	$1.14	$35.75	0.02%
REMERON SLTB TAB 30MG	1	1	$36.29	$1.21	$36.29	0.00%
SUBTOTAL	**19,398**	**5,726**	**$231,949.55**	**$0.38**	**$11.96**	**2.60%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE CAP 150MG	8,475	2,140	$109,432.12	$0.38	$12.91	1.23%
VENLAFAXINE CAP 75MG	6,222	2,475	$76,339.97	$0.37	$12.27	0.85%
VENLAFAXINE TAB 75MG	3,134	962	$70,893.06	$0.72	$22.62	0.79%
VENLAFAXINE CAP 37.5 ER	1,739	1,017	$20,565.41	$0.38	$11.83	0.23%
VENLAFAXINE TAB 37.5MG	1,105	524	$24,007.71	$0.70	$21.73	0.27%
VENLAFAXINE TAB 100MG	606	139	$17,831.34	$0.96	$29.42	0.20%
VENLAFAXINE TAB 50MG	289	91	$7,293.90	$0.82	$25.24	0.08%
VENLAFAXINE TAB 25MG	156	56	$4,163.35	$0.81	$26.69	0.05%
EFFEXOR XR CAP 75MG	37	5	$14,036.27	$10.88	$379.36	0.16%
EFFEXOR XR CAP 150MG	19	6	$9,943.88	$8.50	$523.36	0.11%
EFFEXOR XR CAP 37.5MG	12	8	$131.31	$0.41	$10.94	0.00%
SUBTOTAL	**21,794**	**7,423**	**$354,638.32**	**$0.49**	**$16.27**	**3.97%**
BUPROPION PRODUCTS						
BUPROPION TAB 150MG	8,078	2,666	$156,955.13	$0.62	$19.43	1.76%
BUPROPN HCL TAB 150MG	6,099	2,245	$134,876.81	$0.66	$22.11	1.51%
BUPROPN HCL TAB 300MG	5,803	1,422	$149,066.80	$0.73	$25.69	1.67%
BUPROPION TAB 100MG	1,730	663	$74,752.56	$1.37	$43.21	0.84%
BUPROPION TAB 100MG	1,705	634	$30,857.49	$0.59	$18.10	0.35%
BUPROPION TAB 75MG	1,661	685	$50,869.00	$1.03	$30.63	0.57%
BUPROPION TAB 200MG	1,139	295	$31,442.65	$0.88	$27.61	0.35%
BUPROPION TAB 100MG	77	34	$1,357.14	$0.58	$17.63	0.02%
BUPROPION TAB 150MG	74	44	$1,391.06	$0.58	$18.80	0.02%
BUDEPRION TAB 150MG	56	16	$1,401.63	$0.60	$25.03	0.02%
WELLBUTRIN TAB XL	23	4	$13,768.11	$20.25	$598.61	0.15%
BUDEPRION TAB 100MG	15	7	$315.92	$0.61	$21.06	0.00%
WELLBUTRIN TAB XL	10	1	$4,463.49	$14.88	$446.35	0.05%
BUPROPION TAB 200MG	9	7	$251.65	$0.93	$27.96	0.00%
WELLBUTRIN TAB 150MG	3	2	$277.63	$3.08	$92.54	0.00%
BUDEPRION XL TAB	2	2	$48.16	$0.80	$24.08	0.00%
SUBTOTAL	**26,484**	**8,727**	**$652,095.23**	**$0.76**	**$24.62**	**7.30%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 20MG	6,985	2,683	$59,450.97	$0.24	$8.51	0.67%
PAROXETINE TAB 40MG	5,028	1,269	$61,180.58	$0.34	$12.17	0.69%
PAROXETINE TAB 10MG	2,357	1,008	$19,729.68	$0.25	$8.37	0.22%
PAROXETINE TAB 30MG	1,758	473	$19,892.55	$0.33	$11.32	0.22%
PAROXETINE TAB 25MG	520	138	$47,342.76	$2.66	$91.04	0.53%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
PAROXETIN ER TAB	267	56	$26,366.33	$2.89	$98.75	0.30%
PAROXETIN ER TAB	180	76	$17,862.79	$2.82	$99.24	0.20%
PAXIL SUS 10MG/5ML	50	14	$8,815.68	$6.01	$176.31	0.10%
PAXIL CR TAB 37.5MG	7	1	$1,059.02	$5.04	$151.29	0.01%
PAXIL TAB 40MG	5	1	$2,364.82	$5.26	$472.96	0.03%
SUBTOTAL	**17,157**	**5,719**	**$264,065.18**	**$0.44**	**$15.39**	**2.96%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE TAB	1,384	229	$31,568.70	$0.74	$22.81	0.35%
FLUVOXAMINE TAB 50MG	936	239	$17,102.42	$0.60	$18.27	0.19%
FLUVOXAMINE TAB 25MG	336	88	$5,029.03	$0.49	$14.97	0.06%
SUBTOTAL	**2,656**	**556**	**$53,700.15**	**$0.66**	**$20.22**	**0.60%**
TIER-1 SUBTOTAL	**358,491**	**68,288***	**$3,917,446.09**	**$0.33**	**$10.93**	**43.87%**
DULOXETINE PRODUCTS						
CYMBALTA CAP 60MG	6,571	1,959	$1,896,273.91	$8.48	$288.58	21.24%
DULOXETINE CAP 60MG	5,966	1,835	$1,345,240.35	$6.51	$225.48	15.07%
CYMBALTA CAP 30MG	2,006	744	$633,898.09	$9.74	$316.00	7.10%
DULOXETINE CAP 30MG	1,894	750	$446,180.86	$7.28	$235.58	5.00%
CYMBALTA CAP 20MG	247	91	$71,087.64	$9.17	$287.80	0.80%
DULOXETINE CAP 20MG	198	77	$43,091.93	$6.95	$217.64	0.48%
SUBTOTAL	**16,882**	**5,456**	**$4,435,772.78**	**$7.78**	**$262.75**	**49.68%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE TAB 225MG	615	164	$106,541.12	$4.76	$173.24	1.19%
VENLAFAXINE TAB 150MG	302	92	$27,709.21	$2.93	$91.75	0.31%
VENLAFAXINE TAB 75MG	182	60	$13,520.00	$2.37	$74.29	0.15%
VENLAFAXINE TAB 37.5 ER	57	21	$5,695.88	$3.08	$99.93	0.06%
SUBTOTAL	**1,156**	**337**	**$153,466.21**	**$3.89**	**$132.76**	**1.72%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE CAP	85	18	$31,013.80	$12.26	$364.87	0.35%
FLUVOXAMINE CAP	79	23	$28,629.89	$10.98	$362.40	0.32%
FLUOXETINE CAP 90MG	58	6	$7,591.18	$4.67	$130.88	0.09%
LUVOX CR CAP 150MG	35	12	$23,439.19	$22.45	$669.69	0.26%
LUVOX CR CAP 100MG	17	7	$9,273.61	$16.27	$545.51	0.10%
SUBTOTAL	**274**	**66**	**$99,947.67**	**$11.93**	**$364.77**	**1.12%**
PAROXETINE PRODUCTS						
PEXEVA TAB 20MG	5	2	$1,663.82	$8.00	$332.76	0.02%
SUBTOTAL	**5**	**2**	**$1,663.82**	**$8.00**	**$332.76**	**0.02%**
TIER-2 SUBTOTAL	**18,317**	**3,471***	**$4,690,850.48**	**$7.59**	**$256.09**	**52.53%**
DESVENLAFAXINE PRODUCTS						
PRISTIQ TAB 50MG	470	114	$111,498.98	$6.45	$237.23	1.25%
PRISTIQ TAB 100MG	462	91	$105,904.30	$6.61	$229.23	1.19%
DESVENLAFAX TAB 50MG	9	1	$1,124.79	$5.07	$124.98	0.01%
SUBTOTAL	**941**	**206**	**$218,528.07**	**$6.52**	**$232.23**	**2.45%**
VILAZODONE PRODUCTS						
VIIBRYD TAB 40MG	436	104	$69,160.32	$5.33	$158.62	0.77%
VIIBRYD TAB 20MG	56	12	$9,543.46	$5.49	$170.42	0.11%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
VIIBRYD TAB 10MG	18	6	$6,125.36	$11.34	$340.30	0.07%
VIIBRYD KIT	8	8	$1,268.72	$5.29	$158.59	0.01%
SUBTOTAL	**518**	**130**	**$86,097.86**	**$5.56**	**$166.21**	**0.96%**
LEVOMILNACIPRAN PRODUCTS						
FETZIMA CAP 40MG	27	16	$5,620.56	$6.94	$208.17	0.06%
FETZIMA CAP 80MG	16	7	$3,262.10	$6.80	$203.88	0.04%
FETZIMA CAP 20MG	1	1	$214.36	$7.15	$214.36	0.00%
FETZIMA CAP 120MG	1	1	$214.36	$7.15	$214.36	0.00%
SUBTOTAL	**45**	**25**	**$9,311.38**	**$6.90**	**$206.92**	**0.10%**
FLUOXETINE PRODUCTS						
FLUOXETINE TAB 60MG	22	5	$1,998.46	$3.03	$90.84	0.02%
SUBTOTAL	**22**	**5**	**$1,998.46**	**$3.03**	**$90.84**	**0.02%**
NEFAZODONE PRODUCTS						
NEFAZODONE TAB 250MG	18	2	$587.99	$0.85	$32.67	0.01%
NEFAZODONE TAB 100MG	16	3	$477.19	$0.99	$29.82	0.01%
NEFAZODONE TAB 200MG	14	3	$613.56	$0.91	$43.83	0.01%
NEFAZODONE TAB 50MG	8	1	$235.56	$0.98	$29.45	0.00%
NEFAZODONE TAB 150MG	1	1	$20.29	$0.68	$20.29	0.00%
SUBTOTAL	**57**	**10**	**$1,934.59**	**$0.92**	**$33.94**	**0.02%**
VORTIOXETINE PRODUCTS						
BRINTELLIX TAB 10MG	5	4	$1,154.15	$7.69	$230.83	0.02%
BRINTELLIX TAB 20MG	2	2	$461.66	$7.69	$230.83	0.00%
SUBTOTAL	**7**	**6**	**$1,615.81**	**$7.69**	**$230.83**	**0.02%**
SELEGILINE PRODUCTS						
EMSAM DIS 12MG/24H	2	1	$1,780.08	$29.67	$890.04	0.02%
SUBTOTAL	**2**	**1**	**$1,780.08**	**$29.67**	**$890.04**	0.02%
TIER-3 SUBTOTAL	**1,592**	**332***	**$321,266.25**	**$6.02**	**$201.80**	**3.60%**
TOTAL	**378,400**	**69,663***	**$8,929,562.82**	**$0.72**	**$23.60**	**100.00%**

