Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
June 10, 2015
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 – June 10, 2015

DATE: June 1, 2015

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 June meeting.
Material is arranged in order of the agenda.

Call to Order

Public Comment Forum

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

Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – Appendix B

Action Item – Vote to Prior Authorize Tanzeum™ (Albiglutide), Trulicity™ (Dulaglutide), Cycloset® (Bromocriptine), Jardiance® (Empagliflozin), Invokamet™ (Canagliflozin/Metformin), Xigduo™ XR (Dapagliflozin/Metformin Extended-Release), Glyxambi® (Empagliflozin/Linagliptin), Afrezza® (Insulin Human Inhalation Powder), and Toujeo® (Insulin Glargine) – Appendix C

Action Item – Vote to Prior Authorize Ruconest® (C1 Esterase Inhibitor) – Appendix D

Action Item – Vote to Prior Authorize Hemangeol™ (Propranolol Oral Solution), Sotylize™ (Sotalol Oral Solution), and Prestalia® (Perindopril/Amlodipine) – Appendix E

Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Invega Trinza™ (3-Month Paliperidone Palmitate Injection) – Appendix F

30-Day Notice to Prior Authorize Cholbam™ (Cholic Acid) – Appendix G

30-Day Notice to Prior Authorize Natpara® (Parathyroid Hormone) – Appendix H

Annual Review of ADHD & Narcolepsy Medications and 30-Day Notice to Prior Authorize Zenzedi® (Dextroamphetamine), Evekeo™ (Amphetamine), and Aptensio XR™ (Methylphenidate Extended-Release) – Appendix I

Annual Review of Otic Anti-Infectives and 30-Day Notice to Prior Authorize Xtoro™ (Finafloxacin) – Appendix J

Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Hetlioz® (Tasimelteon) and Belsomra® (Suvorexant) – Appendix K

Annual Review of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations and 30-Day Notice to Prior Authorize Avycaz™ (Ceftazidime/Avibactam) and Zerbaxa™ (Ceftolozane/Tazobactam) – Appendix L

30-Day Notice to Prior Authorize Copaxone® (Glatiramer Acetate) 40mg/mL – Appendix M

FDA and DEA Updates – Appendix N

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – June 10, 2015 @ 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. April 8, 2015 DUR Minutes – Vote
   B. April 8, 2015 DUR Recommendations Memorandum

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

4. **Update on Medication Coverage Authorization Unit/Chronic Medication Adherence Program Update – See Appendix B**
   A. Medication Coverage Activity for April 2015
   B. Pharmacy Help Desk Activity for April 2015
   C. Medication Coverage Activity for May 2015
   D. Pharmacy Help Desk Activity for May 2015
   E. Chronic Medication Adherence Program Update

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

5. **Action Item – Vote to Prior Authorize Tanzeum™ (Albiglutide), Trulicity™ (Dulaglutide), Cycloset® (Bromocriptine), Jardiance® (Empagliflozin), Invokamet™ (Canagliflozin/Metformin), Xigduo™ XR (Dapagliflozin/Metformin Extended-Release), Glyxambi® (Empagliflozin/Linagliptin), Afrezza® (Insulin Human Inhalation Powder), and Toujeo® (Insulin Glargine) – See Appendix C**
   A. College of Pharmacy Recommendations

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

6. **Action Item – Vote to Prior Authorize Ruconest® (C1 Esterase Inhibitor) – See Appendix D**
   A. College of Pharmacy Recommendations

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

7. **Action Item – Vote to Prior Authorize Hemangeol™ (Propranolol Oral Solution), Sotylize™ (Sotalol Oral Solution), and Prestalia® (Perindopril/Amlodipine) – See Appendix E**
   A. College of Pharmacy Recommendations

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

8. Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Invega Trinza™ (3-Month Paliperidone Palmitate Injection) – See Appendix F

A. Current Prior Authorization Criteria
B. Utilization of Atypical Antipsychotics
C. Prior Authorization of Atypical Antipsychotic Medications
D. Market News and Updates
E. Invega Trinza™ (3-Month Paliperidone Palmitate Injection) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Atypical Antipsychotic Medications

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

9. 30-Day Notice to Prior Authorize Cholbam™ (Cholic Acid) – See Appendix G

A. Introduction
B. Cholbam™ (Cholic Acid) Product Summary
C. College of Pharmacy Recommendations

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

10. 30-Day Notice to Prior Authorize Natpara® (Parathyroid Hormone) – See Appendix H

A. Introduction
B. Natpara® (Parathyroid Hormone) Product Summary
C. College of Pharmacy Recommendations

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

11. Annual Review of ADHD & Narcolepsy Medications and 30-Day Notice to Prior Authorize Zenzedi® (Dextroamphetamine), Evekeo™ (Amphetamine), and Aptensio XR™ (Methylphenidate Extended-Release) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of ADHD & Narcolepsy Medications
C. Prior Authorization of ADHD & Narcolepsy Medications
D. Market News and Updates
E. Product Summaries
F. Binge Eating Disorder (BED) Summary
G. College of Pharmacy Recommendations
H. Utilization Details of ADHD & Narcolepsy Medications

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

12. Annual Review of Otic Anti-Infectives and 30-Day Notice to Prior Authorize Xtoro™ (Finafloxacin) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Otic Anti-Infectives
C. Prior Authorization of Otic Anti-Infectives
D. Market News and Updates
E. Xtoro™ (Finafloxacin) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Otic Anti-Infectives

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

13. Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Hetlioz® (Tasimelteon) and Belsomra® (Suvorexant) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Insomnia Medications
C. Prior Authorization of Insomnia Medications
D. Market News and Updates

E. Product Summaries
F. College of Pharmacy Recommendations
G. Utilization Details of Insomnia Medications

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

14. Annual Review of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations and 30-Day Notice to Prior Authorize Avycaz™ (Ceftazidime/Avibactam) and Zerbaxa™ (Ceftolozane/Tazobactam) – See Appendix L

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations
D. Prior Authorization of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations
E. Cephalosporin Utilization Evaluation
F. Market News and Updates
G. Product Summaries
H. College of Pharmacy Recommendations
I. Utilization Details of Cephalosporin Antibiotics
J. Utilization Details of Systemic Antibiotic Special Formulations

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

15. 30-Day Notice to Prior Authorize Copaxone® (Glatiramer Acetate) 40mg/mL – See Appendix M

A. Introduction
B. Current Prior Authorization Criteria
C. Copaxone® (Glatiramer Acetate) Utilization
D. Market News and Updates
E. Discussion
F. College of Pharmacy Recommendations
G. Utilization Details of Copaxone® (Glatiramer Acetate)

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

17. FDA and DEA Updates – Appendix N

Items to be presented by Dr. Muchmore, Chairman:

18. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF APRIL 8, 2015

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.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 Winegardner, D.Ph.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist		x
Krystin Lorg, Pharm.D.; Clinical Pharmacist	x	
Melissa Anderson, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist	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
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): Kenny White		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
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Medicaid Director		x
Joseph Young, Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Mark DeClerk, Lilly	Ty Griffin, Medco	Jim Fowler, AstraZeneca
Danielle Walters, Sanofi	Kelly Devitt, Medco	Jim Chapman, AbbVie
Melvin Nwamadi, Abbott	Kelly Duncan, Dyax	Larry Goolsby, J&J
Chet Steckler, Purdue Pharma	Aaron Shaw, Boehringer	Brian Maves, Pfizer

PRESENT FOR PUBLIC COMMENT:	
Uday Jodhpurkar	Sanofi Pasteur
Jennifer Ward	Eli Lilly
Kimi Vesta	Sanofi
Matthew Bird	AstraZeneca

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**

2A: AGENDA NO. 11 SPEAKER: JENNIFER WARD
2B: AGENDA NO. 11 SPEAKER: KIMI VESTA
2C: AGENDA NO. 11 SPEAKER: MATTHEW BIRD
2D: AGENDA NO. 12 SPEAKER: UDAY JODHPURKAR

ACTION: NONE REQUIRED

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

3A: MARCH 11, 2015 DUR MINUTES – VOTE
3B: MARCH 11, 2015 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore
Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS UPDATE

4A: MEDICATION COVERAGE ACTIVITY FOR MARCH 2015
4B: PHARMACY HELP DESK ACTIVITY FOR MARCH 2015
4C: ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 5: **FISCAL YEAR 2014 ANNUAL REVIEW OF SOONERCARE PHARMACY BENEFIT**

5A: INTRODUCTION
5B: TOTAL ENROLLMENT
5C: TRADITIONAL VERSUS SPECIALTY PHARMACY PRODUCTS
5D: TOP 10 THERAPEUTIC CLASSES BY REIMBURSEMENT
5E: HEPATITIS C DRUG SPENDING
5F: GENERIC MEDICATION PRICE INCREASES
5G: CONCLUSION

5H: TOP 100 REIMBURSED DRUGS BY FISCAL YEAR
5I: TOP 50 MEDICATIONS BY TOTAL NUMBER OF CLAIMS
5J: TOP TRADITIONAL THERAPEUTIC CLASSES BY FISCAL YEAR
5K: TOP SPECIALTY THERAPEUTIC CLASSES BY FISCAL YEAR
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NO ACTION REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE SYLVANT™ (SILTUXIMAB)
6A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ECOZA™ (ECONAZOLE NITRATE), JUBLIA® (EFINACONAZOLE), AND KERYDIN™ (TAVABOROLE)
7A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
Dr. Hardzog-Britt moved to approve; seconded by Dr. Rhymer
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE IZBA® (TRAVOPROST OPHTHALMIC SOLUTION)
8A: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nawaz
Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF ANTIHYPERTENSIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE HEMANGEOL™ (PROPRANOLOL ORAL SOLUTION), SOTYLIZE™ (SOTALOL ORAL SOLUTION), AND PRESTALIA® (PERINDOPRIL/AMLODIPINE)
9A: CURRENT PRIOR AUTHORIZATION CRITERIA
9B: UTILIZATION OF ANTIHYPERTENSIVE MEDICATIONS
9C: PRIOR AUTHORIZATION OF ANTIHYPERTENSIVE MEDICATIONS
9D: MARKET NEWS AND UPDATES
9E: PRODUCT SUMMARIES
9F: COLLEGE OF PHARMACY RECOMMENDATIONS
9G: UTILIZATION DETAILS OF ANTIHYPERTENSIVE MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF HEREDITARY ANGIOEDEMA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE RUCONEST® (C1 ESTERASE INHIBITOR)
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF HEREDITARY ANGIOEDEMA MEDICATIONS
10C: PRIOR AUTHORIZATION OF HEREDITARY ANGIOEDEMA MEDICATIONS
10D: MARKET NEWS AND UPDATES
10E: RUCONEST® (C1 ESTERASE INHIBITOR) PRODUCT SUMMARY
10F: COLLEGE OF PHARMACY RECOMMENDATIONS

10G: UTILIZATION DETAILS OF HEREDITARY ANGIOEDEMA MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF DIABETES MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TANZEUM™(ALBIGLUTIDE), TRULICITY™ (DULAGLUTIDE), CYCLOSET® (BROMOCRIPTINE), JARDIANCE® (EMPAGLIFLOZIN), INVOKAMET™ (CANAGLIFLOZIN/METFORMIN), XIGDUO™ XR (DAPAGLIFLOZIN/METFORMIN EXTENDED-RELEASE), GLYXAMBI® (EMPAGLIFLOZIN/LINAGLIPTIN), AFREZZA® (INSULIN HUMAN INHALATION POWDER), AND TOUJEO® (INSULIN GLARGINE)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF DIABETES MEDICATIONS
11C: PRIOR AUTHORIZATION OF DIABETES MEDICATIONS
11D: MARKET NEWS AND UPDATES
11E: PRODUCT SUMMARIES
11F: COLLEGE OF PHARMACY RECOMMENDATIONS
11G: UTILIZATION DETAILS OF DIABETIC MEDICATIONS
Materials included in agenda packet; presented by Dr. Anderson
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF PEDICULICIDES
12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF PEDICULICIDES
12C: PRIOR AUTHORIZATION OF PEDICULICIDES
12D: MARKET NEWS AND UPDATES
12E: SUMMARY OF PEDICULICIDE MAILING
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
12G: UTILIZATION DETAILS OF PEDICULICIDES
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: FUTURE BUSINESS
14A: ANNUAL REVIEWS
14B: NEW PRODUCT REVIEWS
Materials included in agenda packet; submitted by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ADJOURNMENT
The meeting was adjourned at 5:04 pm.

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

Memorandum

Date: April 09, 2015

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

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

Subject: DUR Board Recommendations From Meeting of April 08, 2015

Recommendation 1: Oral Viscous Lidocaine Claims Analysis Update

NO ACTION REQUIRED.

The FDA recommendations and the educational mailing have been effective in reducing prescribing of oral, viscous lidocaine in the SoonerCare pediatric population. Based on the downward trend in claims in the pediatric population as well as feedback from the prescribers regarding potential appropriate, emergency use of oral viscous lidocaine, the College of Pharmacy does not recommend any changes to the current criteria. Utilization of oral viscous lidocaine will be reassessed periodically to ensure prescribing of this product remains appropriate.

Recommendation 2: Fiscal Year 2014 Annual Review of SoonerCare Pharmacy Benefit

NO ACTION REQUIRED.

Recommendation 3: Vote to Prior Authorize Sylvant™ (Siltuximab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Sylvant™ (siltuximab) with the following criteria:

Sylvant™ (Siltuximab) Approval Criteria:

1. An FDA approved diagnosis of Multicentric Castleman's Disease (also known as giant lymph node hyperplasia); and
2. Member must be Human Immunodeficiency Virus (HIV) and Human Herpesvirus-8 (HHV-8) negative; and
3. Member must be 18 years of age or older; and
4. The following FDA approved dosing restrictions will apply:
    a. 11 mg/kg via intravenous (IV) infusion every three weeks until treatment failure (defined as disease progression based on increase in symptoms, radiologic progression, or deterioration in performance status); and
5. Sylvant™ must be administered in a clinical setting able to provide resuscitation equipment, medications, and trained personnel; and
6. The prescriber must verify that a complete blood count (CBC) will be done prior to each dose for the first 12 months and for an additional three doses thereafter; and
7. Approvals will be for the duration of six months.

Recommendation 4: Vote to Prior Authorize Ecoza™ (Econazole Nitrate), Jublia® (Efinaconazole), and Kerydin™ (Tavaborole)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the addition of Jublia® (efinaconazole) and Kerydin™ (tavaborole) to the Special Prior Authorization tier of the Topical Antifungal Product Based Prior Authorization category with the following criteria:

Jublia® (Efinaconazole) and Kerydin™ (Tavaborole) Approval Criteria:

1. An FDA approved diagnosis of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes;* and
2. A trial of oral antifungals (12 weeks for toenails); and
3. A patient-specific, clinically significant reason why member cannot use Penlac® (ciclopirox solution); and
4. A clinically significant reason the member requires treatment for onychomycosis (cosmetic reasons will not be approved).

Additionally, the College of Pharmacy recommends the addition of Ecoza™ (econazole nitrate) to Tier-2 of the Topical Antifungal Product Based Prior Authorization category. Current criteria for this category will apply.

Topical Antifungal Tier-2 Approval Criteria:

1. Documented, recent trials of at least two Tier-1 topical antifungal products for at least 90 days each; and

2. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage form of that medication in Tier-2 (foams, shampoos, sprays, kits, etc.).
3. Authorization of combination products nystatin/triamcinolone or clotrimazole/betamethasone requires a patient-specific, clinically significant reason why the member cannot use the individual components separately.
4. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).

Topical Antifungal Medications		
Tier-1	**Tier-2**	**Special PA**
ciclopirox cream	butenafine (Mentax®)	**efinaconazole (Jublia®)**
clotrimazole (Rx) cream, solution	ciclopirox solution, shampoo, gel, suspension (Penlac® and Loprox®)	**tavaborole (Kerydin™)**
clotrimazole (OTC)* cream	clotrimazole/betamethasone cream, lotion	
econazole cream	**econazole nitrate (Ecoza™)**	
ketoconazole cream, shampoo	ketoconazole foam (Extina®)	
nystatin cream, ointment, powder	ketoconazole gel (Xolegel™)	
terbinafine (OTC)* cream	luliconazole cream (Luzu™)	
tolnaftate (OTC)*cream	miconazole/zinc oxide/white petrolatum (Vusion®)	
	naftifine (Naftin®)	
	nystatin/triamcinolone cream, ointment	
	oxiconazole (Oxistat®)	
	salicylic acid (Bensal HP®)	
	sertaconazole nitrate (Ertaczo®)	
	sulconazole (Exelderm®)	

*Over-the-counter (OTC) antifungal products are covered for pediatric members 0-20 years of age without prior authorization.

Recommendation 5: Vote to Prior Authorize Izba® (Travoprost Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of Izba® (travoprost) into Tier-2 of the Glaucoma Medications Product Based Prior Authorization (PBPA) category. The existing criteria for this category will apply.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and

2. The member must attempt at least three Tier-1 trials of a minimum of four weeks duration each within the last 120 days. Tier-1 trials may be from any pharmacologic class; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 products; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 products.
5. The member must have had a comprehensive, dilated eye exam within the last 365 day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Glaucoma Medications*	
Tier-1	**Tier-2**
Beta-Blockers	
betaxolol (Betoptic® 0.5%)	betaxolol (Betoptic-S®)
carteolol (Ocupress® 1%)	brimonidine/timolol (Combigan®)
dorzolamide/timolol (Cosopt®)	timolol maleate (Timoptic Ocudose®)
levobunolol (Betagan®)	
metipranolol (OptiPranolol®)	
timolol maleate (Betimol®, Istalol®, Timoptic®, Timoptic-XE®)	
Prostaglandin Analogs	
travoprost 0.004% (Travatan-Z®)	bimatoprost (Lumigan®)
latanoprost (Xalatan®)	tafluprost (Zioptan™)
	travoprost 0.004% (Travatan®)
	unoprostone (Rescula®)
	travoprost 0.003% (Izba®)
Adrenergic Agonists	
dipivefrin (Propine®)	
Alpha-2 Adrenergic Agonists	
brimonidine 0.2%	brimonidine (Alphagan-P® 0.1%, 0.15%)
brinzolamide/brimonidine (Simbrinza™)	apraclonidine (Iopidine®)
	brimonidine/timolol (Combigan®)
Carbonic Anhydrase Inhibitors	
dorzolamide/timolol (Cosopt®)	
dorzolamide (Trusopt®)	
brinzolamide (Azopt®)	
brinzolamide/brimonidine (Simbrinza™)	
acetazolamide (Diamox®)[+]	
methazolamide (Neptazane®)[+]	
([+]Indicates Available Oral Products)	
Cholinergic Agonists/Cholinesterase Inhibitors	
pilocarpine (Isopto® Carpine®, Pilopine HS®)	carbachol (Isopto®, Miostat® 1.5%, 3%)
	echothiophate iodide (Phospholine Iodide®)

*Tier structure based on supplemental rebate participation.