*Total number of unduplicated members.

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[6] Fetzima® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/fetzima/. Last revised 7/21/14. Last accessed 9/26/14.

[7] Fetzima® Prescribing Information, Forest Laboratories, Inc. Available online at: http://www.frx.com/pi/fetzima_pi.pdf. Last revised 7/2014. Last accessed 9/26/14.

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[9] Brintellix® Prescribing Information, Drugs@FDA. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204447s000lbl.pdf. Last revised 9/2013. Last accessed 9/26/14.

Appendix G

Fiscal Year 2014 Annual Review of Biologic Products for the Treatment of Rheumatoid Arthritis, Plaque Psoriasis, and Ankylosing Spondylitis and 30-Day Notice to Prior Authorize Otezla® (Apremilast) and Entyvio™ (Vedolizumab)

Oklahoma Health Care Authority
October 2014

Current Prior Authorization Criteria

Biologic Products		
Tier-1 (DMARDs appropriate to disease state)	**Tier-2***	**Tier-3+**
Methotrexate	Adalimumab (Humira®)	Abatacept (Orencia®)
Hydroxychloroquine	Certolizumab pegol (Cimzia®)	Alefacept (Amevive®)
Sulfasalazine	Etanercept (Enbrel®)	Anakinra (Kineret®)
Minocycline		Golimumab (Simponi®)
Oral Corticosteroids		Infliximab (Remicade®)
Leflunomide		Rituximab (Rituxan®)
Mesalamine		Tocilizumab (Actemra®)
6-Mercaptopurine		Tofacitinib (Xeljanz®)
Azathioprine		Ustekinumab (Stelara®)
NSAIDs		

Tier structure based on supplemental rebate participation.
DMARDs= Disease modifying antirheumatic drugs
*Supplemental rebated products
+ May be rebated to Tier-2 status only

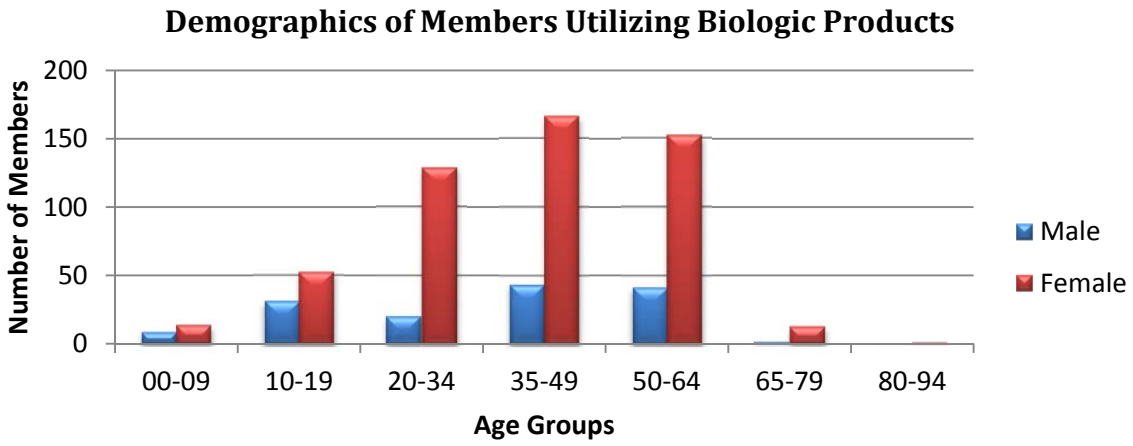
Current tier trial requirements can be found in the recommendations section at the end of this report.

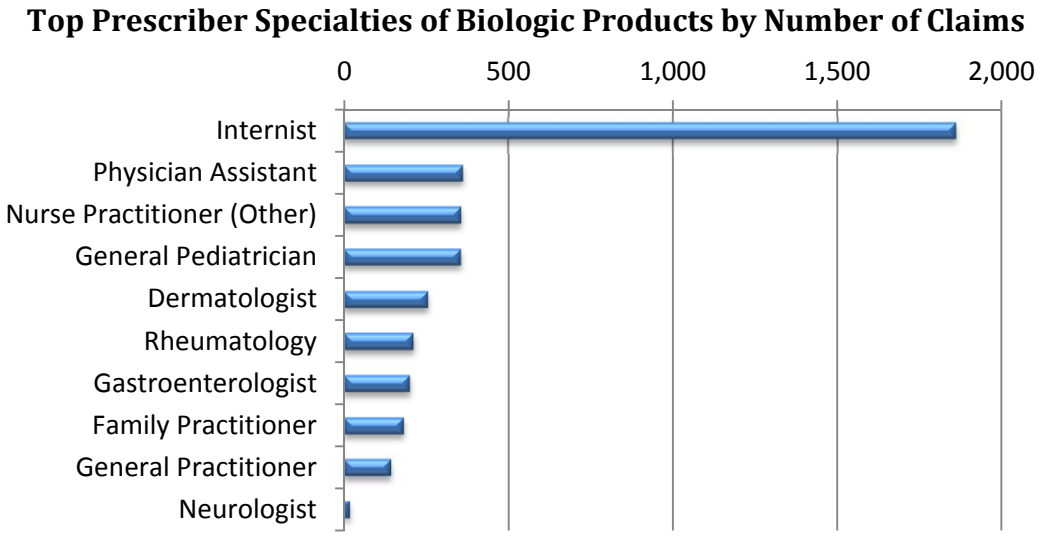
Utilization of Biologic Products

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	595	3,448	$9,473,643.76	$2,747.58	$93.23	23,438	101,616
2014	685	4,001	$12,901,295.07	$3,224.52	$107.93	26,679	119,536
% Change	**15.13%**	**16.04%**	**36.18%**	**17.36%**	**15.77%**	**13.83%**	**17.64%**
Change	**90**	**553**	**$3,427,651.31**	**$476.94**	**$14.70**	**3,241**	**17,920**

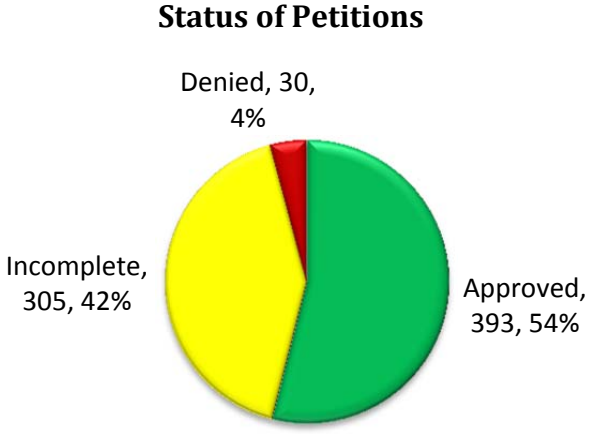
*Total number of unduplicated members.





Prior Authorization of Biologic Products

There was a total of 728 petitions submitted for a total of 407 unique members for biologic products during fiscal year 2014. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



Market News and Updates[1, 2, 3, 4, 5, 6,7]

Anticipated Patent Expirations:

- Rituxan® (rituximab)-09/2016
- Humira® (adalimumab)- 12/2016
- Remicade® (infliximab)-09/2018
- Enbrel® (etanercept)- 12/2028

New Medications/Indications:

- **09/2013:** The FDA granted a new indication for Cimzia® (certolizumab) for the treatment of adult patients with active psoriatic arthritis (PsA). PsA is a form of arthritis that affects some people with psoriasis (Ps). Most people develop Ps first and are later diagnosed with PsA. Joint pain, stiffness and swelling are the main signs and symptoms of PsA. Currently approved treatments for PsA include corticosteroids, tumor necrosis factor (TNF) blockers, and an interleukin-12/interleukin-23 inhibitor. In addition to its approval for PsA, Cimzia® is approved for reducing the signs and symptoms of Crohn's disease, treatment of adult patients with rheumatoid arthritis (RA), and anklylosing spondylitis.
- **09/2013:** The FDA granted a new indication for Stelara® (ustekinumab) for the treatment of moderate-to-severe PsA in adult patients. In addition to its approval for PsA, Stelara® is approved for the treatment of adult patients with moderate-to-severe plaque Ps.
- **03/2014:** The FDA approved Otezla® (apremilast) to treat adults with active PsA.
- **05/2014:** The FDA approved Entyvio™ (vedolizumab) injection to treat adult patients with moderate-to-severe ulcerative colitis (UC) and adult patients with moderate-to-severe Crohn's disease (CD). Entyvio™ is approved to treat those conditions when one or more standard therapies (corticosteroids, immunomodulators, or tumor necrosis factor blocker medications) have not resulted in an adequate response.
- **07/2014:** Janssen Biotech, Inc. announced the FDA approval of Simponi® Aria™ (golimumab) for infusion for the treatment of adults with moderately-to-severely active RA in combination with methotrexate. Simponi® Aria™ is the only fully-human anti-tumor necrosis factor (TNF)-alpha infusible therapy and was previously approved as a subcutaneous injection in patients with moderate-to-severe RA.
- **09/2014:** The FDA granted a new indication for Otezla® (apremilast) for the treatment of patients with moderate-to-severe Ps who are candidates for phototherapy or systemic therapy. Otezla® is the first and only selective inhibitor of phosphodiesterase-4 (PDE-4) approved to treat plaque Ps.

Otezla® (Apremilast)[8] Summary

FDA Approved: March 2014

Indications: Otezla® (apremilast) is indicated for the treatment of adult patients with active PsA and patients with moderate-to-severe Ps who are who are candidates for phototherapy or systemic therapy.

Dosing:

- Otezla® is available as 10mg, 20mg, and 30mg oral tablets.
- The recommended starting dose of Otezla® is 10mg orally once daily. The dose should be titrated over five days to reduce gastrointestinal symptoms associated with initial therapy. Following the five day titration, the recommended maintenance dosage is 30mg by mouth twice daily.
- Otezla® can be administered without regard to meals.
- Otezla® tablets should not be crushed, split, or chewed.

Mechanism of Action: Otezla® is a small-molecule inhibitor of phosphodiesterase-4 (PDE-4) specific for cyclic adenosine monophosphate (cAMP). PDE-4 inhibition results in increased intracellular cAMP levels. The specific mechanism by which Otezla® exerts its therapeutic action in PsA and Ps patients is not well defined.

Efficacy: The safety and efficacy of Otezla® for the treatment of PsA was evaluated in three multi-center, randomized, double-blind, placebo-controlled trials of similar design. A total of 1,493 adult patients with active PsA (≥3 swollen joints and ≥3 tender joints) despite prior or current treatment with DMARD therapy were randomized. Previous treatment with a biologic was allowed. Patients were randomly assigned to placebo, Otezla® 20mg, or Otezla® 30mg given orally twice daily. Patients were allowed to receive stable doses of concomitant methotrexate, sulfasalazine, lefluonomide, low dose oral corticosteroids, and/or nonsteroidal anti-inflammatory drugs (NSAIDs) during the trial. The primary endpoint was the percentage of patients achieving American College of Rheumatology (ACR) 20 response at Week 16. Patients whose tender and swollen joint counts had not improved by at least 20% were considered non-responders at Week 16. The percent of patients achieving ACR 20, 50, and 70 responses in Studies 1, 2, and 3 are presented in the table below. Otezla®, compared with Placebo resulted in a greater improvement in signs and symptoms of PsA as demonstrated by the proportion of patients with an ACR 20 response at Week 16.

	Study 1		Study 2		Study 3	
	Placebo	Otezla®	Placebo	Otezla®	Placebo	Otezla®
ACR 20	19%	38%	19%	32%	18%	41%
ACR 50	6%	16%	5%	11%	8%	15%
ACR 70	1%	4%	1%	1%	2%	4%

Utilization/Cost:

- Otezla® has not been utilized in the SoonerCare population since its approval in March 2014.

Medication	EAC Per mL or Tablet	EAC Per Day or Week	EAC for 28 Days of Therapy
Otezla® Oral Tablet 30mg	$33.00	$66.00	$1,848.00
Methotrexate Oral Tablet 2.5mg	$2.13 +	$25.56*	$102.24
Humira® SQ Pen 40mg	$1,425.77	$1,425.77	$5,703.08

EAC= estimated acquisition cost
+ State maximum allowable cost (SMAC) pricing
*Dosing based on weekly total.
Dosing based on recommended target dose of methotrexate 30mg per week.

Entyvio™ (Vedolizumab)[9] Summary

FDA Approved: May 2014

Indications: Entyvio™ (vedolizumab) is indicated for the treatment of adult patients with moderately-to-severely active UC or CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

Dosing:

- Entyvio™ is available for injection in a single-use 20mL vial containing 300mg of lyophilized Entyvio™ powder. Unopened vials should be refrigerated at 2° to 8°C (36° to 46°F) and retained in the original package to protect from light.
- The recommended dosage of Entyvio™ for both UC and CD is 300mg infused intravenously (IV) over approximately 30 minutes at initiation, two and six weeks, then eight weeks thereafter.
- Entyvio™ should be reconstituted with sterile water for injection and must be diluted in 250mL of sterile 0.9% sodium chloride prior to administration. Administer infusion solution within four hours of reconstitution and dilution.
- Entyvio™ should be administered by a healthcare professional prepared to manage hypersensitivity reactions including anaphylaxis, if they occur. Appropriate monitoring and medical support measures should be available for immediate use. Patients should be observed during infusion and until the infusion is complete.
- Entyvio™ should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.
- Bring patients up-to-date with all immunizations before initiating treatment with Entyvio™.

Mechanism of Action: Entyvio™ is a humanized monoclonal antibody that binds to the α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal addressin cell adhesion molecule-1 (MAdCAM-1) and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. The interaction of the α4β7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation of UC and CD.