Recommendation 6: Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Hemangeol™ (Propranolol Oral Solution), Sotylize™ (Sotalol Oral Solution) and Prestalia® (Perindopril/Amlodipine)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Hereditary Angioedema Medications and 30-Day Notice to Prior Authorize Ruconest® (C1 Esterase Inhibitor)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Tanzeum™ (Albiglutide), Trulicity™ (Dulaglutide), Cycloset® (Bromocriptine), Jardiance® (Empagliflozin), Invokamet™ (Canagliflozin/Metformin), Xigduo™ XR (Dapagliflozin/Metformin Extended-Release), Glyxambi (Empagliflozin/Linagliptin), Afrezza® (Insulin Human Inhalation Powder), and Toujeo® (Insulin Glargine)

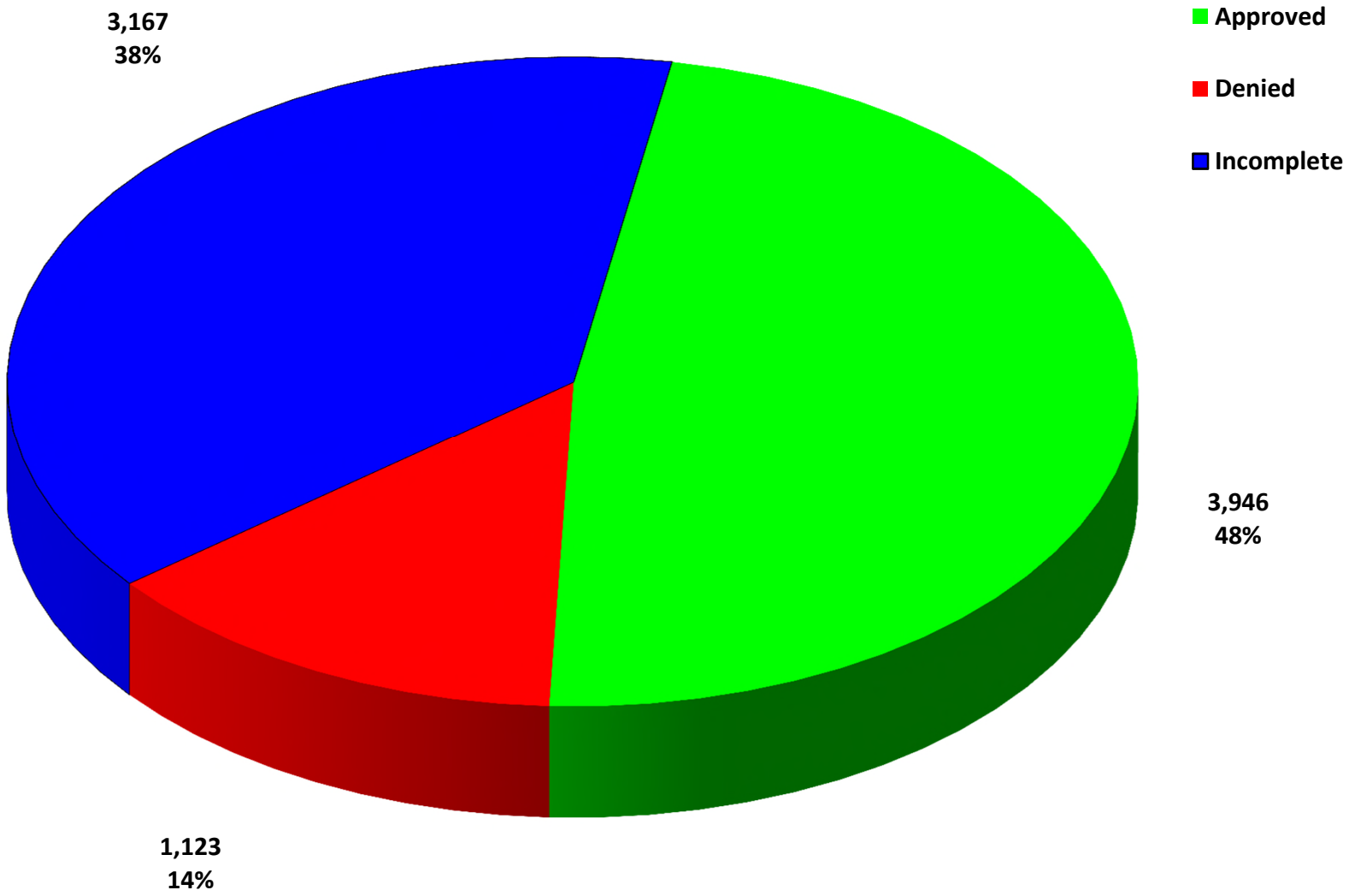
NO ACTION REQUIRED.

Recommendation 9: Annual Review of Pediculicides

NO ACTION REQUIRED.

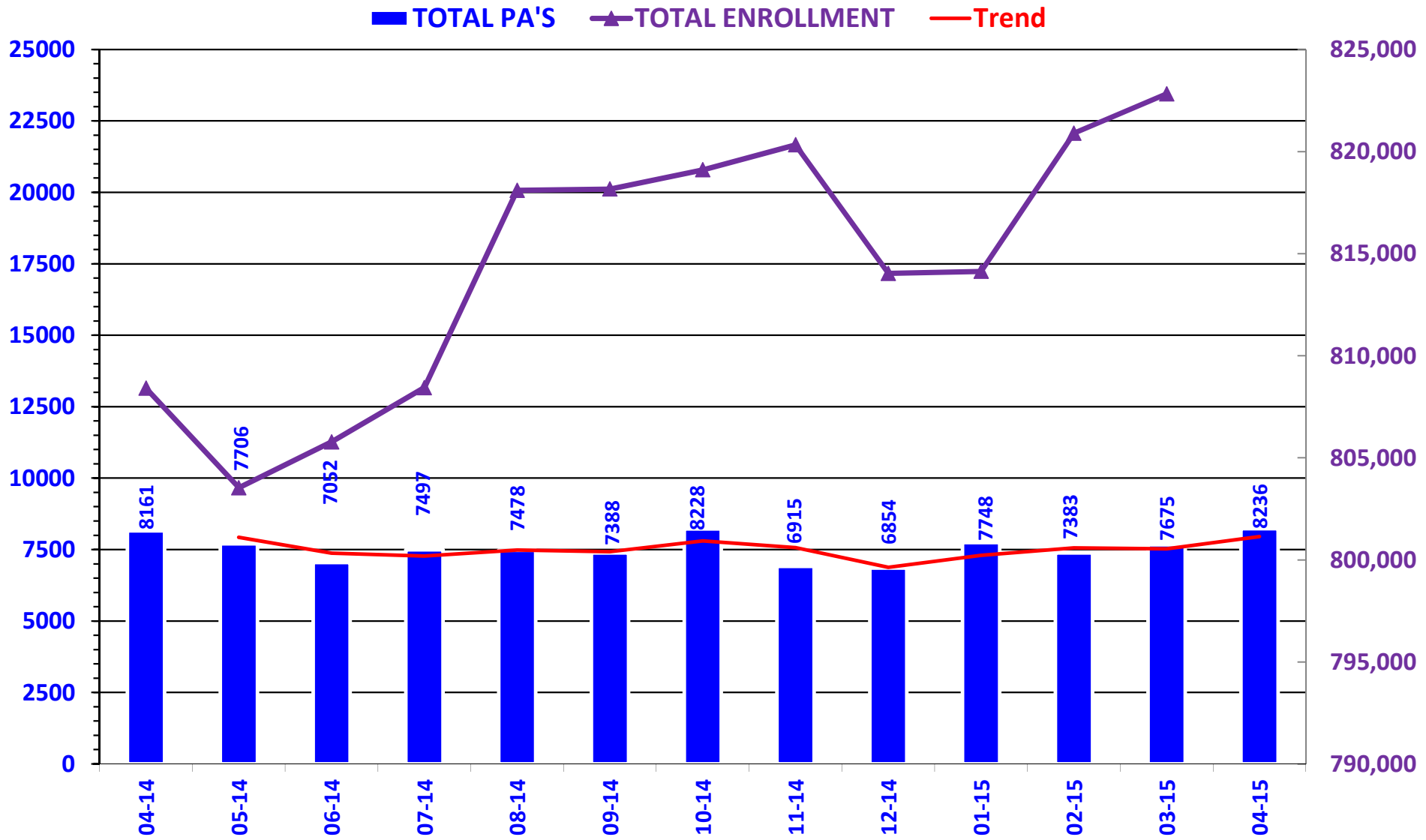
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: APRIL 2015



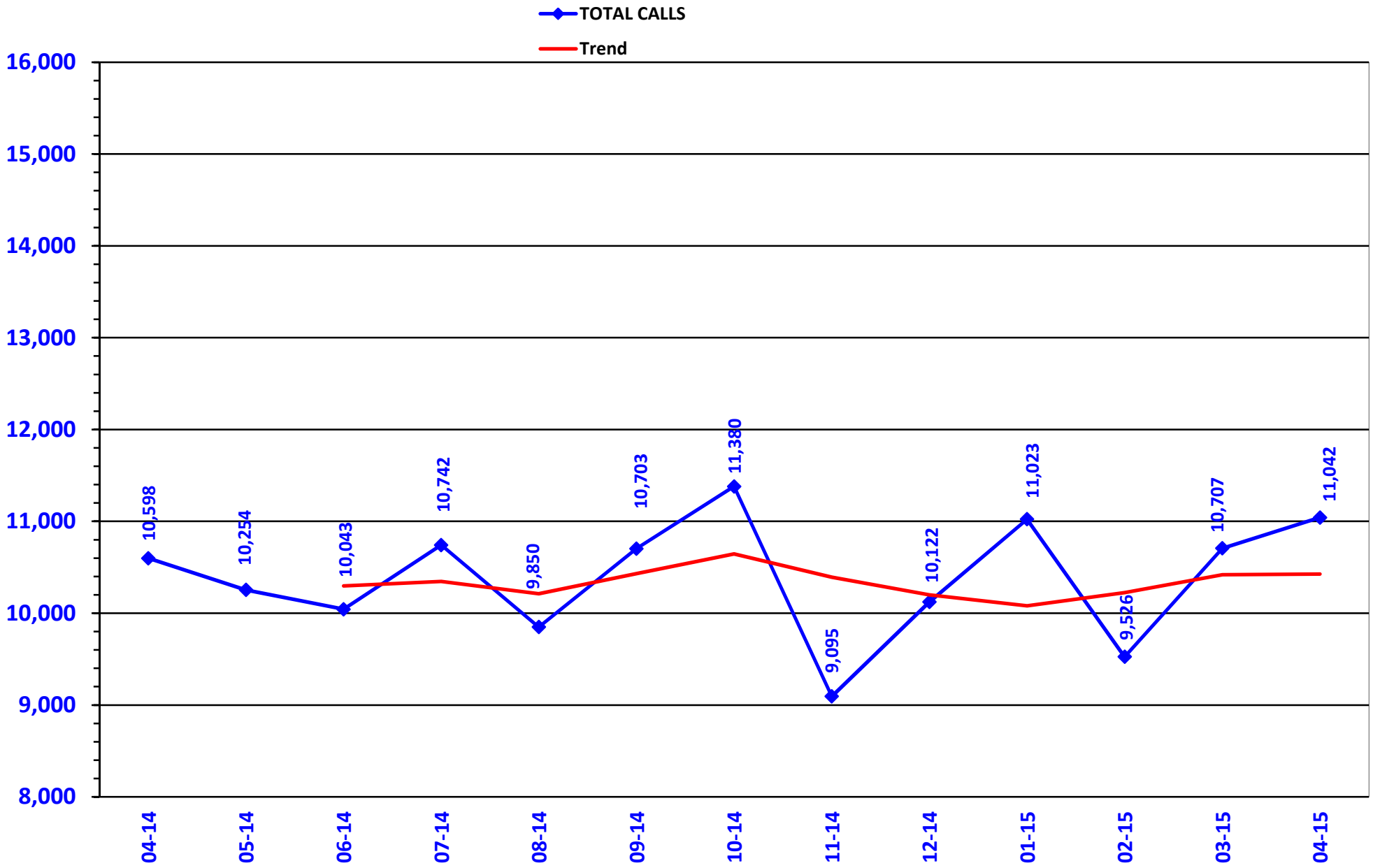
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: APRIL 2014 – APRIL 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
APRIL 2014 – APRIL 2015



Prior Authorization Activity

4/1/2015 Through 4/30/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	434	192	23	219	355
Analgesic - NonNarcotic	20	2	1	17	101
Analgesic, Narcotic	429	235	45	149	162
Angiotensin Receptor Antagonist	38	8	18	12	310
Antiasthma	249	89	32	128	301
Antibiotic	51	21	6	24	77
Anticonvulsant	59	22	6	31	319
Antidepressant	105	18	27	60	359
Antidiabetic	214	87	24	103	357
Antifungal	16	1	10	5	4
Antigout	13	7	3	3	312
Antihistamine	199	144	11	44	345
Antimigraine	38	8	11	19	272
Antiulcers	218	45	70	103	251
Anxiolytic	74	52	7	15	281
Atypical Antipsychotics	456	265	25	166	345
Biologics	75	37	10	28	320
Bladder Control	44	11	9	24	356
Blood Thinners	142	101	3	38	315
Botox	34	17	11	6	359
Cardiovascular	46	24	5	17	330
Cephalosporins	16	10	0	6	4
Chronic Obstructive Pulmonary Disease	19	6	2	11	360
Contraceptive	11	5	0	6	289
Dermatological	98	13	57	28	83
Diabetic Supplies	301	114	33	154	242
Endocrine & Metabolic Drugs	74	54	6	14	119
Erythropoietin Stimulating Agents	31	19	2	10	116
Fibromyalgia	140	42	40	58	350
Fish Oils	11	2	4	5	360
Gastrointestinal Agents	56	13	18	25	106
Glaucoma	14	1	2	11	361
Growth Hormones	99	82	2	15	145
Hematopoietic Agents	10	7	1	2	54
Hepatitis C	147	81	30	36	9
HFA Rescue Inhalers	47	18	4	25	360
Insomnia	44	10	11	23	195
Linzess, Amitiza, and Relistor	79	12	15	52	200
Multiple Sclerosis	41	28	0	13	196
Muscle Relaxant	84	20	26	38	42
Nasal Allergy	174	10	78	86	250
Neurological Agents	55	34	5	16	357
Nsaids	179	25	47	107	299
Ocular Allergy	93	17	25	51	170
Ophthalmic Anti-infectives	45	16	5	24	22
Osteoporosis	23	13	0	10	312
Other*	229	36	38	155	161
Pediculicide	61	22	11	28	13
Prenatal Vitamins	35	0	6	29	0
Statins	72	33	6	33	359
Stimulant	954	437	78	439	338
Suboxone/Subutex	210	141	20	49	82
Synagis	11	4	6	1	109

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

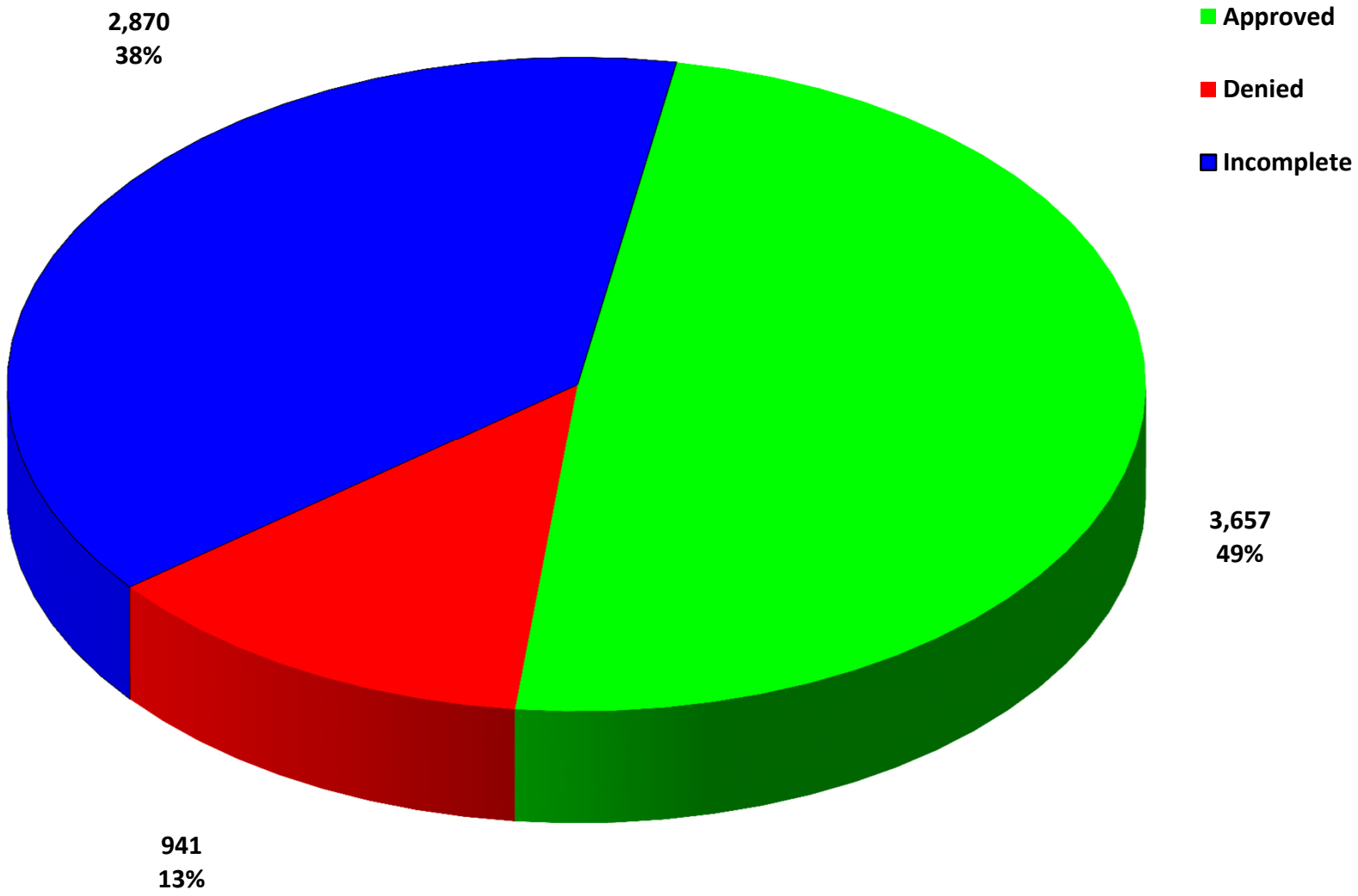
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Testosterone	67	15	11	41	346
Topical Antifungal	58	0	26	32	0
Topical Corticosteroids	80	2	36	42	359
Vitamin	71	17	36	18	339
Pharmacotherapy	72	46	6	20	276
Emergency PAs	5	5	0	0	
Total	**6,770**	**2,796**	**1,050**	**2,924**	
Overrides					
Brand	55	34	9	12	339
Cumulative Early Refill	5	5	0	0	180
Diabetic Supplies	169	110	4	55	282
Dosage Change	346	313	5	28	7
High Dose	6	3	1	2	89
Ingredient Duplication	55	42	1	12	5
Lost/Broken Rx	85	79	4	2	5
NDC vs Age	44	43	0	1	218
Nursing Home Issue	75	67	1	7	4
Opioid Quantity	11	9	2	0	167
Other*	29	25	3	1	8
Quantity vs. Days Supply	719	509	39	171	282
STBS/STBSM	19	19	0	0	78
Stolen	7	3	1	3	3
Temporary Unlock	6	3	3	0	26
Third Brand Request	20	10	6	4	25
Overrides Total	**1,466**	**1,150**	**73**	**243**	
Total Regular PAs + Overrides	**8,236**	**3,946**	**1,123**	**3,167**	

Denial Reasons	
Unable to verify required trials.	2,614
Does not meet established criteria.	1,069
Lack required information to process request.	691

Other PA Activity	
Duplicate Requests	543
Letters	4,658
No Process	11
Changes to existing PAs	497
Helpdesk Initiated Prior Authorizations	882
PAs Missing Information	31

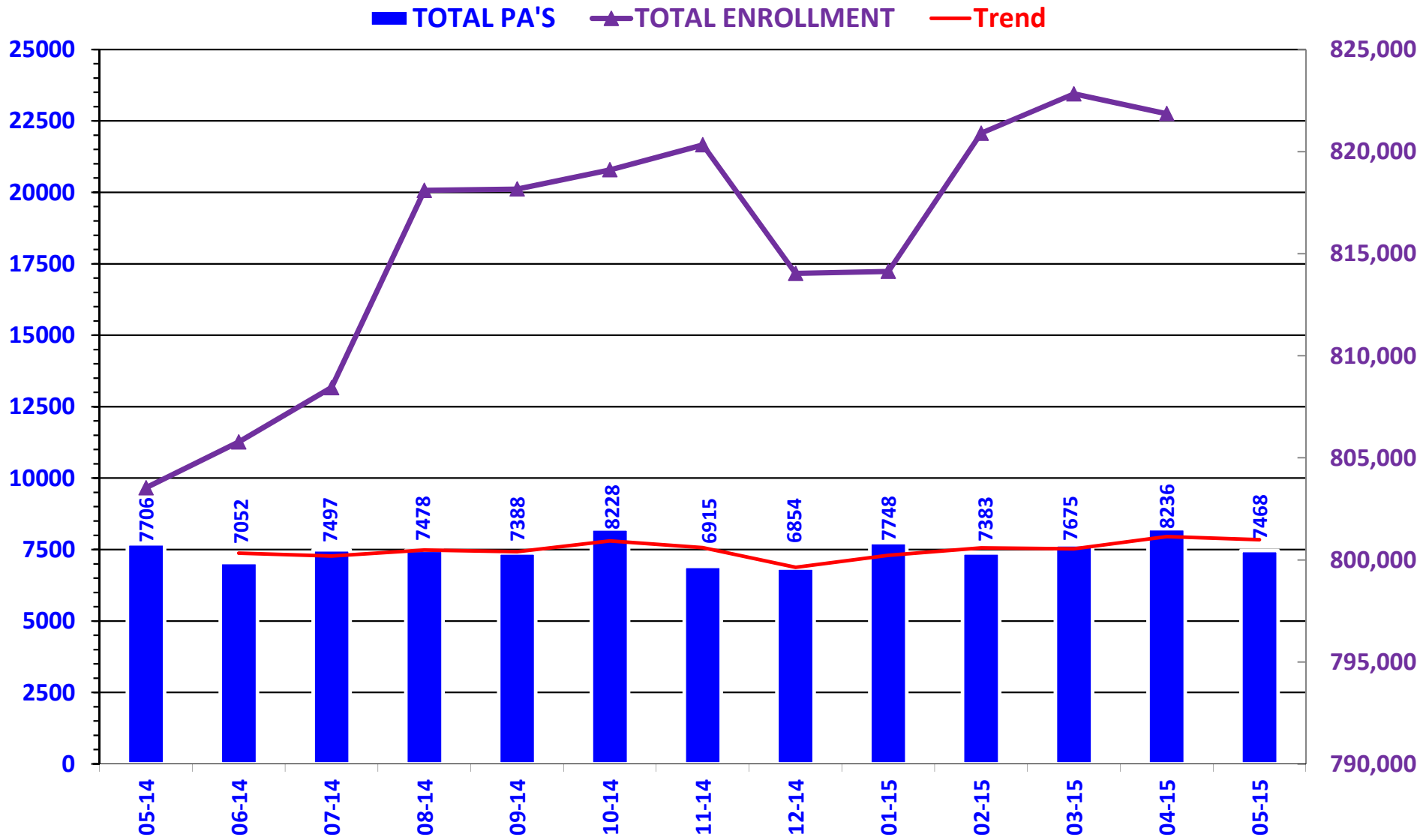
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: MAY 2015



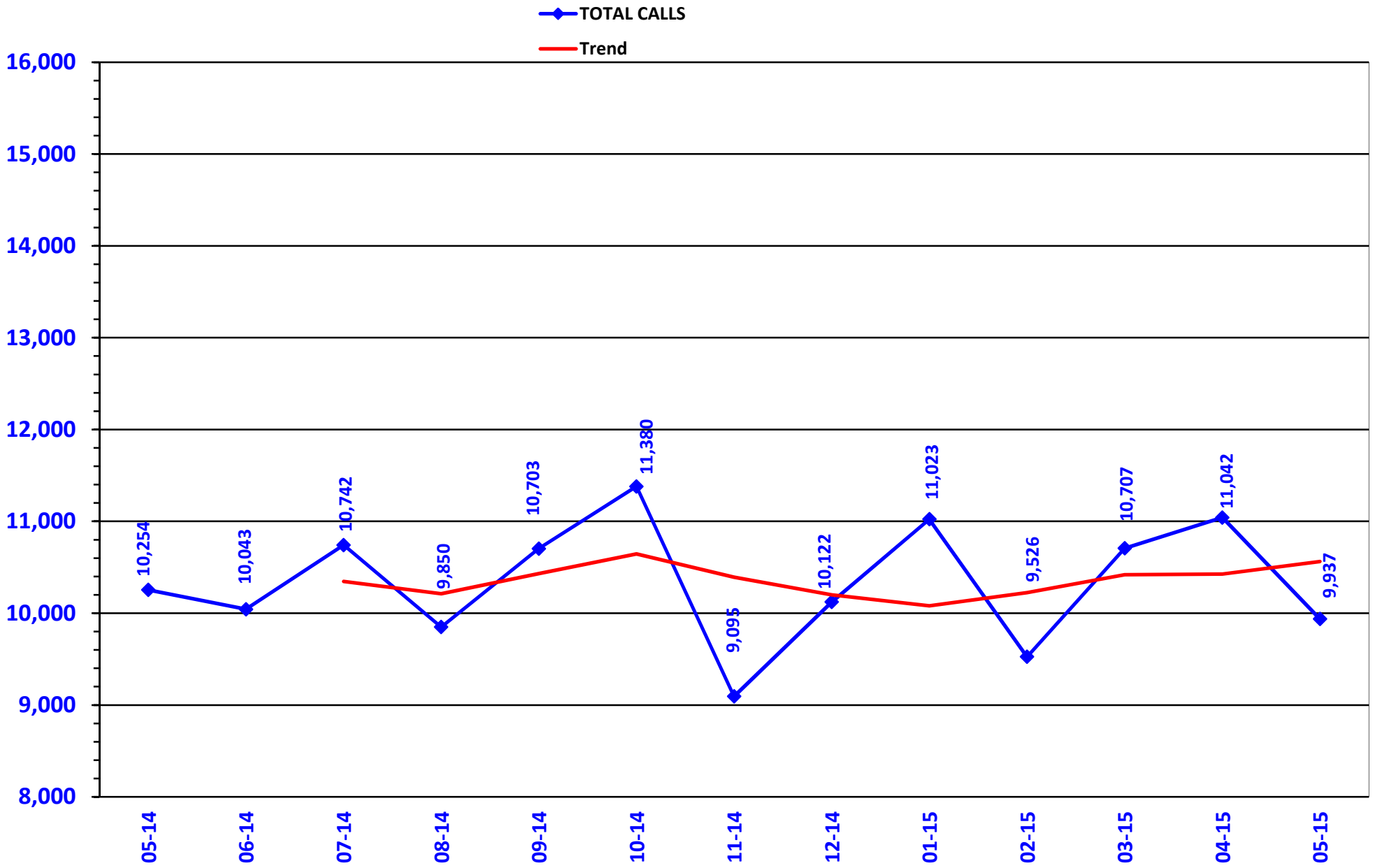
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MAY 2014 – MAY 2015



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MAY 2014 – MAY 2015



Prior Authorization Activity

5/1/2015 Through 5/31/2015

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	306	148	12	146	357
Analgesic - NonNarcotic	21	1	2	18	87
Analgesic, Narcotic	421	243	35	143	163
Angiotensin Receptor Antagonist	26	4	7	15	359
Antiasthma	226	95	16	115	332
Antibiotic	33	13	5	15	127
Anticonvulsant	63	15	12	36	334
Antidepressant	123	31	23	69	348
Antidiabetic	212	80	38	94	355
Antifungal	11	1	6	4	39
Antigout	10	6	0	4	201
Antihistamine	168	150	1	17	354
Antimigraine	27	5	11	11	293
Antiulcers	205	53	59	93	212
Antiviral	10	2	0	8	98
Anxiolytic	73	49	0	24	249
Atypical Antipsychotics	408	222	19	167	339
Biologics	113	61	10	42	334
Bladder Control	37	8	5	24	359
Blood Thinners	128	88	3	37	306
Botox	18	15	3	0	310
Calcium Channel Blockers	12	6	1	5	104
Cardiovascular	27	14	2	11	286
Cephalosporins	11	4	0	7	6
Chronic Obstructive Pulmonary Disease	14	1	4	9	359
Contraceptive	15	3	2	10	250
Dermatological	87	8	52	27	120
Diabetic Supplies	340	178	18	144	271
Endocrine & Metabolic Drugs	71	40	15	16	139
Erythropoietin Stimulating Agents	45	22	6	17	111
Fibromyalgia	162	38	54	70	323
Fish Oils	27	2	7	18	355
Gastrointestinal Agents	62	10	23	29	150
Glaucoma	10	0	1	9	0
Growth Hormones	73	57	6	10	150
Hematopoietic Agents	11	7	0	4	151
Hepatitis C	153	91	27	35	8
HFA Rescue Inhalers	45	19	6	20	332
Insomnia	53	8	13	32	201
Linzess, Amitiza, and Relistor	71	10	17	44	161
Multiple Sclerosis	45	26	1	18	218
Muscle Relaxant	82	20	31	31	32
Nasal Allergy	101	11	33	57	186
Neurological Agents	57	32	6	19	355
Nsaids	162	14	40	108	308
Ocular Allergy	76	16	16	44	206
Ophthalmic Anti-infectives	31	11	0	20	17
Osteoporosis	30	13	3	14	333
Other*	211	33	42	136	252
Otic Antibiotic	17	1	3	13	5
Pediculicide	85	43	12	30	11
Prenatal Vitamins	10	0	4	6	0
Statins	64	18	7	39	355

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Stimulant	779	386	47	346	344
Suboxone/Subutex	173	129	6	38	79
Testosterone	62	15	14	33	320
Topical Antifungal	42	0	22	20	0
Topical Corticosteroids	65	3	17	45	182
Vitamin	69	24	34	11	284
Pharmacotherapy	81	60	0	21	263
Emergency PAs	5	5	0	0	
Total	**6,175**	**2,668**	**859**	**2,648**	
Overrides					
Brand	35	21	5	9	310
Cumulative Early Refill	5	5	0	0	144
Diabetic Supplies	117	80	2	35	222
Dosage Change	346	316	6	24	6
High Dose	3	3	0	0	126
Ingredient Duplication	47	40	1	6	9
Lost/Broken Rx	96	87	4	5	4
NDC vs Age	46	45	1	0	234
Nursing Home Issue	40	40	0	0	4
Opioid Quantity	12	11	1	0	130
Other*	39	31	4	4	9
Quantity vs. Days Supply	580	367	48	165	259
STBS/STBSM	11	10	1	0	45
Stolen	16	16	0	0	4
Temporary Unlock	5	1	4	0	28
Third Brand Request	27	10	8	9	42
Wrong D.S. on Previous Rx	2	2	0	0	7
Overrides Total	**1,293**	**989**	**82**	**222**	
Total Regular PAs + Overrides	**7,468**	**3,657**	**941**	**2,870**	

Denial Reasons	
Unable to verify required trials.	2,522
Does not meet established criteria.	887
Lack required information to process request.	456

Other PA Activity	
Duplicate Requests	471
Letters	4,324
No Process	3
Changes to existing PAs	483
Helpdesk Initiated Prior Authorizations	798
PAs Missing Information	33

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
June 2015

Prescriber Mailing: RAS Antagonists and HMG-CoA Reductase Inhibitors

The College of Pharmacy and the Oklahoma Health Care Authority have started an educational quarterly mailing to prescribers with members on chronic maintenance medications for diabetes, blood pressure, or cholesterol. The purpose of these mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Each mailing includes a prescriber summary report with a "star rating" based on their overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is greater than or equal to 80%. A patient is considered non-adherent if their PDC is less than 80%. Patients must have at least two pharmacy claims for at least one medication in the drug category in the past year to be included in the calculations.

The second mailing was processed in February and addressed adherence to maintenance renin angiotensin system (RAS) antagonists (e.g., angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors) and HMG-CoA reductase inhibitors (i.e., statins). Prescribers with three or more patients on both classes of medications were eligible for inclusion in the mailing if their percentage of patients considered adherent was less than 60% (0 stars) or ≥84% for RAS antagonists and ≥78% for statins (5 stars). The review period was for one year and patients were assigned to prescribers based on their designated medical home provider as of January 2015.

A total of 3,150 RAS antagonist prescribers and 2,388 statin prescribers were evaluated based on the computed adherence claims. These prescribers had 5,237 RAS antagonist members and 3,112 statin members considered non-adherent based on PDC calculations. A total of 345 prescribers were included in the mailing which accounted for 6,672 patients intervened for adherence.

Summary of Mailing

Letters/Prescribers	Count
Total Letters Mailed	345
Members	**Count**
Total Members Included	6,672

Example Star Rating[1]

Report date: 1/31/2015 Prescriber: <Prescriber Name>
NPI: <Prescriber NPI> SoonerCare Provider ID: <Provider ID>
Assigned medical home patients on a RAS antagonist: <7>
Assigned medical home patients on a statin: <8>

Percentage of patients adherent to RAS antagonists: <42.86%>

0 out of 5 stars

Percentage of patients adherent to statins: <50.00%>

0 out of 5 stars

Adherence is shown in the Provider Summary Report as a percentage for RAS antagonists and as a percentage for statins, with a corresponding star rating for each category. The star ratings for the percentage of patients that are adherent to RAS antagonists or statins are based on the 2015 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. A key is shown below to illustrate the star ratings and adherence percentages for each star rating.

RAS antagonists:

5 Stars: Excellent (≥ 84%)

4 Stars: Above Average (≥ 81% to < 84%)

3 Stars: Average (≥ 76% to < 81%)

2 Stars: Below Average (≥ 72% to < 76%)

1 Star: Poor (≥ 60% to < 72%)

0 Stars: Very Poor (< 60%)

Statins:

5 Stars: Excellent (≥ 78%)

4 Stars: Above Average (≥ 75% to < 78%)

3 Stars: Average (≥ 69% to < 75%)

2 Stars: Below Average (≥ 62% to < 69%)

1 Star: Poor (≥ 60% to < 62%)

0 Stars: Very Poor (< 60%)

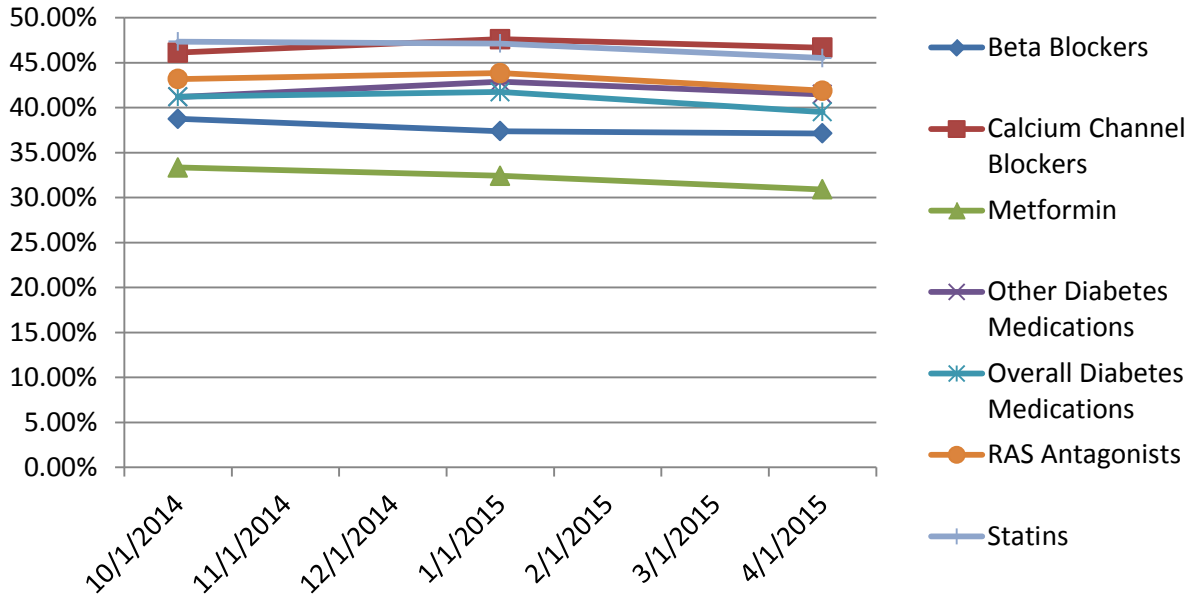
Chronic Medication Adherence PDC by Drug Category

The average member PDC is listed based on drug category below. Also listed is the average prescriber percentage of adherent members (PDC ≥ 80%) for each category and the average star rating for the applicable categories. Star ratings listed as N/A are either subcategories or categories that are not included in Medicare's star ratings thus far.

Drug Category	Member PDC	Prescriber % of Adherent Members	Star Rating
Beta Blockers	66.29%	37.38%	N/A
Calcium Channel Blockers	71.27%	47.60%	N/A
Metformin	62.15%	32.42%	N/A
Other Diabetes Medications	68.22%	42.88%	N/A
Overall Diabetes Medications	68.15%	41.74%	0 stars
RAS Antagonists	69.92%	43.84%	0 stars
Statins	71.98%	47.12%	0 stars

The average member PDC and the percent of adherent members is tracked for all drug categories each time a mailing is processed. The line graph below shows trends in the percentage of adherent members for each drug category since the Chronic Medication Adherence initiative commenced. The line graph below depicts the percentage of adherent members for all of SoonerCare and does not differentiate those members who received a mailing. Of note, the beta blockers and calcium channel blockers are being monitored but have not yet been included in the mailings to prescribers. Topics and dates of previous and current mailings include the following:

- Metformin and other diabetes medications: October 2014
- RAS Antagonists and statins: February 2015
- Metformin and other diabetes medications: May 2015



Medication Compliance Informational Page [2, 3, 4, 5]

Medication adherence is essential for positive therapeutic outcomes. Non-adherence may lead to false medication failure, resulting in unnecessary dose increases and/or medication changes or additions, complications associated with high blood pressure and/or high cholesterol, and increased health-care costs. Patients need to understand the importance of taking their blood pressure and/or cholesterol medications as directed to reduce the risk of serious complications, such as heart disease, stroke, kidney failure, and pre-mature death. Dosing regimens, possible adverse effects, the importance of medication compliance, and long-term serious complications associated with high blood pressure and/or high cholesterol should be discussed with the patient to address any concerns and improve medication adherence, resulting in improved blood pressure and/or cholesterol control and a decreased risk of serious complications.

Please refer to the websites below for helpful patient resources!

- *National Consumers League:* Script Your Future (videos, adherence tools for patients, medication guides)
  http://www.scriptyourfuture.org/cardiovascular/
- *FDA:* High Blood Pressure Medications and You (how hypertension medications work)
  http://www.fda.gov/downloads/Drugs/ResourcesForYou/SpecialFeatures/UCM358489.pdf
- *Million Hearts:* High Blood Pressure (patient fact sheet)
  http://millionhearts.hhs.gov/Docs/MH_PCNA_Blood_Pressure_Fact_Sheet.pdf
- *American Heart Association (AHA):* Life's Simple 7 Heart Health Factors (information and resources)
  http://mylifecheck.heart.org/Multitab.aspx?NavID=3&CultureCode=en-US
- *AHA:* Heart360® (tracks blood pressure, physical activity, cholesterol, glucose, weight, and medications)
  https://www.heart360.org/

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[1] Centers for Medicare & Medicaid Services: *Medicare 2015 Part C & D Star Rating Technical Notes*. Available online at http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PerformanceData.html. Last updated 12/4/14.