Efficacy: The safety and efficacy of Entyvio™ for UC and CD were evaluated in a randomized, double-blind, placebo controlled trials in adult patients with moderately-to-severely active UC or CD. Patients were randomized to Entyvio™ 300mg or placebo. Efficacy assessments were at week six. Concomitant stable dosages of aminosalicylates, corticosteroids, and immunomodulators (azathioprine or 6-mercaptopurine) were permitted through Week 6.

- **UC:** A greater percentage of patients treated with Entyvio™ compared to patients treated with placebo achieved clinical response at week six (26% Placebo vs 47% Entyvio™ $p<0.001$). In addition, a greater percentage of patients treated with Entyvio™ had improvement of endoscopic appearance of the mucosa at week six.
- **CD:** A statistically significantly higher percentage of patients treated with Entyvio™ achieved clinical remission compared to placebo at week six (7% Placebo vs 15% Entyvio™ $p<0.041$).

Utilization/Cost:

- Entyvio™ has not been utilized in the SoonerCare population since its approval in May 2014.

Medication	EAC Per Vial or Tablet	EAC per Dose	EAC for 8 Weeks of Therapy
Entyvio™ Vial 300mg	$5,088.86	$5,088.86	$5,088.86
Remicade® Vial 100mg	$980.22	$3,920.88-$7,841.76*	$3,920.88-$7,841.76*
Humira® SQ Pen 40mg	$1,425.77	$1,425.77	$5,703.08

EAC= estimated acquisition cost
SQ= Subcutaneous
*Dosing based on 80kg patient at a dose of 5-10mg/kg.

Recommendations

The College of Pharmacy recommends the addition of Entyvio™ (vedolizumab) and Otezla® (apremilast) to Tier-3 of the Biologic Products for the Treatment of Rheumatoid Arthritis, Plaque Psoriasis, and Ankylosing Spondylitis Product Based Prior Authorization category with the following criteria:

Entyvio™ (Vedolizumab) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of moderate-to-severely active Crohn's disease (CD) or moderate-to-severely active ulcerative colitis (UC); and
3. A trial of aminosalicylate therapy in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; and
4. A minimum of a 4 week trial of a Tier-2 tumor necrosis factor (TNF) blocker indicated for the treatment of CD or UC that did not yield adequate relief of symptoms or resulted in intolerable adverse effects. Current Tier-2 products include the following:
    a. **UC:** Humira® (adelimumab)
    b. **CD:** Cimzia® (certolizumab), Humira® (adelimumab); and
5. Prior stabilization on the medication documented within the last 100 days.
6. A quantity limit of 300mg every 8 weeks will apply. Approvals will be granted for titration quantities required for initial dosing.
7. Initial approvals will be for the duration of 14 weeks as Entyvio™ should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.

Otezla® (apremilast) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of active psoriatic arthritis (PsA) or moderate-to-severe plaque psoriasis (Ps); and
3. Current Tier-3 approval criteria will apply.
4. A quantity limit of 60 tablets for 30 days will apply. Approvals will be granted for titration quantities required for initial dosing.

Biologic Products		
Tier-1 **(DMARDs appropriate to disease state)**	**Tier-2***	**Tier-3+**
Methotrexate		Abatacept (Orencia®)
Hydroxychloroquine		Adalimumab (Humira®)
Sulfasalazine		Alefacept (Amevive®)
Minocycline		Anakinra (Kineret®)
Oral Corticosteroids		Apremilast (Otezla®)
Leflunomide		Certolizumab pegol (Cimzia®)
Mesalamine		Etanercept (Enbrel®)
6-Mercaptopurine		Golimumab (Simponi®)
Azathioprine		Golimumab (Simponi® Aria™)
NSAIDs		Infliximab (Remicade®)
		Rituximab (Rituxan®)
		Tocilizumab (Actemra®)
		Tofacitinib (Xeljanz®)
		Ustekinumab (Stelara®)
		Vedolizumab (Entyvio™)

Tier structure based on supplemental rebate participation.
DMARDs= Disease modifying antirheumatic drugs
*Supplemental rebated products
+ May be rebated to Tier-2 status only

Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least one Tier-1 product in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 product and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 products.

Utilization Details of Biologic Products: Fiscal Year 2014

Pharmacy Claims

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Adalimumab Products					
HUMIRA PEN KIT 40MG/0.8ML	1,415	277	$4,074,802.38	$97.13	$2,879.72
HUMIRA PEN KIT 40MG/0.8ML PS	67	41	$341,363.19	$169.83	$5,094.97
HUMIRA PEN KIT 40MG/0.8ML CD	31	27	$239,646.61	$262.20	$7,730.54
HUMIRA KIT 40MG/0.8ML	369	85	$1,095,682.50	$100.99	$2,969.33
HUMIRA KIT 20MG/0.4ML	58	10	$170,209.87	$91.86	$2,934.65
Subtotal	**1,940**	**360**	**$5,921,704.55**	**$102.85**	**$3,052.43**
Certolizumab Pegol Products					
CIMZIA INJ KIT (2) 200MG/ML	201	57	$607,521.92	$103.21	$3,022.50
CIMZIA INJ KIT (6) STARTER 200MG/ML	33	33	$280,164.15	$195.37	$8,489.82
Subtotal	**234**	**65**	**$887,686.07**	**$121.27**	**$3,793.53**
Etanercept Products					
ENBREL SRCLK INJ 50MG/ML	901	173	$2,530,192.86	$98.44	$2,808.21
ENBREL INJ 50MG/ML	246	60	$642,961.42	$91.49	$2,613.66
ENBREL INJ KIT 25MG	169	26	$258,912.77	$54.72	$1,532.03
ENBREL INJ 25mg/0.5ML	82	14	$156,117.24	$63.62	$1,903.87
Subtotal	**1,398**	**251**	**$3,588,184.29**	**$89.89**	**$2,566.66**
Tier-2 Subtotal	**3,572**	**609**	**$10,397,574.91**	**$99.20**	**$2,910.86**
Abatacept Products					
ORENCIA INJ 125MG/ML	72	9	$170,359.18	$83.35	$2,366.10
Subtotal	**72**	**9**	**$170,359.18**	**$83.35**	**$2,366.10**
Anakinra Products					
KINERET INJ 100MG/0.67ML	34	6	$87,839.67	$110.49	$2,583.52
Subtotal	**34**	**6**	**$87,839.67**	**$110.49**	**$2,583.52**
Infliximab Products					
REMICADE INJ 100MG	105	24	$503,176.23	$143.76	$4,792.15
Subtotal	**105**	**24**	**$503,176.23**	**$143.76**	**$4,792.15**
Rituximab Products					
RITUXAN INJ 500MG	11	4	$198,916.52	$888.02	$18,083.32
RITUXAN INJ 100MG	4	2	$53,659.92	$638.81	$13,414.98
Subtotal	**15**	**5**	**$252,576.44**	**$820.05**	**$16,838.43**
Tocilizumab Products					
ACTEMRA INJ 400/20ML	10	3	$35,816.65	$161.34	$3,581.67
ACTEMRA INJ 200/10ML	4	1	$4,263.11	$38.06	$1,065.78
Subtotal	**14**	**4**	**$40,079.76**	**$120.00**	**$2,862.84**
Ustekinumab Products					
STELARA 45MG/0.5ML	21	8	$155,094.92	$97.06	$7,385.47
STELARA 90 MCG	15	6	$224,621.27	$193.97	$14,974.75
Subtotal	**36**	**13**	**$379,716.19**	**$137.78**	**$10,547.67**
Golimumab Products					
SIMPONI INJ 50/0.5ML	97	19	$261,768.31	$91.34	$2,698.64
Subtotal	**97**	**19**	**$261,768.31**	**$91.34**	**$2,698.64**
Tier-3 Subtotal	**373**	**80**	**$1,695,515.78**	**$134.53**	**$4,545.62**
Natalizumab Products					
TYSABRI INJ 300/15ML	11	2	$45,089.43	$145.45	$4,099.04