[2] Centers for Disease Control and Prevention: *Heart Disease Facts.* Available online at: http://www.cdc.gov/heartdisease/facts.htm. Last updated 10/29/14.

[3] Ho, P.M., Bryson, C.L., et al. Medication Adherence: Its Importance in Cardiovascular Outcomes. *Circulation.* 2009. 119: 3028-3035.

[4] Krousel-Wood, M., Thomas, S., et al. Medication adherence: a key factor in achieving blood pressure control and good clinical outcomes in hypertensive patients. *Curr Opin Cardiol.* 2004. 19 (4): 357-362.

[5] Gatwood, J., Bailey, J.E. Improving medication adherence in hypercholesterolemia: challenges and solutions. *Vasc Health Risk Manag.* 2014. 2014 (10): 615-625.

Appendix C

Vote to Prior Authorize Tanzeum™ (Albiglutide), Trulicity™ (Dulaglutide), Cycloset® (Bromocriptine), Jardiance® (Empagliflozin), Invokamet™ (Canagliflozin/Metformin), Xigduo™ XR (Dapagliflozin/Metformin Extended-Release), Glyxambi (Empagliflozin/Linagliptin), Afrezza® (Insulin Human Inhalation Powder), and Toujeo® (Insulin Glargine)

Oklahoma Health Care Authority
June 2015

Recommendations

The College of Pharmacy recommends moving Actos® (pioglitazone) and Prandin® (repaglinide) to Tier-1 based on generic availability and state maximum allowable cost. Additionally, the College of Pharmacy recommends the placement of Tanzeum™ (albiglutide), Trulicity™ (dulaglutide), Cycloset® (bromocriptine), Jardiance® (empagliflozin), Invokamet™ (canagliflozin/metformin), Xigduo™ XR (dapagliflozin/metformin extended-release), and Glyxambi® (empagliflozin/linagliptin) into Tier-3 of the Diabetes Medications Product Based Prior Authorization category. Current criteria for this category will apply.

Diabetes Medications Tier-2 Approval Criteria:

1. A trial of a Tier-1 medication (must include a trial of metformin titrated up to maximum dose), or a patient-specific, clinically significant reason why a Tier-1 medication is not appropriate.
2. For initiation with dual or triple therapy, additional Tier-2 medications can be approved based on current AACE or ADA guidelines.

Diabetes Medications Tier-3 Approval Criteria:

1. Member must have tried a Tier-2 medication in the same category and have a documented clinical reason why the Tier-2 medication is not appropriate. (For Tier-3 medications that do not have a similar category in Tier-2, a medication from any category in Tier-2 may be used.)

Diabetes Medications Special Prior Authorization Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least three other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member.

Diabetes Medications*			
Tier-1	**Tier-2+**	**Tier-3**	**Special PA**
Biguanides metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®) **Sulfonylureas** chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide Micronized (Micronase®) tolbutamide **Alpha-Glucosidase Inhibitors** acarbose (Precose®) **Glinides** nateglinide (Starlix®) **repaglinide (Prandin®)** **Thiazolidinedione** **pioglitazone (Actos®)**	**DPP-4 Inhibitors** saxagliptin (Onglyza®) saxagliptin/metformin (Kombiglyze®) sitagliptin (Januvia®) sitagliptin/metformin (Janumet®) sitagliptin/metformin ER (Janumet XR®) **Glinides** repaglinide/metformin (Prandimet®) **GLP-1 Agonists** exenatide (Byetta®) exenatide (Bydureon®) liraglutide (Victoza®)	**DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto™) **Thiazolidinediones** pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®) **Alpha-Glucosidase Inhibitors** miglitol (Glyset®) **SGLT 2 Inhibitor** canagliflozin (Invokana™) **canagliflozin/metformin (Invokamet™)** dapagliflozin (Farxiga™) **dapagliflozin/metformin (Xigduo™ XR)** **empagliflozin (Jardiance®)** **Dopamine Agonist** **bromocriptine (Cycloset®)** **SGLT-2/DPP-4 Inhibitor** **empagliflozin/linagliptin (Glyxambi®)** **GLP-1 Agonists** **albiglutide (Tanzeum™)** **dulaglutide (Trulicity™)**	**Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®) **Amylinomimetic** pramlintide (Symlin®)

* Tier structure based on supplemental rebate participation.

+ Rebated Products

Furthermore, the College of Pharmacy recommends the prior authorization of Afrezza® (insulin human inhalation powder) with the following criteria:

Afrezza® (Insulin Human) Inhalation Powder Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why other rapid-acting injectable insulins are not appropriate; and
4. For the indication of type 1 diabetes, the member must use Afrezza® with a long-acting insulin; and
5. The member must not smoke or have chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD).

Lastly, the College of Pharmacy recommends the prior authorization of Toujeo® (insulin glargine) with the following criteria:

Toujeo® (Insulin Glargine) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why member cannot use Lantus® (insulin glargine), and member must be using a minimum of 100 units of Lantus® (insulin glargine) per injection.

Appendix D

Vote to Prior Authorize
Ruconest® (C1 Esterase Inhibitor)

Oklahoma Health Care Authority
June 2015

Recommendations

The College of Pharmacy recommends prior authorization of Ruconest® (C1 esterase inhibitor) with the following criteria:

Ruconest® (C1 Esterase Inhibitor) Approval Criteria:

1. An FDA approved diagnosis of hereditary angioedema; and
2. Ruconest® must be used for *treatment* of acute attacks of hereditary angioedema; and
3. A patient-specific, clinically significant reason why the member cannot use Berinert® (C1 esterase inhibitor, human).

Appendix E

Vote to Prior Authorize Hemangeol™ (Propranolol Oral Solution), Sotylize™ (Sotalol Oral Solution), and Prestalia® (Perindopril/Amlodipine)

Oklahoma Health Care Authority
June 2015

Recommendations

The College of Pharmacy recommends the prior authorization of Hemangeol™ (propranolol oral solution) and Sotylize™ (sotalol oral solution) with the following criteria:

Hemangeol™ (Propranolol Hydrochloride Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of treatment of proliferating infantile hemangioma requiring systemic therapy; and
2. A patient-specific, clinically significant reason why the member cannot use the generic propranolol solutions (20mg/5mL and 40mg/5mL) which are available without prior authorization.

Sotylize™ (Sotalol Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of life-threatening ventricular arrhythmias or for the maintenance of normal sinus rhythm in patients with highly symptomatic atrial fibrillation/flutter; and
2. A patient-specific, clinically significant reason why the member cannot use sotalol oral tablets in place of the oral solution formulation; and
3. A quantity limit of 64mL per day or 1,920mL per 30 days will apply.

Additionally, the College of Pharmacy recommends the addition of Prestalia® (perindopril/amlodipine) to Tier-3 of the ACE Inhibitor/Calcium Channel Blocker category with the following criteria:

Prestalia® (Perindopril/Amlodipine) Approval Criteria:

1. An FDA approved diagnosis; and
2. Documented trials of inadequate response to two Tier-1 angiotensin converting enzyme inhibitors (ACEIs) in combination with amlodipine; and
3. A patient-specific, clinically significant reason why the member cannot use the individual components separately; and
4. A quantity limit of 30 tablets per 30 days will apply.

Angiotensin Converting Enzyme Inhibitor (ACEI)/ Calcium Channel Blocker (CCB) Combinations*		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE + Tier-1 CCB		benazepril/amlodipine (Lotrel®)
		enalapril/felodipine (Lexxel®)
		perindopril/amlodipine (Prestalia®)
		trandolapril/verapamil (Tarka®)

*Tier-2 criterion applies for Tier-3 medications when there are no Tier-2 medications available.

Antihypertensive Tier-2 Approval Criteria:

(or Tier-3 medication when no Tier-2 medications exist)

1. A documented inadequate response to two Tier-1 medications (trials must include medication from all available classes where applicable); or
2. An adverse drug reaction to all Tier-1 classes of medications; or
3. Previous stabilization on the Tier-2 medication; or
4. A unique indication for which the Tier-1 antihypertensive medications lack

Appendix F

Calendar Year 2014 Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Invega Trinza™ (3-Month Paliperidone Palmitate Injection)

Oklahoma Health Care Authority
June 2015

Current Prior Authorization Criteria

Tier-1 products are available without prior authorization for age five years and older. Prior authorization requests for members younger than five years are reviewed by an OHCA-contracted child psychiatrist.

Atypical Antipsychotic Tier-2 Approval Criteria:

1. Trials of two Tier-1 products (not including clozapine), at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. Trials of two Tier-1 products (not including clozapine), at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
2. Trials 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.

Approval Criteria for Atypical Antipsychotics as Adjunctive Treatment for Major Depression Disorder:

Authorization of Abilify® (aripiprazole), Seroquel XR® (quetiapine extended release), or Symbyax® (olanzapine/fluoxetine) for a diagnosis of major depressive disorder requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and duloxetine) that did not yield adequate response. Tier structure applies.

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

Tier structure based on supplemental rebate participation.
*Mandatory generic plan applies
+ May be rebated to Tier-2 status only
¥ Does not count toward a Tier-1 trial
ER = extended-release

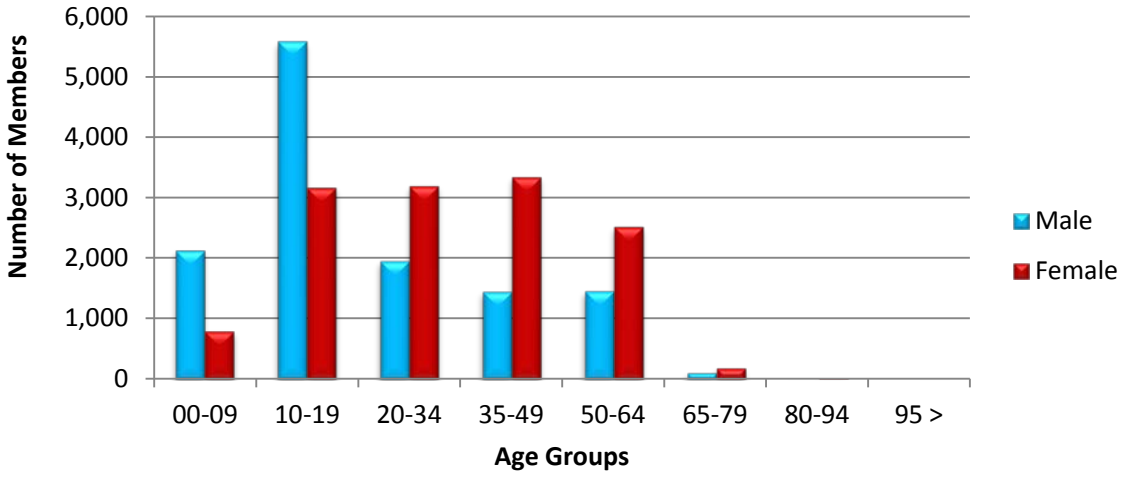
Utilization of Atypical Antipsychotic Medications: Calendar Year 2014

Comparison of Calendar Years

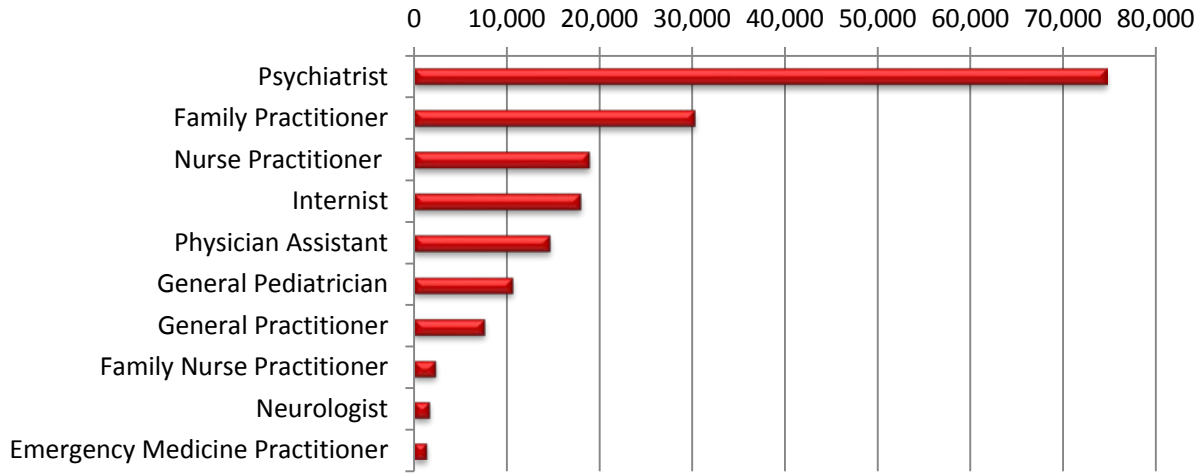
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	26,472	185,074	$48,445,980.50	$261.77	$8.65	7,618,754	5,599,891
2014	25,982	185,349	$52,664,907.67	$284.14	$9.36	7,673,020	5,624,862
% Change	**-1.90%**	**0.10%**	**8.70%**	**8.50%**	**8.20%**	**0.70%**	**0.40%**
Change	**-490**	**275**	**$4,218,927.17**	**$22.37**	**$0.71**	**54,266**	**24,971**

*Total number of unduplicated members.

Demographics of Members Utilizing Atypical Antipsychotic Medications



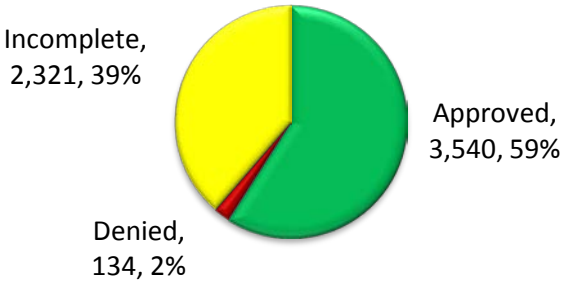
Top Prescriber Specialties of Atypical Antipsychotic Medications by Number of Claims



Prior Authorization of Atypical Antipsychotics

There were 5,995 petitions submitted for the Atypical Antipsychotic Medication Product Based Prior Authorization category during calendar 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.

Status of Petitions



There were 84 petitions submitted for atypical antipsychotics during calendar year 2014 that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations

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

Anticipated Patent Expirations:

- Invega® (paliperidone tablets): October 2014, however, generic is not currently available.
- Fanapt® (iloperidone tablets): November 2016
- Seroquel XR® (quetiapine extended-release tablets): May 2017
- Latuda® (lurasidone tablets): July 2018
- Saphris® (asenapine sublingual tablets): April 2026

New FDA Approvals:

- September 2014: The FDA approved a new dosage form of Abilify Maintena® (aripiprazole extended-release injection), a dual-chamber syringe. The pre-filled, dual chamber syringe contains the sterile water for reconstitution in one chamber and the lyophilized drug in another chamber for an all-in-one reconstitution and administration. The single-use vials for reconstitution will also still be available.
- November 2014: The FDA approved a label expansion for Invega® Sustenna® (paliperidone extended-release injection) to include treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants.
- December 2014: The FDA approved a label expansion for Abilify Maintena® (aripiprazole extended-release injection) to include treatment of acutely relapsed adults with schizophrenia based on a 12-week short-term trial with concomitant oral aripiprazole for the first two weeks.
- March 2015: Saphris® (asenapine) was granted approval by the FDA as monotherapy for the acute treatment of manic or mixed episodes associated with bipolar-1 disorder in pediatric patients (ages 10-17 years).
- April 2015: The patent for Abilify® (aripiprazole tablets) expired in April 2015 and generic aripiprazole tablets are currently available through multiple generic manufacturers; however, generic pricing is currently comparable to the brand formulation price.
- May 2015:The FDA approved Invega Trinza™ (3-month Paliperidone palmitate injection), a 3-month injection indicated for the treatment of schizophrenia in patients after they have been adequately treated with Invega Sustenna® (1-month paliperidone injection) for at least four months. It is the first and only four-times-a-year treatment for schizophrenia.

Invega Trinza™ (3-Month Paliperidone Palmitate Injection)[7,8] Product Summary

Indications: Invega Trinza™ (3-Month paliperidone palmitate injection), a 3-month injection, is an atypical antipsychotic indicated for the treatment of schizophrenia in patients after they have been adequately treated with Invega Sustenna® (1-month paliperidone palmitate extended-release injectable suspension) for at least four months.

Dosing:

- Invega Trinza™ is available as an extended-release injectable suspension in the following strengths:
  - 273mg
  - 410mg
  - 546mg
  - 819mg
- Invega Trinza™ should only be used after the patient has been adequately treated with the 1-month paliperidone injection for at least four months.
- Invega Trinza™ should be administered once every three months by a health care professional.
- The starting dose of Invega Trinza™ is based on the last dose of Invega® Sustenna® given.
- Invega Trinza™ is not recommended in moderate to severe renal impairment (creatinine clearance < 50 mL/min)

Mechanism of Action:

- Paliperidone palmitate is hydrolyzed to paliperidone. The mechanism of action of paliperidone is unknown. It has been proposed that the therapeutic activity of paliperidone in schizophrenia is mediated through a combination of central dopamine Type-2 (D2) and serotonin Type-2 (5HT2A) receptor antagonism.

Contraindications:

- Known hypersensitivity to paliperidone, risperidone, or to any excipients in the formulation.

Warnings and Precautions:

- Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients with Dementia-Related Psychosis: There is an increased incidence of cerebrovascular adverse reactions (e.g. stroke, transient ischemic attack, including fatalities) in patients using Invega Trinza™. Invega Trinza™ is not approved for use in patients with dementia-related psychosis.
- Neuroleptic Malignant Syndrome (NMS): NMS should be managed with immediate discontinuation of drug and close monitoring.
- QT Prolongation: Avoid use of Invega Trinza™ with drugs that also increase QT interval and in patients with risk factors for prolonged QT interval.
- Tardive Dyskinesia: Discontinue Invega Trinza™ if clinically appropriate.
- Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include:
  - Hyperglycemia and Diabetes Mellitus: Monitor for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients with diabetes or patients at risk for diabetes.
  - Dyslipidemia: Undesirable alterations have been observed.
  - Weight Gain: Significant weight gain has been reported. Monitor weight gain.

- Orthostatic Hypotension and Syncope: Use Invega Trinza™ with caution in patients with known cardiovascular or cerebrovascular disease and patients predisposed to hypotension.
- Leukopenia, Neutropenia, and Agranulocytosis: Monitor complete blood count in patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia. Consider discontinuation if there is a clinically significant decline in WBC in the absence of other causative factors.
- Hyperprolactinemia: Prolactin elevations can occur and persist during chronic administration of Invega Trinza™.
- Potential for Cognitive and Motor Impairment: Patients should use caution when operating machinery while on Invega Trinza™ therapy.
- Seizures: Use Invega Trinza™ cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.

Adverse Reactions: The most common adverse reactions during clinical trials were the following (incidence of ≥5% and occurring at least twice as often as placebo):

- Injection Site Reaction
- Weight Increase
- Headache
- Upper Respiratory Tract Infection
- Akathisia
- Parkinsonism

Clinical Studies:

- The efficacy of Invega Trinza™ was evaluated in a long-term, double-blind, placebo-controlled, randomized-withdrawal trial with a primary efficacy endpoint of time to first relapse.
- A total of 506 patients entered the three phase trial consisting of 17-week flexible dose open-label period with 1-month paliperidone in which the dose could be adjusted at weeks 5 and 9. Patients had to be clinically stable on 1-month paliperidone at week 17 to enter the second part of the trial, a 12-week open-label treatment period with Invega Trinza™. A total of 379 patients received a single-dose of Invega Trinza™ which was a 3.5 multiple of the last dose of 1-month paliperidone. Patients had to remain stable before entry into the third period of study which was the double-blind treatment period. In the third period, 305 stabilized patients were randomized 1:1 to receive placebo or Invega Trinza™.
- The Invega Trinza™ treated patients showed a statistically significant longer time to relapse compared to placebo. The median time to relapse in the placebo group (23%) was 274 days. The median time to relapse in the Invega Trinza™ group could not be estimated due to low percentage (7.4%) of subjects with relapse.

Cost and Launch Date:

- Cost information is currently unavailable. Janssen Pharmaceuticals anticipates that Invega Trinza™ will be commercially available by mid-June.

Recommendations

The College of Pharmacy recommends the following:

1. Moving aripiprazole tablets to Tier-1 when the state maximum allowable cost is comparable to other Tier-1 generic medications.
2. After moving aripiprazole tablets to Tier-1, the College of Pharmacy recommends requiring a trial of aripiprazole as one of the Tier-1 trials for authorization of a Tier-2 medication.
    a. If an aripiprazole tablets trial is inappropriate for the member, a patient-specific, clinically significant reason would need to be provided; or
    b. An FDA approved diagnosis not covered by aripiprazole.
3. Additionally, after moving aripiprazole tablets to Tier-1 the College of Pharmacy recommends adding a required trial of aripiprazole to the approval criteria for atypical antipsychotics as adjunctive treatment for major depressive disorder.
4. Lastly, the College of Pharmacy recommends placing Invega Trinza™ into Tier-3 of the atypical antipsychotic product based prior authorization category. Current criteria for this category will apply.

Atypical Antipsychotic Tier-2 Approval Criteria:

1. Trials of two Tier-1 products at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
    a. One of the Tier-1 trials must include a trial with aripiprazole unless member has a patient-specific, clinically significant reason why aripiprazole is not appropriate or an FDA approved diagnosis not covered by aripiprazole.
    b. Clozapine does not count towards a Tier-1 trial.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. Trials of two Tier-1 products at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
    a. One of the Tier-1 trials must include a trial with aripiprazole unless member has a patient-specific, clinically significant reason why aripiprazole is not appropriate or an FDA approved diagnosis not covered by aripiprazole.
    b. Clozapine does not count towards a Tier-1 trial.
2. Trials 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.

Approval Criteria for Atypical Antipsychotics as Adjunctive Treatment for Major Depression Disorder:

Authorization of Seroquel XR® (quetiapine extended release) or Symbyax® (olanzapine/fluoxetine) for a diagnosis of major depressive disorder requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and duloxetine) and a trial of aripiprazole tablets that did not yield adequate response. Tier structure applies.

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

Tier structure based on supplemental rebate participation.
*Mandatory generic plan applies
+ May be rebated to Tier-2 status only
¥ Does not count toward a Tier-1 trial
ER = extended-release

Utilization Details of Atypical Antipsychotic Medications: Calendar Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 UTILIZATION						
RISPERIDONE ORAL PRODUCTS						
RISPERIDONE TAB 1MG	19,807	4,756	$170,351.56	$0.28	$8.60	0.32%
RISPERIDONE TAB 0.5MG	15,237	3,952	$149,456.26	$0.32	$9.81	0.28%
RISPERIDONE TAB 2MG	10,417	2,572	$117,124.72	$0.36	$11.24	0.22%
RISPERIDONE TAB 0.25MG	6,763	1,771	$56,341.72	$0.27	$8.33	0.11%
RISPERIDONE TAB 3MG	5,312	1,029	$60,427.80	$0.37	$11.38	0.11%
RISPERIDONE TAB 4MG	2,976	568	$39,896.97	$0.42	$13.41	0.08%
RISPERIDONE SOL 1MG/ML	1,156	194	$44,805.56	$1.24	$38.76	0.09%
RISPERIDONE TAB 0.5MG OD	295	79	$18,781.55	$2.11	$63.67	0.04%
RISPERIDONE TAB 1MG ODT	179	54	$13,716.72	$2.56	$76.63	0.03%
RISPERIDONE TAB 2MG ODT	141	38	$17,434.62	$3.52	$123.65	0.03%
RISPERIDONE TAB 0.25 ODT	71	22	$12,547.46	$6.04	$176.72	0.02%
RISPERIDONE TAB 3MG ODT	38	11	$10,387.34	$9.20	$273.35	0.02%
RISPERDAL TAB 0.25MG	34	7	$4,286.34	$4.20	$126.07	0.01%
RISPERDAL TAB 3MG	33	4	$30,558.00	$30.87	$926.00	0.06%
RISPERDAL TAB 1MG	24	3	$16,445.99	$23.23	$685.25	0.03%
RISPERIDONE TAB 4MG ODT	23	5	$11,601.10	$17.74	$504.40	0.02%
RISPERDAL SOL 1MG/ML	18	3	$11,307.95	$22.89	$628.22	0.02%
RISPERDAL TAB 4MG	12	1	$18,598.31	$51.95	$1,549.86	0.04%
RISPERDAL TAB 2MG	11	5	$3,667.49	$11.11	$333.41	0.01%
QUETIAPINE PRODUCTS						
QUETIAPINE TAB 100MG	8,908	2,623	$117,276.46	$0.42	$13.17	0.22%
QUETIAPINE TAB 200MG	7,026	1,854	$122,486.42	$0.56	$17.43	0.23%
QUETIAPINE TAB 300MG	6,485	1,515	$186,967.59	$0.92	$28.83	0.36%
QUETIAPINE TAB 50MG	6,104	1,959	$74,415.25	$0.40	$12.19	0.14%
QUETIAPINE TAB 400MG	5,661	1,072	$145,977.41	$0.82	$25.79	0.28%
QUETIAPINE TAB 25MG	3,941	1,263	$44,868.73	$0.38	$11.39	0.09%
QUETIAPINE TAB 200MG	132	62	$2,796.33	$0.71	$21.18	0.01%
SEROQUEL TAB 100MG	23	9	$314.38	$0.46	$13.67	0.00%
SEROQUEL TAB 25MG	16	8	$202.25	$0.46	$12.64	0.00%
SEROQUEL TAB 400MG	14	2	$15,966.97	$38.02	$1,140.50	0.03%
SEROQUEL TAB 300MG	10	1	$15,675.36	$52.25	$1,567.54	0.03%
SEROQUEL TAB 50MG	3	1	$56.94	$0.63	$18.98	0.00%
SEROQUEL TAB 200MG	1	1	$13.67	$0.46	$13.67	0.00%
CLOZAPINE PRODUCTS						
CLOZAPINE TAB 100MG	5,323	387	$430,712.53	$4.20	$80.92	0.82%
CLOZAPINE TAB 50MG	934	85	$38,624.68	$2.43	$41.35	0.07%
CLOZAPINE TAB 200MG	857	83	$74,650.10	$4.99	$87.11	0.14%
CLOZAPINE TAB 25MG	640	72	$20,127.65	$1.80	$31.45	0.04%
CLOZARIL TAB 100MG	54	5	$64,407.83	$56.70	$1,192.74	0.12%
OLANZAPINE PRODUCTS						
OLANZAPINE TAB 20MG	4,252	856	$83,814.15	$0.60	$19.71	0.16%
OLANZAPINE TAB 10MG	4,097	1,232	$47,225.16	$0.37	$11.53	0.09%
OLANZAPINE TAB 5MG	2,624	983	$25,321.68	$0.31	$9.65	0.05%
OLANZAPINE TAB 15MG	1,855	470	$30,786.87	$0.52	$16.60	0.06%
OLANZAPINE TAB 2.5MG	794	316	$7,160.57	$0.29	$9.02	0.01%
OLANZAPINE TAB 20MG	689	125	$12,938.46	$0.62	$18.78	0.02%
OLANZAPINE TAB 20MG ODT	550	224	$178,207.64	$5.95	$324.01	0.34%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
OLANZAPINE TAB 10MG ODT	430	159	$50,337.10	$3.34	$117.06	0.10%
OLANZAPINE TAB 7.5MG	349	102	$3,565.40	$0.35	$10.22	0.01%
OLANZAPINE TAB 15MG ODT	286	102	$56,089.13	$4.27	$196.12	0.11%
OLANZAPINE TAB 5MG ODT	239	104	$17,421.62	$2.30	$72.89	0.03%
OLANZAPINE 5MG TAB	69	13	$660.95	$0.32	$9.58	0.00%
OLANZAPINE TAB 10MG	54	35	$656.42	$0.41	$12.16	0.00%
ZYPREXA TAB 20MG	41	4	$45,659.88	$37.12	$1,113.66	0.09%
OLANZAPINE TAB 15MG	26	8	$326.08	$0.42	$12.54	0.00%
ZYPREXA TAB 15MG	13	2	$10,532.73	$27.01	$810.21	0.02%
OLANZAPINE TAB 15 MG	12	11	$184.73	$0.51	$15.39	0.00%
ZYPREXA TAB 2.5MG	12	2	$3,625.05	$10.07	$302.09	0.01%
ZYPREXA TAB 10MG	11	2	$5,286.69	$16.02	$480.61	0.01%
OLANZAPINE INJ 10MG	8	4	$639.75	$45.70	$79.97	0.00%
ZYPREXA TAB 5MG	4	2	$1,558.33	$12.99	$389.58	0.00%
OLANZAPINE TAB 15MG	1	1	$16.75	$0.54	$16.75	0.00%
ZIPRASIDONE PRODUCTS						
ZIPRASIDONE CAP 80MG	2,753	493	$326,485.80	$3.82	$118.59	0.62%
ZIPRASIDONE CAP 40MG	1,842	641	$156,472.11	$2.79	$84.95	0.30%
ZIPRASIDONE CAP 60MG	1,562	396	$164,516.40	$3.42	$105.32	0.31%
ZIPRASIDONE CAP 20MG	1,483	570	$165,515.88	$3.73	$111.61	0.31%
GEODON CAP 80MG	100	19	$22,797.01	$7.60	$227.97	0.04%
GEODON CAP 40MG	51	13	$10,371.90	$7.00	$203.37	0.02%
GEODON CAP 60MG	26	6	$3,839.86	$4.92	$147.69	0.01%
GEODON CAP 20MG	17	7	$3,200.73	$6.47	$188.28	0.01%
GEODON INJ 20MG	8	7	$1,188.22	$30.47	$148.53	0.00%
RISPERDONE INJECTABLE PRODUCTS						
RISPERDAL INJ 50MG	701	88	$786,189.93	$42.57	$1,121.53	1.49%
RISPERDAL INJ 25MG	366	64	$169,677.95	$21.55	$463.60	0.32%
RISPERDAL INJ 37.5MG	245	51	$199,447.06	$32.28	$814.07	0.38%
RISPERDAL INJ 12.5MG	35	5	$10,365.81	$10.71	$296.17	0.02%
TIER-1 SUBTOTAL	**134,284**	**33,193**	**$4,765,361.81**	**$9.76**	**$249.71**	**9.06%**
TIER-2 UTILIZATION						
ARIPIPRAZOLE ORAL PRODUCTS						
ABILIFY TAB 10MG	7,378	1,849	$6,065,616.56	$26.30	$822.12	11.52%
ABILIFY TAB 5MG	7,013	1,830	$5,467,110.42	$25.90	$779.57	10.38%
ABILIFY TAB 15MG	4,806	1,171	$3,789,209.70	$25.00	$788.43	7.19%
ABILIFY TAB 20MG	3,432	757	$3,948,047.71	$37.05	$1,150.36	7.50%
ABILIFY TAB 30MG	2,748	463	$3,339,289.48	$37.70	$1,215.17	6.34%
ABILIFY TAB 2MG	2,155	552	$1,715,724.76	$26.16	$796.16	3.26%
ABILIFY SOL 1MG/ML	160	40	$147,649.72	$30.51	$922.81	0.28%
ABILIFY DISC TAB 10MG	16	3	$11,769.92	$24.52	$735.62	0.02%
ABILIFY DISC TAB 15MG	10	2	$8,107.01	$29.48	$810.70	0.02%
PALIPERIDONE INJECTABLE PRODUCTS						
INVEGA SUST INJ 234/1.5	2,722	436	$5,292,754.29	$67.71	$1,944.44	10.05%
INVEGA SUST INJ 156MG/ML	1,508	300	$1,962,468.42	$45.63	$1,301.37	3.73%
INVEGA SUST INJ 117/0.75	446	81	$433,583.82	$34.18	$972.16	0.82%
INVEGA SUST INJ 78/0.5ML	50	13	$32,541.05	$22.41	$650.82	0.06%
INVEGA SUST INJ 39/0.25	4	3	$1,297.71	$11.28	$324.43	0.00%
LURASIDONE PRODUCTS						
LATUDA TAB 40MG	2,234	634	$1,690,357.03	$24.39	$756.65	3.21%
LATUDA TAB 80MG	1,702	429	$1,442,352.71	$27.72	$847.45	2.74%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
LATUDA TAB 120MG	759	169	$856,845.84	$35.81	$1,128.91	1.63%
LATUDA TAB 20MG	561	236	$390,462.11	$23.26	$696.01	0.74%
LATUDA TAB 60MG	369	137	$282,436.87	$25.09	$765.41	0.54%
QUETIAPINE EXTENDED-RELEASE PRODUCTS						
SEROQUEL XR TAB 400MG	1,554	260	$1,566,173.56	$32.58	$1,007.83	2.97%
SEROQUEL XR TAB 300MG	1,380	279	$1,172,553.73	$27.00	$849.68	2.23%
SEROQUEL XR TAB 200MG	577	142	$289,289.43	$15.23	$501.37	0.55%
SEROQUEL XR TAB 150MG	437	114	$185,860.95	$13.88	$425.31	0.35%
SEROQUEL XR TAB 50MG	313	82	$97,666.13	$9.74	$312.03	0.19%
PALIPERIDONE ORAL PRODUCTS						
INVEGA TAB 6MG	1,324	278	$1,333,835.94	$32.82	$1,007.43	2.53%
INVEGA TAB 9MG	762	142	$976,893.68	$38.28	$1,282.01	1.85%
INVEGA TAB 3MG	467	116	$396,939.92	$27.64	$849.98	0.75%
INVEGA TAB 1.5MG	40	10	$29,048.57	$25.66	$726.21	0.06%
ASENAPINE ORAL PRODUCTS						
SAPHRIS SUB 10MG	990	234	$597,525.62	$20.15	$603.56	1.13%
SAPHRIS SUB 5MG	472	156	$269,289.75	$18.48	$570.53	0.51%
ARIPIPRAZOLE INJECTABLE PRODUCTS						
ABILIFY MAIN INJ 400MG	752	133	$1,196,057.27	$55.62	$1,590.50	2.27%
ABILIFY MAIN INJ 300MG	98	25	$118,259.53	$41.91	$1,206.73	0.22%
ABILIFY INJ 9.75MG	7	1	$205.10	$14.65	$29.30	0.00%
ILOPERIDONE PRODUCTS						
FANAPT TAB 6MG	596	143	$401,542.82	$22.60	$673.73	0.76%
FANAPT TAB 8MG	501	108	$337,208.86	$23.95	$673.07	0.64%
FANAPT TAB 12MG	367	63	$257,733.50	$25.05	$702.27	0.49%
FANAPT TAB 4MG	287	70	$202,396.94	$24.24	$705.22	0.38%
FANAPT TAB 10MG	190	31	$132,293.23	$24.70	$696.28	0.25%
FANAPT TAB 2MG	119	40	$82,991.88	$23.20	$697.41	0.16%
FANAPT TAB 1MG	10	5	$7,697.94	$23.33	$769.79	0.01%
FANAPT PAK	6	6	$656.04	$18.74	$109.34	0.00%
TIER-2 SUBTOTAL	**49,322**	**11,543**	**$46,529,745.52**	**$16.25**	**$452.87**	**88.33%**
TIER-3 UTILIZATION						
CLOZAPINE ORALLY DISINTEGRATING PRODUCTS						
FAZACLO TAB 100/ODT	583	53	$600,912.24	$40.84	$1,030.72	1.14%
CLOZAPINE TAB 100/ODT	329	30	$184,210.16	$27.89	$559.91	0.35%
FAZACLO TAB 25MG ODT	233	17	$59,624.92	$11.21	$255.90	0.11%
FAZACLO TAB 150MG	182	22	$149,048.97	$31.10	$818.95	0.28%
FAZACLO TAB 200MG	176	20	$267,283.19	$52.01	$1,518.65	0.51%
CLOZAPINE TAB 25MG ODT	117	8	$18,251.84	$11.23	$156.00	0.03%
OLANZAPINE/FLUOXETINE COMBINATION PRODUCTS						
OLANZ/FLUOX CAP 6-25MG	42	6	$17,805.16	$12.01	$423.93	0.03%
OLANZ/FLUOX CAP 12-50MG	28	6	$31,728.97	$25.18	$1,133.18	0.06%
SYMBYAX CAP 12-50MG	19	3	$13,449.48	$23.60	$707.87	0.03%
OLANZ/FLUOX CAP 12-25MG	15	4	$16,517.87	$18.99	$1,101.19	0.03%
SYMBYAX CAP 6-25MG	10	2	$4,258.26	$14.19	$425.83	0.01%
OLANZ/FLUOX CAP 6-50MG	4	1	$4,404.98	$12.24	$1,101.25	0.01%
OLANZ/FLUOX CAP 3-25MG	3	1	$752.76	$8.36	$250.92	0.00%
CLOZAPINE ORAL SOLUTION PRODUCTS						
VERSACLOZ 50MG/ML	2	1	$1,551.54	$48.49	$775.77	0.00%
TIER-3 SUBTOTAL	**1,743**	**174**	**$1,369,800.34**	**$17.10**	**$483.26**	**2.59%**
TOTAL	**185,349**	**25,982***	**$52,664,907.67**	**$9.36**	**$284.14**	**100.00%**

*Total number of unduplicated members.

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Appendix G

30-Day Notice to Prior Authorize Cholbam™ (Cholic Acid)

Oklahoma Health Care Authority
June 2015

Introduction[1,2,3,4,5,6,7]

Cholic acid is a primary bile acid synthesized from cholesterol and produced by the liver. Bile acids are stored in the gallbladder and secreted into the intestine to help digest fat, oil, and fat-soluble vitamins by aiding in combining fatty substances with digestive enzymes to assist in absorption.

Bile acids are produced from cholesterol with the help of sixteen enzymes. A genetic mutation that causes defects or deficiency in any of these enzymes can lead to a failure in normal bile acid production and formation of abnormal bile acids. These defects are known as bile acid synthesis disorders (B.A.S.D.) and can present in two different ways, single enzyme defects with intact peroxisomal structure and peroxisomal biogenesis disorders.

The estimated incidence of B.A.S.D. due to single enzyme defects is 1 to 9 per one million live births. There are at least ten different disorders in which there is a deficiency of a single peroxisomal enzyme but the structure of the peroxisome is intact.

Peroxisomal biogenesis disorders are a group of disorders that occur due to a genetically inherited condition in which an individual lacks normal peroxisomes resulting in multiple metabolic abnormalities. Peroxisomes are cellular organelles that are a part of important cellular functions, such as beta-oxidation of very-long-chain fatty acids (VLCFA), production of plasmalogens, and synthesis of bile acid. Zellweger Syndrome, Neonatal Adrenoleukodystrophy, and Infantile Refsum disease, listed in decreasing severity, are peroxisomal biogenesis disorders of the Zellweger Syndrome spectrum. Zellweger Syndrome is the most common and severe peroxisomal disorder which is estimated to occur in 1 in 50,000-100,000 people in the United States.