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Subtotal	**11**	**2**	**$45,089.43**	**$145.45**	**$4,099.04**
Canakinumab Products					
ILARIS 180MG/1.2ML VIAL	45	7	$763,114.95	$421.38	$16,958.11
Subtotal	**45**	**7**	**$763,114.95**	**$421.38**	**$16,958.11**
Tysabri and Ilaris Subtotal	**56**	**9**	**$808,204.38**	**$381.05**	**$14,432.22**
Total	**4,001**	**685**	**$12,901,295.07**	**$107.93**	**$3,224.52**

*Total number of unduplicated members

Medical Claims

Product Utilized	Total Claims	Total Members	Total Cost	Units
Certolizumab Pegol Products				
CIMZIA INJ J0717	1	1	$2,372.00	400
Subtotal	**1**	**1**	**$2,372.00**	**400**
Abatacept Products				
ORENCIA INJ J0129	17	3	$32,988.25	1,200
Subtotal	**17**	**3**	**$32,988.25**	**1,200**
Golimumab Products				
SIMPONI ARIA IV INJ J1602	1	1	$8,863.19	371
Subtotal	**1**	**1**	**$8,863.19**	**371**
Infliximab Products				
REMICADE INJ J1745	114	29	$384,228.77	5,995
Subtotal	**114**	**29**	**$384,228.77**	**5,995**
Natalizumab Products (For CD/UC Diagnosis)				
TYSABRI INJ J2323	6	1	$23,709.00	1,800
Subtotal	**6**	**1**	**$23,709.00**	**1,800**
Tocilizumab Products				
ACTEMRA INJ J3262	46	8	$86,987.82	23,486
Subtotal	**46**	**8**	**$86,987.82**	**23,486**
Rituximab Products (For RA/SJA Diagnosis)				
RITUXAN INJ J9310	28	11	$158,058.50	257
Subtotal	**28**	**11**	**$158,058.50**	**257**
Total	**213**	**54**	**$697,207.53**	**33,509**

[1] US $67 billion worth of biosimilar patents expiring before 2020." Generics and Biosimilars Initiatives. Available online at: www.gavionline.net/Biosimilars/General/US-67-billion-worth-of-biosimilar-patents-expiring-before-2020. Last accessed 09/2014.

[2] FDA Approves Cimzia for Treatment of Adult Patients with Active Psoriatic Arthritis. Available online at: http://www.drugs.com/newdrugs/fda-approves-cimzia-adult-patients-active-psoriatic-arthritis-3914.html . Last revised 09/30/13. Last accessed 09/2014.

[3] FDA Oks Stelara for Psoriatic Arthritis. Available at: http://www.medpagetoday.com/Rheumatology/Arthritis/41808. Last revised 09/2013. Last accessed 09/2014.

[4] FDA News Release: Otezla. FDA. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm390091.htm. Last revised 03/2014. Last accessed 09/2014.

[5] FDA News Release: FDA Approves Entyvio to Treat Ulcerative Colitis and Crohn's Disease. FDA. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm398065.htm. Last revised 05/2014. Last accessed 09/2014.

[6]Janssen Biotech Inc: Simponi Aria For Infusion Recieves FDA Approval For Treatment Of Moderately to Severely Active Rheumatoid Arthritis. Available online at: http://www.investor.jnj.com/releasedetail.cfm?releaseid=778787. Last revised 07/2014. Last accessed 09/2014.

[7] Rosenthal, Mary. New Indication Granted for Otezla to Treat Plaque Psoriasis. Avaialble online at: http://www.pharmacypracticenews.com/ViewArticle.aspx?d=Clinical&d_id=50&i=September+2014&i_id=1098&a_id=28296. Last revised 09/2014. Last accessed 09/2014.

[8] Otezla Product Information. Celgene Corporation. Available online at: http://www.otezlapro.com/prescribing-information/. Last revised 09/2014. Last accessed 09/2014.

[9] Entyvio Product Information. Millennium Pharmaceuticals Inc. and under license by Takeda Pharmaceuticals America. Available online at: http://www.entyvio.com/?gclid=COn33cTR_8ACFZKHaQodUWoA9Q. Last revised 05/2014. Last accessed 09/2014.

Appendix H

Fiscal Year 2014 Annual Review of Bladder Control Medications

Oklahoma Health Care Authority
October 2014

Current Prior Authorization Criteria

Tier-1 products are available without a prior authorization for all members. Hyoscyamine is available without prior authorization and can be used as adjunctive therapy, but does not count as a Tier-1 trial.

Tier-2 Approval Criteria:

1. Trials of all Tier-1 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique FDA approved indication not covered by Tier-1 medications

Tier-3 Approval Criteria:

1. Trials of all Tier-2 medications that yielded an inadequate clinical response or adverse effects; or
2. A unique FDA approved indication not covered by lower tiered medications

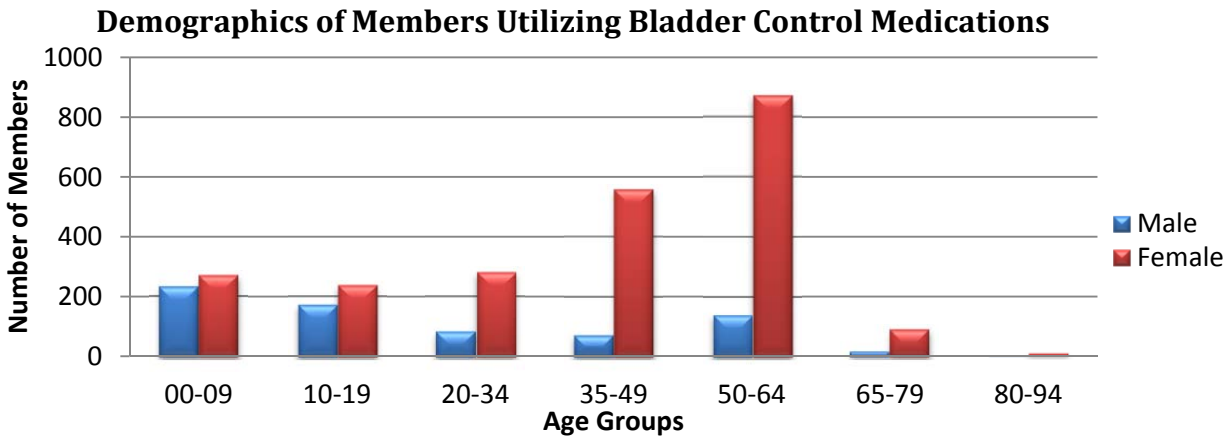
Bladder Control Medications		
Tier-1	**Tier-2**	**Tier-3**
oxybutynin (Ditropan®)	oxybutynin ER (Ditropan XL®)	darifenacin (Enablex®)
trospium ER (Sanctura XR™)		fesoterodine (Toviaz™)
		flavoxate (Urispas®)
		mirabegron (Myrbetriq™)
		oxybutynin patch (Oxytrol®)
		oxybutynin gel (Gelnique™)
		solifenacin (Vesicare®)
		tolterodine (Detrol®)
		tolterodine ER (Detrol LA®)
		trospium (Sanctura™)

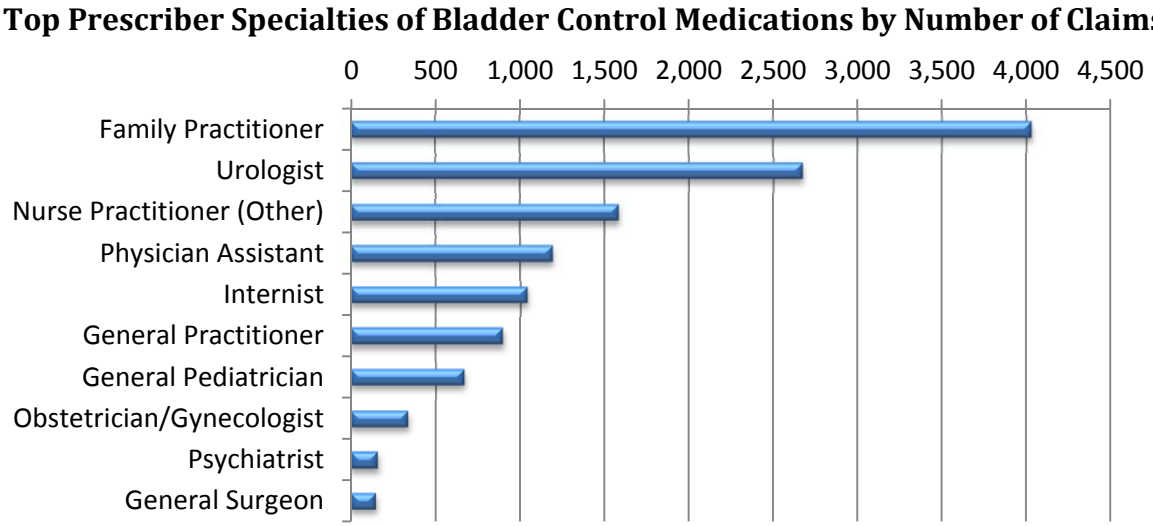
Utilization of Bladder Control Medications