B.A.S.D. come with several consequences that can be detrimental to a person's health including cholestasis, malnutrition due to inability to digest fatty foods and fat-soluble vitamins, and hepatotoxicity due to an accumulation of incompletely formed bile acids. If untreated, the more severe cases can progress to cause life-threatening complications including cirrhosis and liver failure requiring a liver transplant. There are no current guidelines to treat B.A.S.D. and treatment has been directed toward specific symptoms in affected individuals. Supplemental treatment with fat-soluble vitamins is essential for individuals with malabsorption. Ursodeoxycholic acid (trade name Ursodiol®) has shown to provide short-term benefit to some patients with B.A.S.D, however long-term benefit is limited because it cannot compensate for the basic underlying pathophysiology and patients still experience adverse outcomes. Chenodeoxycholic acid (trade name Chenodiol®) is a bile acid that has shown benefit in small studies to treat individuals specifically with cerebrotendinous xanthomatosis, an autosomal recessive lipid storage disease caused by disruption of bile acid synthesis; however, chenodeoxycholic acid is only FDA approved to aid in gallstone dissolution.

Treatment with oral cholic acid therapy increases the bile acid concentration in the digestive system to facilitate the absorption of fats and fat-soluble vitamins leading to a normal growth rate. Oral bile acid also blocks the affected bile production pathway so the abnormal bile acids and toxic substances cannot be produced, and improves bile flow to prevent cholestasis. Cholbam™ (cholic acid) is an oral bile acid FDA approved in March 2015 in ages three weeks and older, and is the first FDA approved treatment for B.A.S.D.

Cholbam™ (Cholic Acid) Product Summary[5,8,9]

FDA Approved: March 2015

Indications: Cholbam™ (cholic acid) is a bile acid indicated for the following:

1. Treatment of bile acid disorders due to single enzyme defects (SEDs).
2. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat-soluble vitamin absorption.

Limitations of Use: The safety and effectiveness of Cholbam™ on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established.

Dosing: Cholic acid is available in 50mg and 250mg strength capsules.

- The recommended dosage is 10mg/kg to 15 mg/kg once daily or in two divided doses, in pediatric patients and adults.
- The recommended dosage in patients with concomitant familial hypertriglyceridemia is 11mg/kg to 17mg/kg once daily or in two divided doses and is adjusted based on clinical response.
- Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase, bilirubin, and international normalized ration (INR) should be monitored every month for the first three months, every three months for the next nine months, every six months during the next three years and annually thereafter. The lowest dose of cholic acid that effectively maintains liver function should be administered.
- Cholic acid should be discontinued if liver function does not improve within three months of starting treatment, if complete biliary obstruction develops, or if there are persistent clinical or laboratory indicators of worsening liver function or cholestasis; liver function should be monitored and consideration should be given to restarting at a lower dose when parameters return to baseline.
- Cholic acid should be taken with food.
- Cholic acid should not be crushed or chewed. For patients unable to swallow the capsules, the capsules can be opened and the contents mixed with drink/food.

Mechanism of Action:

- Cholic acid is a primary bile acid synthesized from cholesterol in the liver. In bile acid synthesis disorders due to SEDs in the biosynthetic pathway, and in PDs including Zellweger spectrum disorders, deficiency of primary bile acids leads to unregulated accumulation of intermediate bile acids and cholestasis. Bile acids facilitate fat digestion and absorption by forming mixed micelles, and facilitate absorption of fat-soluble vitamins in the intestine.
- Endogenous bile acids including cholic acid enhance bile flow and provide the physiologic feedback inhibition of bile acid synthesis. The mechanism of action of cholic acid has not been fully established; however, it is known that cholic acid and its conjugates are endogenous ligands of the nuclear receptor, farnesoid X receptor (FXR). FXR regulates enzymes and transporters that are involved in bile acid synthesis and in the enterohepatic circulation to maintain bile acid homeostasis under normal physiologic conditions.

Contraindications: None.

Warnings and Precautions:

- Exacerbation of Liver Impairment: Monitor liver function and discontinue cholic acid if liver function worsens while on treatment.

Adverse Reactions:

- The most common adverse reactions reported with cholic acid use (≥1%) are diarrhea, reflux esophagitis, malaise, jaundice, skin lesion, nausea, abdominal pain, intestinal polyp, urinary tract infection, and peripheral neuropathy.

Efficacy:

- The efficacy of Cholbam™ for the treatment of patients with bile acid synthesis disorders due to SEDs (n = 50) and PDs (n = 29), including Zellweger spectrum disorders was based on a non-randomized, open-label trial of patients treated over an 18-year period. At the start of cholic acid treatment, the average age was 4 years in those with SED while the majority of patients with PDs were less than 2 years of age. Patients received cholic acid therapy for an average of 4.8 to 6 years.
- The response to treatment was evaluated by improvements in baseline liver function tests, a liver biopsy, and weight. Survival at the end of 3 years of treatment was also measured. Overall, 64% (28/44) of SED patients were responders, with 67% of patients having survived more than 3 years.
- Overall, 46% (11/24) of PD patients were responders, with 42% of patients having survived more than 3 years.

Utilization/Cost: There have been no pharmacy claims for Cholbam™ (cholic acid) since its approval in March 2015.

Medication Name	Strength	Cost/Capsule+	Cost/Day*	Cost/Year*
Cholbam™ (cholic acid)	50mg	$291.28	$6,990.72	$2,516,659.20
Cholbam™ (cholic acid	250mg	$876.48	$4,382.40	$1,577,664.00

+ Estimated acquisition cost per capsule.

*Dosing based on recommended dose of 15mg/kg for an 80kg patient.

Recommendations

The College of Pharmacy recommends the prior authorization of Cholbam™ (cholic acid) with the following criteria:

Cholbam™ (Cholic Acid) Approval Criteria:

1. An FDA approved diagnosis of:
    a. Treatment of bile acid disorders due to single enzyme defects (SEDs); or
    b. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat-soluble vitamin absorption; and
2. The prescriber must verify that AST, ALT, GGT, alkaline phosphatase, bilirubin and INR will be monitored every month for the first 3 months, every 3 months for the next 9 months, every 6 months during the next three years and annually thereafter.
3. Cholbam™ should be discontinued if liver function does not improve within 3 months of starting treatment, if complete biliary obstruction develops, or if there are persistent clinical or laboratory indicators of worsening liver function or cholestasis.
4. Initial approval will be for 3 months to monitor for compliance and liver function tests.
5. Continuation approvals will be granted for the duration of one year.
6. A quantity limit of 120 capsules per 30 days will apply. Quantity limit requests will be based on members' recent weight taken within the last 30 days.

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Appendix H

30-Day Notice to Prior Authorize
Natpara® (Parathyroid Hormone Injection)

Oklahoma Health Care Authority
June 2015

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

Hypoparathyroidism is a rare, complex endocrine deficiency disease that affects approximately 60,000 people in the United States. It is characterized by low serum calcium levels, elevated serum phosphorus levels, and absent or abnormally low levels of parathyroid hormone (PTH) in the systemic circulation. The most common cause of hypoparathyroidism is irreversible damage to or removal of the parathyroid glands during neck surgery during thyroidectomy, parathyroidectomy, or radical neck dissection. Non-surgical causes include inherited disorders such as DiGeorge's syndrome, autoimmune diseases, tumors, and idiopathic causes.

PTH plays a central role in maintaining the homeostasis of calcium and phosphorus in the body. When PTH is released in adequate levels, it works with vitamin D and calcitonin to maintain calcium and phosphorous levels in the blood stream through activity in the bowel, kidneys, and bones. PTH stimulates bone resorption via osteoclasts, releasing calcium and phosphate in the blood stream. In the kidney, PTH stimulates renal reabsorption of calcium allowing increased calcium returned to the bloodstream and promotes phosphate excretion. PTH also enhances the conversion of endogenous vitamin D to its active vitamin D metabolite which then increases the absorption of calcium and phosphate in the intestine.

When PTH secretion is compromised, bone cannot be adequately resorbed in response to low levels of serum calcium consequently resulting in bone formation outpacing bone resorption which can lead to abnormal bone formation, hypermineralization, and/or adynamic bone disease. When PTH is absent or low, the kidneys are unable to reabsorb calcium and maintain the proper levels of calcium in the blood stream. Increased calcium excretion may result in additional negative effects including nephrocalcinosis, kidney stones, and/or chronic kidney disease. The lack of phosphate excretion in the kidneys may lead to hyperphosphatemia which can result in deposition of calcium-phosphate complexes in soft tissues. Insufficient PTH also means the advanced vitamin D conversion does not occur resulting in less effective intestinal absorption of calcium.

The symptoms of hypoparathyroidism resulting from hypocalcemia and hyperphosphatemia can be widespread and effect several vital functions. Neuromuscular symptoms can include muscle cramping, twitching, tetany, spasms (ex. bronchospasms), paresthesias of the face and extremities, and seizures. Cardiac function may be compromised including prolonged QT interval, arrhythmia, depressed systolic function, and heart failure. Other complications include premature cataracts, calcifications of brain tissue, and psychiatric conditions.

There are currently no formal guidelines for the management of hypoparathyroidism; however, the goal of hypoparathyroidism treatment is to control symptoms while minimizing complications. Standard treatment has been supplementation with oral calcium and vitamin D;

however, increased intake of calcium and vitamin D can lead to the worsening of hypercalciuria and associated adverse effects on renal and central nervous systems. Thiazide diuretics such as hydrochlorothiazide enhance distal renal tubular calcium reabsorption and may provide some benefit in treating hypoparathyroidism. Several small studies have demonstrated benefit with treating patients with teriparatide (PTH 1-34), the fully active but truncated amino-terminal fragment of the parathyroid hormone (PTH 1-84); however, teriparatide, trade name Forteo®, is only FDA approved to treat osteoporosis.

In January 2015, the FDA approved Natpara® (parathyroid hormone, PTH 1-84) as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism. Natpara® is produced by recombinant DNA technology using a modified strain of *E. coli*. Natpara® carries a boxed warning that bone cancer (osteosarcoma) has been observed in rat studies. Natpara® is only available through a restricted Risk Evaluation and Mitigation Strategy (REMS) program.

Natpara® (Parathyroid Hormone Injection) Product Summary [4, 5, 6]

FDA Approved: January 2015

Indications: Natpara® (parathyroid hormone injection) is a parathyroid hormone indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitations of Use:

- Because of the potential risk of osteosarcoma, Natpara® is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.
- Natpara® was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations.
- Natpara® was not studied in patients with acute post-surgical hypoparathyroidism.

Dosing:

- Natpara® is available as a multiple-dose, dual-chamber glass cartridge containing sterile powder and diluent in 4 dosage strengths, 25mcg, 50mcg, 75mcg, and 100mcg, to be used with a Q-Cliq™ pen for injection.
- The dose of Natpara® should be individualized to achieve a serum calcium level in the lower half of the normal range.
- Confirm vitamin D stores are sufficient and serum calcium is above 7.5mg/dL before starting Natpara®.
- The starting dose of Natpara® is 50mcg injected once daily in the thigh. When starting Natpara®, the dose of active vitamin D should be decreased by 50%, if serum calcium is above 7.5mg/dL.
- Serum calcium levels should be monitored every 3 to 7 days after starting or adjusting the Natpara® dose and when adjusting either active vitamin D or calcium supplements dosing while using Natpara®.
- The dose of Natpara® may be increased in increments of 25mcg every four weeks up to a maximum of 100mcg if serum calcium cannot be maintained above 8mg/dL without an active form of vitamin D and/or calcium supplementation.

- The dose of Natpara® may be decreased as low as 25mcg per day if total serum calcium is repeatedly above 9mg/dL after the active form of vitamin D has been discontinued and calcium supplementation has been decreased to a dose sufficient to meet daily requirements.
- The maintenance dose should be the lowest dose that achieves a total serum calcium (albumin-corrected) within the lower half of the normal total serum calcium range (approximately 8 and 9mg/dL), without the need for active forms of vitamin D and with calcium supplementation sufficient to meet daily requirements.
- Serum calcium and 24-hour urinary calcium should be monitored per standard of care once a maintenance dose is achieved.

Mechanism of Action:

- Natpara® is a parathyroid hormone. Parathyroid hormone raises serum calcium by increasing renal tubular calcium reabsorption, increasing intestinal calcium absorption (i.e., by converting 25-OH vitamin D to 1,25 $(OH)_2$ vitamin D), and by increasing bone turnover which releases calcium into the circulation.

Contraindications: None.

Warnings and Precautions:

- Potential Risk of Osteosarcoma: Natpara® should be prescribed only to patients who cannot be well-controlled on calcium and active vitamin D. Natpara® use should be avoided in patients who are at increased risk for osteosarcoma.
- Severe Hypercalcemia: Serum calcium should be monitored when starting or adjusting the Natpara® dose and when making changes to co-administered drugs known to raise serum calcium.
- Severe Hypocalcemia: Severe hypocalcemia can occur with interruption or discontinuation of Natpara® treatment. Monitor serum calcium and replace calcium and vitamin D.
- Digoxin Toxicity: Hypercalcemia increases the risk of digoxin toxicity. In patients using Natpara® concomitantly with digoxin, monitor serum calcium more frequently and increase monitoring when initiating or adjusting Natpara®.

Adverse Reactions:

- The most common adverse reactions associated with Natpara® and occurring in greater than 10% of individuals were: paresthesia, hypocalcemia, headache, hypercalcemia, nausea, hypoaesthesia, diarrhea, vomiting, arthralgia, hypercalciuria, and pain in extremity.

Efficacy: The safety and effectiveness of Natpara® were evaluated in a trial of 124 patients with hypoparathyroidism. Response was defined as obtaining a greater than or equal to 50% reduction from baseline in the dose of active vitamin D, a greater than or equal to 50% reduction from baseline in the dose of calcium supplementation, and an albumin-corrected total serum calcium concentration of 7.5-10.6mg/dL.

- Results showed that 42% (p-value <0.001) of Natpara®-treated patients achieved normal blood calcium levels on reduced doses of calcium supplements and active forms of vitamin D, compared to 3% of placebo-treated patients.

Utilization/Cost: There have been no pharmacy claims for Natpara® (parathyroid hormone) since its approval in January 2015.

Medication Name	Strength	Cost/Cartridge +	Cost/Month*	Cost/Year*
Natpara® 50mcg cartridge	50mcg	$4,180.00	$8,360.00	$100,320.00

+ Estimated acquisition cost. Each cartridge supplies 14 doses.
*Recommended starting dose is 50mcg once daily. Currently, all strengths of Natpara® are flat priced.

Recommendations

The College of Pharmacy recommends the prior authorization of Natpara® (parathyroid hormone) with the following criteria:

Natpara® (Parathyroid Hormone) Approval Criteria:

1. An FDA approved diagnosis as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism; and
    a. Natpara® is not FDA approved for hypoparathyroidism caused by calcium-sensing receptor mutations.
    b. Natpara® is not FDA approved for hypoparathyroidism due to acute post-surgery.
2. Magnesium deficiency must be ruled out; and
3. Member must have pretreatment serum calcium above 7.5mg/dL before starting Natpara®; and
4. Prescriber must verify the member has sufficient 25-hydroxyvitamin D level per standard of care; and
5. Member must be unable to be adequately well-controlled on calcium supplements and active forms of vitamin D alone; and
6. Health care provider and dispensing pharmacy must be certified through the Natpara® REMS Program; and
7. A quantity limit of two cartridges (each package contains two 14-day cartridges) per 28 days will be set. The maximum covered dose will be 100mcg per day.

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Appendix I

Calendar Year 2014 Annual Review of ADHD & Narcolepsy Medications and 30-Day Notice to Prior Authorize Zenzedi® (Dextroamphetamine), Evekeo™ (Amphetamine), and Aptensio XR™ (Methylphenidate Extended-Release)

Oklahoma Health Care Authority
June 2015

Current Prior Authorization Criteria

ADHD & Narcolepsy Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

ADHD & Narcolepsy Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant; and
3. A trial with at least one long-acting Tier-2 stimulant that did not yield adequate response:
    a. Trials should have been within the last 365 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why member cannot use the available long-acting capsule formulation.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
    a. An FDA approved diagnosis; and
    b. Recent trials with a long-acting Tier-1 stimulant and a long-acting Tier-2 stimulant, and a trial of Intuniv® and Strattera® within the past six months, unless contraindicated, that did not yield adequate results; and
    c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate release tablets.

ADHD & Narcolepsy Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, and ProCentra® Solution Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available stimulant medications.
2. Daytrana®, Quillivant XR®, and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets.
3. Provigil®, Nuvigil®, and Xyrem® Criteria:
    a. An FDA approved diagnosis; and
    b. Use of Provigil® or Nuvigil® requires a patient-specific, clinically significant reason why member cannot use stimulant medications to improve wakefulness during the daytime.
    c. Use of Xyrem® requires recent trials with Tier-1 and Tier-2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past 6 months, unless contraindicated, that did not yield adequate results.
    d. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
    e. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0-4 years of age. All prior authorization requests for members younger than the age of 5 years must be reviewed by an OHCA contracted psychiatrist.

ADHD & Narcolepsy Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Daytrana™ (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) Methylin® (methylphenidate soln & chew tabs) Nuvigil® (armodafinil) ProCentra™ (dextroamphetamine) Provigil® (modafinil) Quillivant XR® (methylphenidate ER) Xyrem® (sodium oxybate)
Short-Acting			
Adderall® (amphetamine/ dextroamphetamine)			
Long-Acting			
Vyvanse® (lisdexamfetamine)	Adderall XR® brand name only (amphetamine/ dextroamphetamine ER)	amphetamine/ dextroamphetamine ER (generic Adderall XR®)	
Methylphenidate			
Short-Acting			
Focalin® (dexmethylphenidate) Methylin® (methylphenidate) Ritalin® (methylphenidate)			
Long-Acting			
Metadate CD® brand name only (methylphenidate ER) Metadate ER® (methylphenidate ER) Methylin ER® (methylphenidate ER) Ritalin SR® (methylphenidate ER)	Focalin XR® (dexmethylphenidate ER) Ritalin LA® brand name only (methylphenidate ER)	Concerta® (methylphenidate ER) methylphenidate ER (generic Metadate CD®) methylphenidate ER (generic Ritalin LA®)	
Non-Stimulants			
Intuniv® brand name only (guanfacine ER) Strattera® (atomoxetine)	guanfacine ER (generic Intuniv®)	Kapvay® (clonidine ER)	

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation.
ER = Extended-Release
SR = Sustained-Release

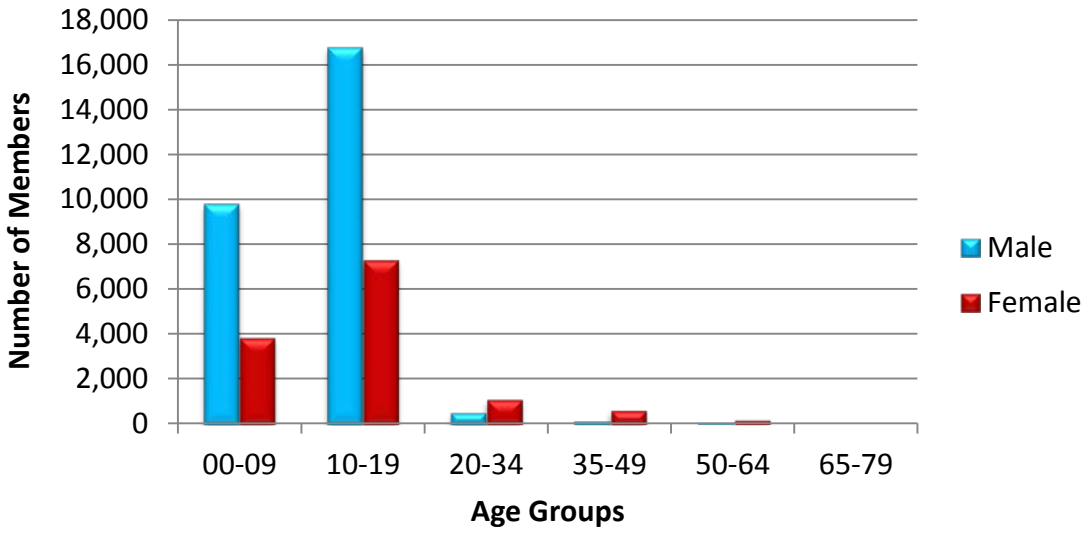
Utilization of ADHD & Narcolepsy Medications: Calendar Year 2014

Comparison of Calendar Years

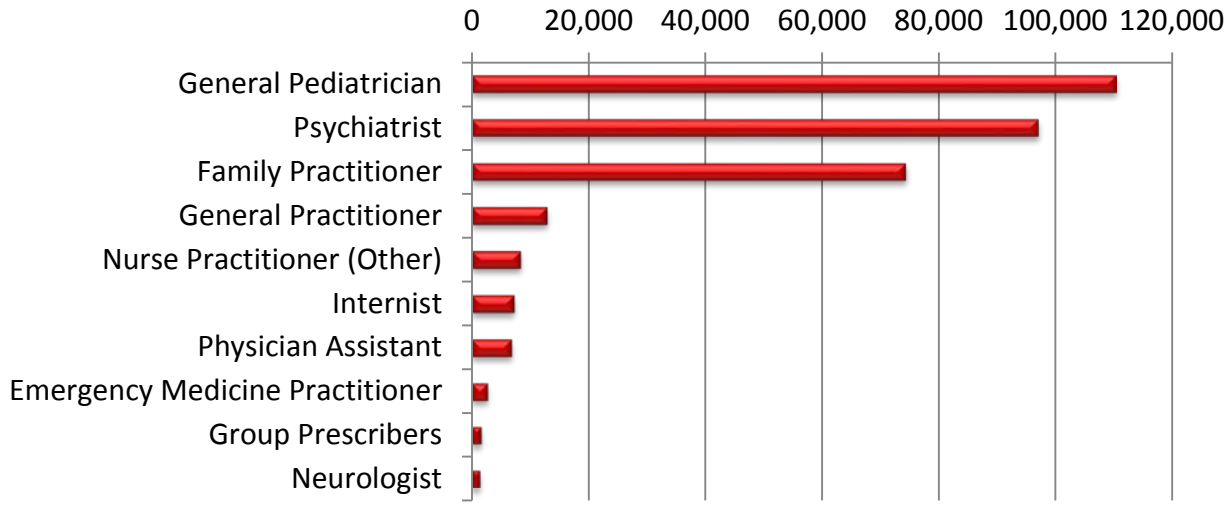
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	40,403	323,861	$55,687,197.54	$171.95	$5.80	11,217,973	9,607,851
2014	40,382	330,774	$60,639,202.28	$183.33	$6.17	11,569,680	9,833,872
% Change	**-0.10%**	**2.10%**	**8.90%**	**6.60%**	**6.40%**	**3.10%**	**2.40%**
Change	**-21**	**6,913**	**$4,952,004.74**	**$11.38**	**$0.37**	**351,707**	**226,021**

*Total number of unduplicated members.