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	3,012	12,892	$806,100.83	$62.53	$2.00	980,281	402,177
2014	3,069	13,277	$918,469.49	$69.18	$2.23	990,162	412,568
% Change	**1.90%**	**3.00%**	**13.90%**	**10.60%**	**11.50%**	**1.00%**	**2.60%**
Change	**57**	**385**	**$112,368.66**	**$6.65**	**$0.23**	**9,881**	**10,391**

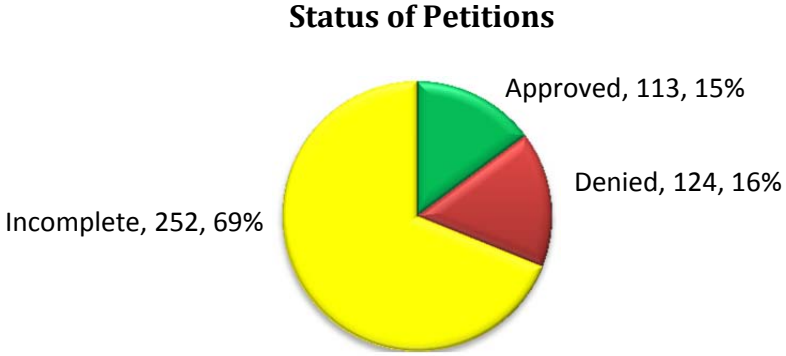
*Total number of unduplicated members.





Prior Authorization of Bladder Control Medications

There was a total of 489 petitions submitted for bladder control medications during fiscal year 2014. Computer edits are in place to detect Tier-1 medication in member's recent claims history and generate automated prior authorization where possible. The following chart shows the status of the submitted petitions.



Market News and Updates[1, 2]

Anticipated Patent Expirations:

- Enablex® (darifenacin)-08/2016
- Vesicare® (solifenacin)-11/2018
- Gelnique™ (oxybutynin gel)- 6/2022
- Toviaz™ (fesoterodine)-06/2027

Recommendations

The College of Pharmacy recommends the following changes to the Bladder Control Medication Prior Authorization category:

1. Move Ditropan XL ® (oxybutynin extended-release) from Tier-2 to Tier-1 based on generic availability and State Maximum Allowable Cost (SMAC).
2. Move Detrol® immediate-release (tolterodine) and Sanctura™ immediate-release (trospium) from Tier-3 to Tier-2 based on generic availability and State Maximum Allowable Cost (SMAC).
3. Move Sanctura XR™ (trospium) from Tier-1 to Tier-3.

Bladder Control Medications		
Tier-1	**Tier-2**	**Tier-3**
oxybutynin (Ditropan®)	tolterodine (Detrol®)	darifenacin (Enablex®)
oxybutynin ER (Ditropan XL®)	trospium (Sanctura™)	fesoterodine (Toviaz™)
		flavoxate (Urispas®)
		mirabegron (Myrbetriq™)
		oxybutynin patch (Oxytrol®)
		oxybutynin gel (Gelnique™)
		solifenacin (Vesicare®)
		tolterodine ER (Detrol LA®)
		trospium ER (Sanctura XR™)

Utilization Details of Bladder Control Medications

Product Utilized	Total Claims	Total Members	Total Cost	Units/ Day	Claims/ Member	Cost/ Claim	%Cost
Proposed Tier-1 Medications							
OXYBUTYNIN SYP 5MG/5ML	1,025	345	$10,558.31	9.68	2.97	$10.30	1.15%
OXYBUTYNIN TAB 5MG	7,946	2,191	$231,335.71	2.23	3.63	$29.11	25.19%
OXYBUTYNIN TAB 5 MG ER	343	65	$15,528.69	1.32	5.28	$45.27	1.69%
OXYBUTYNIN TAB 10MG ER	570	112	$24,999.78	1.33	5.09	$43.86	2.72%
OXYBUTYNIN TAB 15MG ER	288	49	$11,760.31	1.15	5.88	$40.83	1.28%
Subtotal	**10,172**	**2,762**	**$294,182.80**	**2.79**	**3.68**	**$28.92**	**32.03%**
Proposed Tier-2 Medications							
TOLTERODINE TAB 1MG	78	11	$12,425.98	2.11	7.09	$159.31	1.35%
TOLTERODINE TAB 2MG	503	68	$65,687.84	1.84	7.4	$130.59	7.15%
TROSPIUM CL TAB 20MG	35	6	$5,678.13	2.46	5.83	$162.23	0.62%
Subtotal	**616**	**85**	**$83791.95**	**1.91**	**7.25**	**$136.03**	**9.12%**
Proposed Tier-3 Medications							
DETROL LA CAP 2MG	42	10	$9,779.09	1.11	4.2	$232.84	1.06%
DETROL LA CAP 4MG	388	75	$98,475.33	1.06	5.17	$253.80	10.72%
ENABLEX TAB 7.5MG	69	11	$11,423.42	0.91	6.27	$165.56	1.24%
ENABLEX TAB 15MG	159	16	$29,416.45	1.1	9.94	$185.01	3.20%
FLAVOXATE TAB 100MG	27	6	$1,980.90	2.82	4.5	$73.37	0.22%
MYRBETRIQ TAB 25MG	28	5	$6,831.25	1	5.6	$243.97	0.74%
MYRBETRIQ TAB 50MG	15	4	$3,533.70	1	3.75	$235.58	0.38%
OXYTROL DIS 3.9MG/24	7	2	$3,929.44	0.34	3.5	$561.35	0.43%
SANCTURA XR CAP 60MG	116	37	$29,406.52	1.15	3.14	$253.50	3.20%
TOLTERODINE CAP 2MG ER	34	7	$7,223.62	1.16	4.86	$212.46	0.79%
TOLTERODINE CAP 4MG ER	234	61	$49,374.87	1.05	3.84	$211.00	5.38%
TOVIAZ TAB 4MG	11	4	$1,912.61	1	2.75	$173.87	0.21%
TOVIAZ TAB 8MG	54	7	$9,857.25	1	7.71	$182.54	1.07%
TROSPIUM CHL CAP 60MG ER	974	333	$183,301.77	1.03	2.92	$188.19	19.96%
VESICARE TAB 5MG	182	31	$54,203.00	1.09	5.87	$297.82	5.90%
VESICARE TAB 10MG	149	32	$39,845.52	1.02	4.66	$267.42	4.34%
Subtotal	**2489**	**641**	**$540,494.74**	**1.06**	**3.88**	**$217.15**	**58.84%**
Total	**13,277**	**3,069***	**$918,469.49**	**2.4**	**4.33**	**$69.18**	**100%**

*Total number of unduplicated members

[1]FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm Last revised 9/22/14. Last accessed 9/22/14.

[2] FDA: News Release: FDA approves over-the-counter Oxytrol for Women to treat overactive bladder. Available online at: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm336815.htm Last revised 01/25/2013. Last accessed 9/22/14.

Appendix I

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

FDA NEWS RELEASE

For Immediate Release: September 18th, 2014

FDA approves Trulicity to treat type 2 diabetes

The U.S. Food and Drug Administration approved Trulicity (dulaglutide), a once-weekly subcutaneous injection to improve glycemic control, along with diet and exercise, in adults with type 2 diabetes.

Type 2 diabetes affects about 26 million people and accounts for more than 90 percent of diabetes cases diagnosed in the United States. Over time, high blood sugar levels can increase the risk for serious complications, including heart disease, blindness, and nerve and kidney damage.