Demographics of Members Utilizing ADHD & Narcolepsy Medications



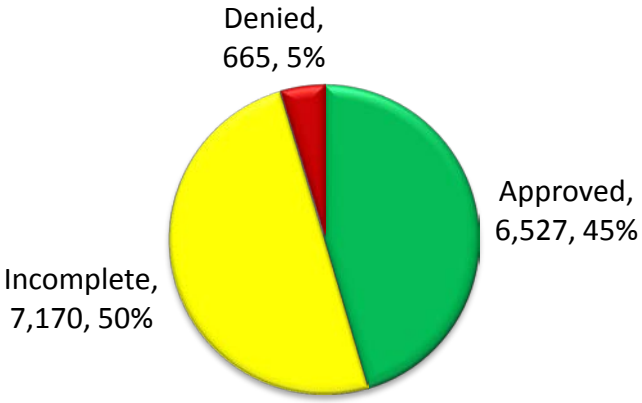
Top Prescriber Specialties of ADHD & Narcolepsy Medications by Number of Claims



Prior Authorization of ADHD & Narcolepsy Medications

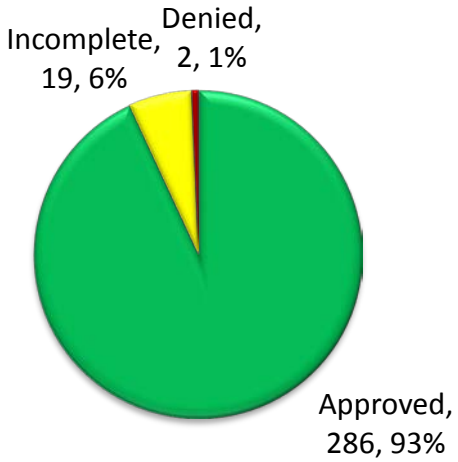
There were 14,362 petitions submitted for the ADHD & narcolepsy medication category during calendar year 2014. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



There were 307 petitions submitted for a total of 228 unique members for the ADHD & narcolepsy medication category during calendar year 2014 that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations



Market News and Updates[1,2]

Anticipated Patent Expirations:

- Strattera® (atomoxetine capsules): May 2017
- Focalin XR® (dexmethylphenidate ER capsules): November 2019
- Intuniv® (guanfacine ER tablets): January 2023
- Vyvanse® (lisdexamfetamine capsules): June 2023
- Nuvigil® (armodafinil tablets): June 2024
- Daytrana™ (methylphenidate ER patches): October 2025
- Quillivant XR® (methylphenidate ER suspension): February 2031
- Xyrem® (sodium oxybate solution): March 2033

New FDA Approvals:

- The FDA approved Zenzedi® (dextroamphetamine) in 2011 and Evekeo™ (amphetamine) in 2012; however, both medications just recently became available on the market.
- In January 2015, the FDA approved Vyvanse® (lisdexamfetamine) for the treatment of moderate-to-severe binge eating disorder (BED) in adults age 18 years or older. Vyvanse® is the first medication approved by the FDA for the treatment of moderate-to-severe BED.
- In April 2015, Aptensio XR™ (methylphenidate extended-release) was approved by the FDA and recently became available on the market.

Zenzedi® (Dextroamphetamine Sulfate Tablets) Product Summary[3,4]

Indications: Zenzedi® (dextroamphetamine) is indicated for the treatment of narcolepsy and for the treatment of attention deficit disorder with hyperactivity (ADHD).

Dosing:

- Zenzedi® is available as 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg, and 30mg oral, immediate-release tablets.
- The recommended dose of Zenzedi® for the treatment of narcolepsy is 5mg to 60mg per day in divided doses, based on the individual patient response.
- The recommended starting dose of Zenzedi® for the treatment of ADHD is 2.5mg daily for pediatric patients from three to five years of age, and 5mg once or twice daily for pediatric patients six years of age and older. The maximum recommended dose for the treatment of ADHD is 40mg per day. Only in rare case will it be necessary to exceed a total of 40mg per day.
- Regardless of indication, amphetamines, including Zenzedi®, should be administered at the lowest effective dosage and dosage should be individually adjusted.
- The first dose of Zenzedi® should be taken upon awakening, with additional (one or two) doses given at intervals of four to six hours. Late evening doses should be avoided because of the resulting insomnia.
- Where possible, treatment with Zenzedi® for ADHD should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.

Mechanism of Action: Zenzedi® (dextroamphetamine) is a central nervous system (CNS) stimulant and is the dextro isomer of the compound *d,l*-amphetamine sulfate, a sympathomimetic amine of the amphetamine group. Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

Contraindications:

- Advanced arteriosclerosis
- Symptomatic cardiovascular disease
- Moderate-to-severe hypertension
- Hyperthyroidism
- Glaucoma
- Agitated states
- Patients with a history of drug abuse
- During or within 14 days following the administration of monoamine oxidase inhibitors (MAOIs)
- Known hypersensitivity or idiosyncrasy to the sympathomimetic amines, including Zenzedi®

Safety:

- Zenzedi® has a boxed warning for a high potential for abuse. Prolonged use may lead to drug dependence and must be avoided. Misuse may cause sudden death and serious cardiovascular adverse events.
- Zenzedi® may cause sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems. CNS stimulant medications, including Zenzedi®, cause a modest increase in average blood pressure and average heart rate, and individuals may have larger increases.
- CNS stimulants, including Zenzedi®, may exacerbate symptoms of behavioral disturbance and thought disorder in patients with a pre-existing psychotic disorder, and may induce a mixed/manic episode in patients with bipolar disorder.
- CNS stimulants, including Zenzedi®, have been associated with weight loss and slowing of growth weight in pediatric patients. Growth (weight and height) should be closely monitored in pediatric patients treated with CNS stimulants.

Adverse Reactions: Common adverse reactions to Zenzedi® include increased heart rate, elevation of blood pressure, restlessness, dizziness, insomnia, headache, xerostomia, unpleasant taste, anorexia, weight loss, and aggressive behavior.

Efficacy: Zenzedi® was approved through an Abbreviated New Drug Application (ANDA) based on previous dextroamphetamine clinical trials.

Estimated Acquisition Cost: $5.60 per tablet

Evekeo™ (Amphetamine Sulfate Tablets) Product Summary[5,6]

Indications: Evekeo™ (amphetamine) is indicated for the treatment of narcolepsy, ADHD, and exogenous obesity.

Dosing:

- Evekeo™ is available as 5mg and 10mg oral, immediate-release tablets.
- The recommended dose of Evekeo™ for the treatment of narcolepsy is 5mg to 60mg per day in divided doses, based on the individual patient response.
- The recommended starting dose of Evekeo™ for the treatment of ADHD is 2.5mg daily for pediatric patients from three to five years of age, and 5mg once or twice daily for pediatric patients six years of age and older. The maximum recommended dose for the treatment of ADHD is 40mg per day. Only in rare cases will it be necessary to exceed a total of 40mg per day.
- Regardless of indication, amphetamines, including Evekeo™, should be administered at the lowest effective dosage and dosage should be individually adjusted.
- The first dose of Evekeo™ should be taken upon awakening, with additional (one or two) doses given at intervals of four to six hours. Late evening doses should be avoided because of the resulting insomnia.
- Where possible, treatment with Evekeo™ for ADHD should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.
- The recommended dose of Evekeo™ for exogenous obesity is 30mg per day, taken in divided doses of 5mg to 10mg, 30 to 60 minutes before meals. Evekeo™ is not recommended for the treatment of exogenous obesity in pediatric patients under twelve years of age.

Mechanism of Action: Evekeo™ (amphetamine) is a CNS stimulant and is a sympathomimetic amine of the amphetamine group. Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action.

Contraindications:

- Advanced arteriosclerosis
- Symptomatic cardiovascular disease
- Moderate to severe hypertension
- Hyperthyroidism
- Agitated states
- Patients with a history of drug abuse
- During or within 14 days following the administration of MAOIs
- Known hypersensitivity or idiosyncrasy to the sympathomimetic amines, including Evekeo™

Safety:

- Evekeo™ has a boxed warning for a high potential for abuse. Prolonged use may lead to drug dependence and must be avoided. Misuse may cause sudden death and serious cardiovascular adverse events.

- Evekeo™ may cause sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems. CNS stimulant medications, including Evekeo™, cause a modest increase in average blood pressure and average heart rate, and individuals may have larger increases.
- CNS stimulants, including Evekeo™, may exacerbate symptoms of behavioral disturbance and thought disorder in patients with a pre-existing psychotic disorder, and may induce a mixed/manic episode in patients with bipolar disorder.
- CNS stimulants, including Evekeo™, have been associated with weight loss and slowing of growth weight in pediatric patients. Growth (weight and height) should be closely monitored in pediatric patients treated with CNS stimulants.

Adverse Reactions: Common adverse reactions to Evekeo™ include increased systolic arterial pressure, weight loss, abdominal pain, loss of appetite, xerostomia, dizziness, headache, insomnia, and feeling nervous.

Efficacy: Evekeo™ was approved through an ANDA based on previous amphetamine clinical trials.

Cost Comparison:

Medication Name	Strength	Cost/Unit	Cost/Month
Evekeo™ (amphetamine)	10mg	5.24^{+}	$943.20
Adderall® (amphetamine)	10mg	$0.97*	$174.60

+Estimated Acquisition Cost (EAC)
*State Maximum Allowable Cost (SMAC)
Dosing based on maximum dose of 60mg/day.

Aptensio XR™ (Methylphenidate Extended-Release Capsules) Product Summary[7,8]

Indications: Aptensio XR™ (methylphenidate extended-release) is indicated for the treatment of ADHD.

Dosing:

- Aptensio XR™ is available as 10mg, 15mg, 20mg, 30mg, 40mg, 50mg, and 60mg oral, extended-release capsules.
- The recommended starting dose of Aptensio XR™ for the treatment of ADHD in patients six years of age and older is 10mg once daily in the morning with or without food.
- The dose of Aptensio XR™ may be titrated weekly in increments of 10mg. The dose should be individualized according to the needs and response of the patient. Daily doses above 60mg have not been studied and are not recommended.
- Aptensio XR™ may be taken whole or the capsule may be opened and the entire contents sprinkled onto applesauce. Patients should take the applesauce with sprinkled beads immediately in its entirety without chewing.
- Pharmacological treatment for ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of Aptensio XR™, and adjust dose as needed.

Mechanism of Action: Aptensio XR™ (methylphenidate) is a CNS stimulant.

Contraindications:

- During or within 14 days following the administration of MAOIs
- Hypersensitivity to methylphenidate or other components of the product

Safety:

- Aptensio XR™ has a boxed warning for a high potential for abuse and dependence. The risk of abuse should be assessed prior to prescribing, and signs and symptoms of abuse and dependence should be monitored while on therapy.
- Aptensio XR™ may cause sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems. Stimulant medications, including Aptensio XR™, cause an increase in blood pressure and heart rate, and all patients should be monitored for hypertension and tachycardia.
- Stimulants, including Aptensio XR™, may exacerbate symptoms of behavioral disturbance and thought disorder in patients with a pre-existing psychotic disorder, may induce a mixed/manic episode in patients with bipolar disorder, and may cause psychotic or manic symptoms in patients without a prior history of psychotic illness or mania.
- CNS stimulants, including Aptensio XR™, have been associated with weight loss and slowing of growth weight in pediatric patients. Growth (weight and height) should be closely monitored in pediatric patients treated with CNS stimulants.

Adverse Reactions: The most common adverse reactions leading to discontinuation of Aptensio XR™ in clinical trials were insomnia, nausea, and rapid heart rate. Other common adverse reactions include abdominal pain, pyrexia, headache, and decreased appetite.

Efficacy:

- The efficacy of Aptensio XR™ for the treatment of ADHD was established in a randomized, double-blind, placebo-controlled, flexible-dose, single center, cross-over trial in 26 pediatric patients aged six to twelve years (Study 1), and in a second randomized, double-blind, placebo-controlled, fixed-dose, multicenter trial in 221 pediatric patients aged six to seventeen years (Study 2).
- The primary efficacy endpoint for Study 1 was the average Swanson, Kotkin, Agler, M. Flynn, and Pelham (SKAMP) total score, comparing Aptensio XR™ to placebo. SKAMP is a validated 13-item teacher-rated scale that assesses the manifestations of ADHD in a classroom setting.
- Following a two to four week open-label dose optimization phase, patients were randomly assigned to Aptensio XR™ (dose from open-label phase) or placebo. After one week of treatment, patients were evaluated over a period of twelve hours. Subsequently, patients were given the opposite treatment for one week and returned for a second evaluation.
- The SKAMP total scores were statistically significantly better for Aptensio XR™ than for placebo at the test day average and at all time points post-dosing in Study 1.
- The primary efficacy endpoint for Study 2 was the mean decrease from baseline to the end of week one in the ADHD Rating Scale-IV (ADHD-RS-IV) total score. ADHD-RS-IV is an

18-item questionnaire that measures the core symptoms of ADHD and includes both hyperactive/impulsive and inattentive subscales.

- For both the 20mg/day and 40mg/day doses, Aptensio XR™ was superior to placebo in reduction of the ADHD-RS-IV total score at the end of week one, but not for the 10mg/day or 15mg/day doses in Study 2.

Cost Comparison:

Medication Name	Strength	Cost/Unit	Cost/Month
Aptensio XR™ (methylphenidate ER)	60mg	$6.86+	$205.80
methylphenidate ER (generic Concerta®)	54mg	$6.65*	$199.50

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

Binge Eating Disorder (BED) Summary[9,10,11,12]

Binge Eating Disorder (BED) is a type of eating disorder that is characterized by recurrent binge eating without the regular use of compensatory measures to counter the binge eating. BED differs from Bulimia Nervosa, which is characterized by a cycle of bingeing and compensatory behaviors (e.g. self-induced vomiting, laxative use, exercising excessively) designed to nullify the extra calories from the binge eating episode.

Symptoms of BED include frequent episodes of consuming very large amounts of food (but without behaviors to prevent weight gain), a feeling of being out of control during the binge eating episodes, feelings of strong shame or guilt regarding the binge eating, and indications that the binge eating is out of control, such as eating when not hungry, eating to the point of discomfort, or eating alone because of shame about the behavior. Health consequences of BED are most commonly associated with clinical obesity and include hypertension, hyperlipidemia, heart disease, diabetes mellitus, gallbladder disease, and musculoskeletal problems.

BED is the most common type of eating disorder, although it's estimated that 57% of patients with BED never receive treatment. The prevalence of BED is estimated to be approximately 1% to 5% of the general population, and affects women slightly more often than men. Patients who struggle with BED can be of normal weight or heavier than average weight. BED is often associated with symptoms of depression, and binge eating episodes occur, on average, at least once a week over a three month period.

The goals of treatment of BED are to reduce binge eating episodes, and when necessary, to lose weight. The most effective and long-lasting treatment for an eating disorder is some form of psychotherapy or counseling, coupled with careful attention to medical and nutritional needs. Some medications have been shown to be helpful. Recommended care is provided by a multidisciplinary team including but not limited to a psychologist, psychiatrist, social worker, nutritionist, and/or primary care physician. Care should be coordinated and provided by a healthcare professional with expertise and experience in dealing with eating disorders. Examples of psychotherapy useful for the treatment of BED include:

- **Cognitive Behavioral Therapy (CBT):** CBT may help patients with BED cope better with issues that can trigger binge-eating episodes, such as negative feelings about their body

or a depressed mood. CBT may give patients a better sense of control over their behavior and help them regular eating patterns.

- **Interpersonal Psychotherapy:** This type of therapy focuses on relationships with other people. The goal is to improve interpersonal skills (how the patients relate to others, including family, friends, and coworkers). This may help reduce binge eating that is triggered by poor relationships and unhealthy communication skills.
- **Dialectical Behavioral Therapy:** This form of therapy can help patients learn behavioral skills to help them tolerate stress, regulate their emotions, and improve their relationships with others, all of which can reduce the desire to binge eat.

Medications that may help reduce symptoms of BED include:

- **Topiramate:** As an off label use, topiramate has been found to reduce binge eating episodes. However, the risk of side effects may outweigh the benefits.
- **Selective Serotonin Reuptake Inhibitors (SSRIs):** SSRIs may be helpful in the treatment of BED. It is not clear how SSRIs can reduce binge eating, but it may relate to the treatment of co-occurring depression.
- **Vyvanse® (lisdexamfetamine):** Lisdexamfetamine is the first medication approved by the FDA for the treatment of moderate-to-severe BED. The efficacy of lisdexamfetamine in the treatment of BED was established in two 12-week randomized, double-blind, multi-center, parallel-group, placebo-controlled, dose-optimization trials in adults (aged 18 to 55 years) with moderate-to-severe BED. The primary efficacy outcome for the two studies was defined as the change from baseline at week 12 in the number of binge days per week. Patients from both studies on lisdexamfetamine had a statistically significantly greater reduction from baseline in mean number of binge days per week at week 12.