Trulicity is a glucagon-like peptide-1 (GLP-1) receptor agonist, a hormone that helps normalize blood sugar levels. The drug's safety and effectiveness were evaluated in six clinical trials in which 3,342 patients with type 2 diabetes received Trulicity. Patients receiving Trulicity had an improvement in their blood sugar control as observed with reductions in HbA1c level.

Trulicity has been studied as a stand-alone therapy and in combination with other type 2 diabetes therapies, including metformin, sulfonylurea, thiazolidinedione, and prandial insulin. Trulicity should not be used to treat people with type 1 diabetes; those who have increased ketones in their blood or urine (diabetic ketoacidosis); those with severe stomach or intestinal problems; or as first-line therapy for patients who cannot be managed with diet and exercise.

Trulicity has a boxed warning that tumors of the thyroid gland (thyroid C-cell tumors) have been observed in rodent studies with Trulicity but that it is unknown whether Trulicity causes thyroid C-cell tumors, including a type of thyroid cancer called medullary thyroid carcinoma (MTC), in humans. Trulicity should not be used in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia syndrome type 2 (a disease in which patients have tumors in more than one gland in their body, which predisposes them to MTC).

The FDA is requiring the following post-marketing studies for Trulicity:

- a clinical trial to evaluate dosing, efficacy, and safety in pediatric patients;
- a study to assess potential effects on sexual maturation, reproduction, and CNS development and function in immature rats;
- a medullary thyroid carcinoma (MTC) case registry of at least 15 years duration to identify any increase in MTC incidence related to Trulicity;
- a clinical trial comparing Trulicity with insulin glargine on glycemic control in patients with type 2 diabetes and moderate or severe renal impairment; and
- a cardiovascular outcomes trial to evaluate the cardiovascular risk of Trulicity in patients with high baseline risk of cardiovascular disease.

The FDA approved Trulicity with a Risk Evaluation and Mitigation Strategy (REMS), which consists of a communication plan to inform health care professionals about the serious risks associated with Trulicity.

In clinical trials, the most common side effects observed in patients treated with Trulicity were nausea, diarrhea, vomiting, abdominal pain, and decreased appetite.

Trulicity is manufactured by Indianapolis-based Eli Lilly and Company.

FDA NEWS RELEASE

For Immediate Release: September 16th, 2014

FDA approves Movantik for opioid-induced constipation

The U.S. Food and Drug Administration approved Movantik (naloxegol), an oral treatment for opioid-induced constipation in adults with chronic non-cancer pain.

Opioids are a class of drugs that are used to treat and manage pain. A common side effect associated with the use of these drugs are that they reduce the gastrointestinal tract's motility, making bowel movements difficult and causing patients to strain, have hard or lumpy stools or experience a sensation of incomplete

evacuation. Movantik belongs to a class of drugs called peripherally acting opioid receptor antagonists, which are used to decrease the constipating effects of opioids.
Movantik's safety and effectiveness were established in two clinical trials of 1,352 participants who had taken opioids for at least four weeks for non-cancer related pain and had opioid-induced constipation. Participants were randomly assigned to receive 12.5 mg or 25 mg of Movantik or placebo once daily for 12 weeks. The trials were designed to measure the change in the number of bowel movements per week from the start of the study.
Results of the first trial showed that 44 percent of participants receiving 25 mg of Movantik and 41 percent of participants receiving 12.5 mg of Movantik experienced an increase in bowel movements per week, compared to 29 percent of participants receiving placebo. The second trial showed similar results.
Common side effects of Movantik include abdominal pain, diarrhea, headache and the experience of excessive gas in the stomach or intestinal area.
The FDA is requiring a postmarketing study to further evaluate the potential risk of cardiovascular adverse events in patients taking Movantik. In June, the FDA held a public meeting to discuss what studies might be required to assess the cardiac safety of peripherally acting opioid receptor antagonists, including Movantik, intended to treat opioid-induced constipation.
Movantik is distributed by AstraZeneca Pharmaceuticals LP, based in Wilmington, Delaware.

FDA NEWS RELEASE

For Immediate Release: September 10th, 2014

FDA approves weight-management drug Contrave

The U.S. Food and Drug Administration approved Contrave (naltrexone hydrochloride and bupropion hydrochloride extended-release tablets) as treatment option for chronic weight management in addition to a reduced-calorie diet and physical activity.
The drug is approved for use in adults with a body mass index (BMI) of 30 or greater (obesity) or adults with a BMI of 27 or greater (overweight) who have at least one weight-related condition such as high blood pressure (hypertension), type 2 diabetes, or high cholesterol (dyslipidemia).
BMI, which measures body fat based on an individual's weight and height, is used to define the obesity and overweight categories. According to the Centers for Disease Control and Prevention, more than one-third of adults in the United States are obese.
Contrave is a combination of two FDA-approved drugs, naltrexone and bupropion, in an extended-release formulation. Naltrexone is approved to treat alcohol and opioid dependence. Bupropion is approved to treat depression and seasonal affective disorder and as an aid to smoking cessation treatment.
The effectiveness of Contrave was evaluated in multiple clinical trials that included approximately 4,500 obese and overweight patients with and without significant weight-related conditions treated for one year. All patients received lifestyle modification that consisted of a reduced- calorie diet and regular physical activity.
Results from a clinical trial that enrolled patients without diabetes showed that patients had an average weight loss of 4.1 percent over treatment with placebo at one year. In this trial, 42 percent of patients treated with Contrave lost at least 5 percent of their body weight compared with 17 percent of patients treated with placebo. Results from another clinical trial that enrolled patients with type 2 diabetes showed that patients had an average weight loss of 2 percent over treatment with placebo at one year. In this trial, 36 percent of patients treated with Contrave lost at least 5 percent of their body weight compared with 18 percent of patients treated with placebo.
Patients using Contrave at the maintenance dose should be evaluated after 12 weeks to determine if the treatment is working. If a patient has not lost at least 5 percent of baseline body weight, Contrave should be discontinued, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.
Because it contains bupropion, Contrave has a boxed warning to alert health care professionals and patients to the increased risk of suicidal thoughts and behaviors associated with antidepressant drugs. The warning also notes that serious neuropsychiatric events have been reported in patients taking bupropion for smoking cessation.
Contrave can cause seizures and must not be used in patients who have seizure disorders. The risk of seizure is dose-related. Contrave should be discontinued and not restarted in patients who experience a seizure while being treated with Contrave.

Contrave can also raise blood pressure and heart rate and must not be used in patients with uncontrolled high blood pressure. The clinical significance of the increases in blood pressure and heart rate observed with Contrave treatment is unclear, especially for patients with heart-related and cerebrovascular (blood vessel dysfunction impacting the brain) disease, since patients with a history of heart attack or stroke in the previous six months, life-threatening arrhythmias, or congestive heart failure were excluded from the clinical trials. Blood pressure and pulse should be measured prior to starting the drug and should be monitored at regular intervals, particularly among patients with controlled high blood pressure prior to treatment.
Other products containing bupropion should not be taken along with Contrave. The drug should not be used in patients who have eating disorders (bulimia or anorexia nervosa). Contrave should also not be taken by patients who are using opioids or treatments for opioid dependence, or who are experiencing acute opiate withdrawal. Patients undergoing an abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs should not take Contrave. Women who are pregnant or trying to become pregnant should not take Contrave.
The most common adverse reactions reported with Contrave include nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea.
The FDA is requiring the following post-marketing requirements:

- a cardiovascular outcomes trial to assess the cardiovascular risk associated with Contrave use;
- two efficacy, safety, and clinical pharmacology studies in pediatric patients (one in patients 12 to 17 years of age, and one in patients 7 to 11 years of age);
- a nonclinical (animal) juvenile toxicity study with a particular focus on growth and development as well as behavior, learning, and memory;
- a study to evaluate the effect of Contrave on cardiac conduction;
- clinical trials to evaluate dosing in patients with hepatic or renal impairment;
- a clinical trial to evaluate the potential for interactions between Contrave and other drugs.

Contrave is distributed by Takeda Pharmaceuticals America Inc. of Deerfield, Illinois for Orexigen Therapeutics, Inc. of La Jolla, California.

FDA NEWS RELEASE

For Immediate Release: September 4th, 2014

FDA approves Keytruda for advanced melanoma

The U.S. Food and Drug Administration granted accelerated approval to Keytruda (pembrolizumab) for treatment of patients with advanced or unresectable melanoma who are no longer responding to other drugs.
Melanoma, which accounts for approximately 5 percent of all new cancers in the United States, occurs when cancer cells form in skin cells that make the pigment responsible for color in the skin. According to the National Cancer Institute, an estimated 76,100 Americans will be diagnosed with melanoma and 9,710 will die from the disease this year.
Keytruda is the first approved drug that blocks a cellular pathway known as PD-1, which restricts the body's immune system from attacking melanoma cells. Keytruda is intended for use following treatment with ipilimumab, a type of immunotherapy. For melanoma patients whose tumors express a gene mutation called BRAF V600, Keytruda is intended for use after treatment with ipilimumab and a BRAF inhibitor, a therapy that blocks activity of BRAF gene mutations.
The five prior FDA approvals for melanoma include: ipilimumab (2011), peginterferon alfa-2b (2011), vemurafenib (2011), dabrafenib (2013), and trametinib (2013).
The FDA granted Keytruda breakthrough therapy designation because the sponsor demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies. It also received priority review and orphan product designation. Priority review is granted to drugs that have the potential, at the time the application was submitted, to be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan product designation is given to drugs intended to treat rare diseases.
The FDA action was taken under the agency's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier

patient access to promising new drugs while the company conducts confirmatory clinical trials. An improvement in survival or disease-related symptoms has not yet been established.
Keytruda's efficacy was established in 173 clinical trial participants with advanced melanoma whose disease progressed after prior treatment. All participants were treated with Keytruda, either at the recommended dose of 2 milligrams per kilogram (mg/kg) or at a higher dose of 10 mg/kg. In the half of the participants who received Keytruda at the recommended dose of 2 mg/kg, approximately 24 percent had their tumors shrink. This effect lasted at least 1.4 to 8.5 months and continued beyond this period in most patients. A similar percentage of patients had their tumor shrink at the 10 mg/kg dose.
Keytruda's safety was established in the trial population of 411 participants with advanced melanoma. The most common side effects of Keytruda were fatigue, cough, nausea, itchy skin (pruritus), rash, decreased appetite, constipation, joint pain (arthralgia) and diarrhea. Keytruda also has the potential for severe immune-mediated side effects. In the 411 participants with advanced melanoma, severe immune-mediated side effects involving healthy organs, including the lung, colon, hormone-producing glands and liver, occurred uncommonly.
Keytruda is marketed by Merck & Co., based in Whitehouse Station, New Jersey.

Safety Announcements

FDA Drug Safety Communication: FDA approves label changes for asthma drug Xolair (omalizumab), including describing slightly higher risk of heart and brain adverse events

[September 26th, 2014] A U.S. Food and Drug Administration (FDA) review of safety studies suggests a slightly increased risk of problems involving the heart and blood vessels supplying the brain among patients being treated with the asthma drug Xolair (omalizumab) than in those who were not treated with Xolair. As a result, we have added information about these potential risks to the drug label. Patients taking Xolair should continue to take the medication as prescribed and discuss any questions or concerns with their health care professionals.
FDA approved Xolair in 2003 to treat patients 12 years and older with moderate to severe persistent asthma who have a positive skin or blood test to year-round allergens in the air and whose symptoms are not well-controlled by asthma medicines called inhaled corticosteroids. Xolair has been shown to decrease the number of asthma attacks in these patients. Asthma is a chronic disease that affects the airways in the lungs and can cause serious trouble breathing, so it is important to take all asthma medicines exactly as they are prescribed. Xolair is also approved for patients 12 years and older with chronic hives without a known cause—a condition called chronic idiopathic urticaria or CIU—who continue to have hives that are not controlled by H1 antihistamine treatment.
Our review of a 5-year safety study found a slightly higher rate of heart and brain blood vessel problems occurred in patients being treated with Xolair compared to those patients not treated with Xolair. The heart and brain blood vessel problems included mini-strokes known as transient ischemic attacks or TIAs; heart attacks; sudden, unexpected chest pain; high blood pressure in the arteries of the lungs called pulmonary hypertension; and blood clots in the lungs and veins. Although the data are suggestive of a serious safety signal, due to weaknesses in how the safety study was designed and carried out, we are unable to definitively confirm or determine the exact increased level of these risks with Xolair.
To further evaluate the heart and brain risks noted in the 5-year safety study, we reviewed a combined analysis of 25 randomized double-blind clinical trials comparing Xolair to a placebo. An increased risk of heart- and brain-related problems in patients treated with Xolair was not noted in this combined analysis, but the low number of these events, the young patient population, and the short duration of follow-up prevent us from making any definite conclusions about the absence of a risk. As a result of our review of the safety study and the combined clinical trials, we have added information about the potential risks of heart- and brain-related problems to the Adverse Reactions section of the drug label.
Some previous clinical trials have shown slightly higher rates of various cancers in patients treated with Xolair compared with non-Xolair-treated patients. Our review of the 5-year safety study found no difference in the rates of cancer between those patients being treated with Xolair and those who were not being treated with Xolair. However, due to limitations in the 5-year study, we cannot rule out a potential risk of

cancer with Xolair, so we have added this information to the Warnings and Precautions section of the drug label.

Safety Announcements

Potassium Chloride Injection (Baxter): Recall - Shipping Carton Mislabeling

[September 17th, 2014] Baxter International Inc. announced a voluntary recall of one lot of Potassium Chloride Injection 10mEq per 100mL, product code 2B0826 (Lot # P318220, NDC # 0338-0709-48) to the hospital/pharmacy/nurse level. The recall is being initiated due to a labeling error on the shipping cartons in a single lot. Shipping cartons labeled for this specific lot number of Potassium Chloride Injection may contain units of Gentamicin Sulfate Injection, 80 mg in 100 mL, product code 2B0862.
As both products are packaged in 100mL containers, have similar code numbers and red labeling on the front panel, there is a potential risk of medication error or delay in therapy for patients that require high concentration potassium chloride.
The affected lot of Potassium Chloride Injection was distributed to customers in the United States between May 26, 2014, and August 8, 2014. There have been no reported adverse events associated with this situation to date.
BACKGROUND: Potassium Chloride is indicated for treatment of potassium deficiency and administered intravenously. Gentamicin Sulfate is an antibacterial drug for intravenous administration.
RECOMMENDATION: It is recommended that healthcare professionals carefully review the product label before administering.
Consumers with questions regarding this recall can call Baxter at 1-800-422-9837, Monday through Friday, between the hours of 8:00 a.m. and 5:00 p.m. Central Time, or e-mail Baxter at onebaxter@baxter.com.
Consumers should contact their physician or healthcare provider if they have experienced any problems that may be related to using this drug product.
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:

Current Drug Shortages Index (as of October 1, 2014):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Amikacin Injection	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Barium Sulfate for Suspension	***Currently in Shortage***
Bupivacaine Hydrochloride (Marcaine, Sensorcaine) Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection[12]	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Cidofovir Injection	***Currently in Shortage***
Clindamycin Phosphate (Cleocin) Injection	***Currently in Shortage***
Clonidine HCL Injection (Duraclon)	***Currently in Shortage***
Cyanocobalamin (Vitamin B12) Injection	***Currently in Shortage***

Daunorubicin Hydrochloride Solution for Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dexmethylphenidate Hydrochloride (Focalin) Tablet	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) CR	***Currently in Shortage***
Doxorubicin (Adriamycin) Lyophilized Powder	***Currently in Shortage***
Ephedrine Sulfate Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Erythrocin Lactobionate Lyophilized Powder for Injection	***Currently in Shortage***
Famotidine Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Sodium Injection	***Currently in Shortage***
Fortaz Injection	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***
Heparin Sodium Injection	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Irrigation Solutions	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Memantine Hydrochloride (Namenda) XR Capsules	***Currently in Shortage***
Methazolamide (Neptazane) Tablets	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride Tablets	***Currently in Shortage***
Morphine Sulfate (Astramorph PF, Duramorph, Infumorph) Injection (Preservative Free)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nalbuphine Hydrochloride (Nubain) Injection	***Currently in Shortage***
Nitroglycerin (Nitronal) Injection	***Currently in Shortage***