Recommendations

The College of Pharmacy recommends the following changes to the ADHD & Narcolepsy Medications Product Based Prior Authorization (PBPA) category:

1. Place Zenzedi® (dextroamphetamine) into the Special PA category.
    a. The existing criteria for other dextroamphetamine products in the Special PA category will apply.
2. Place Evekeo™ (amphetamine) into the Special PA category based on estimated acquisition cost and FDA approved indications.
    a. Evekeo™ (amphetamine) will require a covered diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available stimulant medications.
    a. A quantity limit of 90 tablets per 30 days will apply.
3. Place Aptensio XR™ (methylphenidate ER) into Tier-3 based on estimated acquisition cost.
    a. The existing criteria for this category will apply.
    b. A quantity limit of 30 capsules per 30 days will apply.
4. Add specific criteria for the new indication of binge eating disorder (BED) for Vyvanse® (lisdexamfetamine).

ADHD & Narcolepsy Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

ADHD & Narcolepsy Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant; and
3. A trial with at least one long-acting Tier-2 stimulant that did not yield adequate response:
    a. Trials should have been within the last 365 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why the member cannot use the available long-acting capsule formulation.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
    a. An FDA approved diagnosis; and
    b. Recent trials with a long-acting Tier-1 stimulant and a long-acting Tier-2 stimulant, and a trial of Intuniv® and Strattera® within the past six months, unless contraindicated, that did not yield adequate results; and
    c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate release tablets.

ADHD & Narcolepsy Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra® Solution, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available stimulant medications.
2. Daytrana®, Quillivant XR®, and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and
    b. A patient-specific, clinically significant reason why member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets.
3. Provigil®, Nuvigil®, and Xyrem® Criteria:
    a. An FDA approved diagnosis; and

b. Use of Provigil® or Nuvigil® requires a patient-specific, clinically significant reason why member cannot use stimulant medications to improve wakefulness during the daytime.
c. Use of Xyrem® requires recent trials with Tier-1 and Tier-2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past six months, unless contraindicated, that did not yield adequate results.
d. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
e. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0-4 years of age. All prior authorization requests for members under the age of 5 years must be reviewed by an OHCA contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria: Binge Eating Disorder (BED)
    a. An FDA approved diagnosis of moderate-to-severe binge eating disorder; and
    b. Member must be 18 years or older; and
    c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
    d. Authorizations will not be granted for a diagnosis of weight loss. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
    e. A quantity limit of 30 capsules per 30 days will apply; and
    f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

ADHD & Narcolepsy Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Daytrana™ (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) **Evekeo™ (amphetamine sulfate)** Methylin® (methylphenidate soln & chew tabs) Nuvigil® (armodafinil) ProCentra™ (dextroamphetamine) Provigil® (modafinil) Quillivant XR® (methylphenidate ER) Xyrem® (sodium oxybate) **Zenzedi® (dextroamphetamine)**
Short-Acting			
Adderall® (amphetamine/ dextroamphetamine)			
Long-Acting			
Vyvanse® (lisdexamfetamine)	Adderall XR® brand name only (amphetamine/ dextroamphetamine ER)	amphetamine/ dextroamphetamine ER (generic Adderall XR®)	
Methylphenidate			
Short-Acting			
Focalin® (dexmethylphenidate) Methylin® (methylphenidate) Ritalin® (methylphenidate)			
Long-Acting			
Metadate CD® brand name only (methylphenidate ER) Metadate ER® (methylphenidate ER) Methylin ER® (methylphenidate ER) Ritalin SR® (methylphenidate ER)	Focalin XR® (dexmethylphenidate ER) Ritalin LA® brand name only (methylphenidate ER)	**Aptensio XR™ (methylphenidate ER)** Concerta® (methylphenidate ER) methylphenidate ER (generic Metadate CD®) methylphenidate ER (generic Ritalin LA®)	
Non-Stimulants			
Intuniv® brand name only (guanfacine ER) Strattera® (atomoxetine)	guanfacine ER (generic Intuniv®)	Kapvay® (clonidine ER)	

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation.
ER = Extended-Release
SR = Sustained-Release

Utilization Details of ADHD & Narcolepsy Medications: Calendar Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
METHYLPHENIDATE PRODUCTS						
METHYLPHENID TAB 36MG ER	19,729	3,477	$3,724,432.20	$6.32	$188.78	6.14%
METHYLPHENID TAB 54MG ER	15,827	2,516	$2,649,503.47	$5.61	$167.40	4.37%
METHYLPHENID TAB 27MG ER	9,689	1,954	$1,466,162.64	$5.06	$151.32	2.42%
METHYLPHENID TAB 10MG	9,079	2,325	$355,461.74	$1.31	$39.15	0.59%
METHYLPHENID TAB 5MG	7,256	2,218	$217,376.38	$1.01	$29.96	0.36%
METHYLPHENID TAB 18MG ER	5,762	1,326	$847,552.36	$4.94	$147.09	1.40%
METHYLPHENID TAB 20MG	3,494	769	$237,485.00	$2.28	$67.97	0.39%
METADATE CD CAP 20MG	3,074	1,363	$603,930.94	$6.66	$196.46	1.00%
METADATE CD CAP 10MG	2,023	1,044	$394,049.51	$6.67	$194.78	0.65%
METHYLPHENID TAB 20MG ER	2,005	720	$122,567.06	$2.05	$61.13	0.20%
METADATE CD CAP 30MG	1,829	736	$360,815.61	$6.68	$197.27	0.60%
METADATE CD CAP 40MG	1,138	386	$305,805.92	$9.11	$268.72	0.50%
DAYTRANA DIS 30MG/9HR	713	101	$162,712.61	$7.61	$228.21	0.27%
METHYLPHENID TAB 20MG SR	706	271	$42,567.86	$2.02	$60.29	0.07%
METHYLPHENID TAB 10MG ER	681	322	$31,258.44	$1.53	$45.90	0.05%
METHYLPHENID SOL 5MG/5ML	470	129	$124,615.02	$8.84	$265.14	0.21%
METADATE CD CAP 60MG	407	114	$132,952.59	$11.01	$326.66	0.22%
METADATE CD CAP 50MG	366	126	$117,037.53	$10.81	$319.77	0.19%
DAYTRANA DIS 20MG/9HR	309	67	$80,051.19	$8.64	$259.07	0.13%
METHYLPHENID SOL 10MG/5ML	265	72	$84,788.17	$10.35	$319.96	0.14%
DAYTRANA DIS 15MG/9HR	237	50	$56,675.25	$7.97	$239.14	0.09%
METADATE TAB 20MG ER	231	96	$13,424.29	$1.96	$58.11	0.02%
QUILLIVANT SUS XR	225	59	$51,861.59	$7.25	$230.50	0.09%
RITALIN LA CAP 30MG	213	60	$47,035.28	$7.31	$220.82	0.08%
RITALIN LA CAP 20MG	207	65	$38,770.78	$6.33	$187.30	0.06%
RITALIN LA CAP 40MG	204	38	$41,601.24	$6.80	$203.93	0.07%
DAYTRANA DIS 10MG/9HR	191	55	$44,446.52	$7.51	$232.70	0.07%
METHYLIN TAB 10MG	147	44	$2,957.14	$0.69	$20.12	0.00%
RITALIN LA CAP 10MG	138	48	$23,723.74	$5.81	$171.91	0.04%
METHYLPHENID CAP 30MG ER	92	15	$11,502.76	$4.16	$125.03	0.02%
METHYLPHENID CAP 20MG ER	90	17	$11,018.79	$4.08	$122.43	0.02%
RITALIN TAB 10MG	68	19	$2,966.96	$1.61	$43.63	0.00%
RITALIN TAB 20MG SR	62	19	$6,273.59	$3.37	$101.19	0.01%
CONCERTA TAB 36MG	58	8	$15,211.49	$8.75	$262.27	0.03%
METHYLPHENID CAP 40MG ER	54	9	$6,811.70	$4.20	$126.14	0.01%
METHYLPHENID CAP 30MG	44	11	$6,321.47	$4.90	$143.67	0.01%
METHYLPHENID CAP 20MG	32	9	$9,238.60	$10.15	$288.71	0.02%
METHYLPHENID CAP 40MG	25	8	$4,754.98	$6.52	$190.20	0.01%
METHYLPHENID CAP 60MG	24	10	$5,896.01	$8.19	$245.67	0.01%
METHYLIN SOL 10MG/5ML	18	7	$5,878.78	$10.67	$326.60	0.01%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
METHYLIN SOL 5MG/5ML	18	10	$5,965.21	$11.21	$331.40	0.01%
CONCERTA TAB 54MG	17	4	$4,589.13	$9.00	$269.95	0.01%
CONCERTA TAB 18MG	10	2	$2,282.06	$7.61	$228.21	0.00%
RITALIN TAB 20MG	9	1	$1,527.73	$5.66	$169.75	0.00%
METHYLIN TAB 20MG ER	9	9	$390.81	$1.45	$43.42	0.00%
METHYLPHENID CAP 50MG	7	3	$1,710.44	$8.14	$244.35	0.00%
METHYLPHENID CAP 10MG	5	4	$719.47	$4.80	$143.89	0.00%
METHYLIN TAB 5MG	5	4	$72.66	$0.48	$14.53	0.00%
METHYLIN TAB 20MG	3	2	$84.51	$0.94	$28.17	0.00%
CONCERTA TAB 27MG	2	1	$316.06	$5.27	$158.03	0.00%
METHYLIN TAB 10MG ER	1	1	$26.09	$0.87	$26.09	0.00%
SUBTOTAL	**87,268**	**13,744***	**$12,485,181.37**	**$4.80**	**$143.07**	**20.59%**
LISDEXAMFETAMINE PRODUCTS						
VYVANSE CAP 30MG	18,962	5,825	$3,863,264.63	$6.88	$203.74	6.37%
VYVANSE CAP 20MG	14,843	5,426	$3,007,192.69	$6.86	$202.60	4.96%
VYVANSE CAP 40MG	13,024	3,448	$2,666,676.46	$6.89	$204.75	4.40%
VYVANSE CAP 50MG	9,950	2,338	$2,028,172.87	$6.84	$203.84	3.34%
VYVANSE CAP 70MG	7,170	1,180	$1,475,944.24	$6.89	$205.85	2.43%
VYVANSE CAP 60MG	6,095	1,262	$1,237,759.63	$6.80	$203.08	2.04%
SUBTOTAL	**70,044**	**13,645***	**$14,279,010.52**	**$6.87**	**$203.86**	**23.55%**
AMPHETAMINE/DEXTROAMPHETAMINE PRODUCTS						
AMPHETAMINE TAB 10MG	12,236	3,021	$576,853.79	$1.59	$47.14	0.95%
AMPHETAMINE TAB 5MG	7,708	2,245	$349,363.59	$1.54	$45.32	0.58%
ADDERALL XR CAP 20MG	7,376	1,537	$1,707,963.70	$7.75	$231.56	2.82%
ADDERALL XR CAP 30MG	7,286	1,133	$1,628,718.25	$7.48	$223.54	2.69%
AMPHETAMINE TAB 20MG	6,947	1,458	$386,155.65	$1.86	$55.59	0.64%
ADDERALL XR CAP 15MG	5,034	1,072	$1,120,525.17	$7.47	$222.59	1.85%
ADDERALL XR CAP 10MG	4,933	1,172	$1,098,993.20	$7.50	$222.78	1.81%
AMPHETAMINE TAB 30MG	3,611	633	$189,272.81	$1.76	$52.42	0.31%
ADDERALL XR CAP 25MG	2,839	556	$631,906.25	$7.46	$222.58	1.04%
AMPHETAMINE TAB 15MG	2,486	632	$127,744.40	$1.73	$51.39	0.21%
ADDERALL XR CAP 5MG	1,056	321	$236,738.20	$7.52	$224.18	0.39%
AMPHETAMINE TAB 7.5MG	473	138	$23,518.39	$1.68	$49.72	0.04%
AMPHETAMINE CAP 20MG ER	305	53	$54,912.60	$6.01	$180.04	0.09%
AMPHETAMINE TAB 12.5MG	218	48	$14,873.86	$2.29	$68.23	0.02%
AMPHETAMINE CAP 30MG ER	215	41	$26,479.00	$4.14	$123.16	0.04%
AMPHETAMINE CAP 10MG ER	126	24	$15,821.50	$4.22	$125.57	0.03%
ADDERALL TAB 10MG	78	59	$16,029.92	$7.07	$205.51	0.03%
AMPHETAMINE CAP 15MG ER	71	17	$8,809.72	$4.16	$124.08	0.01%
AMPHETAMINE CAP 25MG ER	58	10	$7,317.02	$4.21	$126.16	0.01%
ADDERALL TAB 15MG	51	23	$13,436.24	$8.84	$263.46	0.02%
ADDERALL TAB 5MG	44	23	$9,386.32	$7.11	$213.33	0.02%
ADDERALL TAB 20MG	38	26	$10,167.28	$9.30	$267.56	0.02%
ADDERALL TAB 30MG	30	16	$7,043.17	$8.10	$234.77	0.01%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AMPHETAMINE CAP 5MG ER	29	10	$3,687.08	$4.28	$127.14	0.01%
ADDERALL TAB 7.5MG	3	3	$882.80	$9.81	$294.27	0.00%
SUBTOTAL	**63,251**	**9,747***	**$8,266,599.91**	**$4.39**	**$130.70**	**13.63%**
DEXMETHYLPHENIDATE PRODUCTS						
FOCALIN XR CAP 10MG	6,932	1,586	$1,543,260.02	$7.46	$222.63	2.54%
FOCALIN XR CAP 20MG	6,803	1,365	$1,565,615.07	$7.72	$230.14	2.58%
DEXMETHYLPH TAB 10MG	6,147	1,515	$282,533.25	$1.54	$45.96	0.47%
DEXMETHYLPH TAB 5MG	4,423	1,344	$141,477.64	$1.08	$31.99	0.23%
DEXMETHYLPH CAP 15MG ER	4,368	1,102	$787,029.11	$6.05	$180.18	1.30%
DEXMETHYLPH CAP 30MG ER	2,982	591	$497,287.14	$5.58	$166.76	0.82%
FOCALIN XR CAP 5MG	2,241	595	$487,890.52	$7.33	$217.71	0.80%
FOCALIN XR CAP 15MG	2,077	847	$458,579.59	$7.43	$220.79	0.76%
FOCALIN XR CAP 25MG	2,039	427	$500,650.31	$8.23	$245.54	0.83%
DEXMETHYLPH CAP 40MG ER	750	136	$139,177.90	$6.25	$185.57	0.23%
DEXMETHYLPH TAB 2.5MG	722	341	$21,076.88	$1.02	$29.19	0.03%
FOCALIN XR CAP 30MG	409	247	$85,777.93	$7.04	$209.73	0.14%
FOCALIN XR CAP 35MG	365	72	$93,763.03	$8.58	$256.89	0.15%
FOCALIN TAB 5MG	359	180	$15,066.13	$1.42	$41.97	0.02%
FOCALIN TAB 10MG	333	167	$21,689.09	$2.21	$65.13	0.04%
FOCALIN TAB 2.5MG	246	91	$8,490.51	$1.17	$34.51	0.01%
FOCALIN XR CAP 40MG	160	79	$36,608.49	$7.78	$228.80	0.06%
DEXMETHYLPHE CAP 5MG ER	30	20	$5,719.42	$6.35	$190.65	0.01%
DEXMETHYLPHE CAP 5MG	12	10	$2,145.45	$5.96	$178.79	0.00%
SUBTOTAL	**41,398**	**5,814***	**$6,693,837.48**	**$5.44**	**$161.69**	**11.04%**
GUANFACINE PRODUCTS						
INTUNIV TAB 2MG	13,047	2,426	$3,549,016.34	$9.13	$272.02	5.85%
INTUNIV TAB 3MG	10,280	1,845	$2,827,173.85	$9.22	$275.02	4.66%
INTUNIV TAB 4MG	6,909	1,074	$1,911,037.87	$9.28	$276.60	3.15%
INTUNIV TAB 1MG	4,954	1,221	$1,337,823.74	$9.15	$270.05	2.21%
GUANFACINE TAB 2MG ER	411	314	$102,812.72	$8.35	$250.15	0.17%
GUANFACINE TAB 3MG ER	391	293	$98,139.94	$8.47	$251.00	0.16%
GUANFACINE TAB 4MG ER	313	234	$80,595.42	$8.60	$257.49	0.13%
GUANFACINE TAB 1MG ER	134	98	$34,201.90	$8.51	$255.24	0.06%
SUBTOTAL	**36,439**	**4,898***	**$9,940,801.78**	**$9.16**	**$272.81**	**16.39%**
ATOMOXETINE PRODUCTS						
STRATTERA CAP 40MG	8,104	2,321	$2,216,375.38	$9.26	$273.49	3.66%
STRATTERA CAP 25MG	6,768	2,172	$1,799,684.77	$9.07	$265.91	2.97%
STRATTERA CAP 60MG	4,885	1,198	$1,293,947.49	$8.89	$264.88	2.13%
STRATTERA CAP 80MG	3,349	830	$960,533.51	$9.42	$286.81	1.58%
STRATTERA CAP 18MG	3,120	1,206	$812,112.19	$9.17	$260.29	1.34%
STRATTERA CAP 10MG	2,121	861	$555,210.02	$9.46	$261.77	0.92%
STRATTERA CAP 100MG	918	185	$270,669.60	$9.24	$294.85	0.45%
SUBTOTAL	**29,265**	**6,314***	**$7,908,532.96**	**$9.18**	**$270.24**	**13.04%**
CLONIDINE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
CLONIDINE TAB 0.1MG ER	2,196	306	$537,341.90	$8.21	$244.69	0.89%
KAPVAY TAB 0.1 MG	161	58	$54,371.78	$11.33	$337.71	0.09%
SUBTOTAL	**2,357**	**321***	**$591,713.68**	**$8.42**	**$251.05**	**0.98%**
MODAFINIL PRODUCTS						
MODAFINIL TAB 200MG	304	44	$174,049.92	$19.23	$572.53	0.29%
MODAFINIL TAB 100MG	25	11	$10,928.72	$15.77	$437.15	0.02%
SUBTOTAL	**329**	**54***	**$184,978.64**	**$18.98**	**$562.25**	**0.31%**
ARMODAFINIL PRODUCTS						
NUVIGIL TAB 250MG	129	20	$63,589.12	$16.43	$492.94	0.10%
NUVIGIL TAB 150MG	79	22	$41,922.79	$17.78	$530.67	0.07%
NUVIGIL TAB 200MG	5	3	$2,671.21	$17.81	$534.24	0.00%
SUBTOTAL	**213**	**39***	**$108,183.12**	**$16.96**	**$507.90**	**0.18%**
DEXTROAMPHETAMINE PRODUCTS						
DEXTROAMPHET CAP 15MG ER	78	12	$20,308.21	$8.78	$260.36	0.03%
DEXTROAMPHET TAB 10MG	64	12	$7,477.64	$3.99	$116.84	0.01%
DEXTROAMPHET CAP 10MG ER	22	7	$4,429.79	$6.87	$201.35	0.01%
DEXTROAMPHET CAP 5MG ER	20	3	$1,799.03	$3.00	$89.95	0.00%
DEXTROAMPHET TAB 5MG	7	4	$402.82	$2.07	$57.55	0.00%
DEXTROAMPHET SOL 5MG/5ML	2	2	$541.88	$9.03	$270.94	0.00%
SUBTOTAL	**193**	**34***	**$34,959.37**	**$6.15**	**$181.14**	**0.06%**
SODIUM OXYBATE PRODUCTS						
XYREM SOL 500MG/ML	17	5	$145,403.45	$286.79	$8,553.14	0.24%
SUBTOTAL	**17**	**5***	**$145,403.45**	**$286.79**	**$8,553.14**	**0.24%**
TOTAL	**330,774**	**40,382***	**$60,639,202.28**	**$6.17**	**$183.33**	**100.00%**

*Total number of unduplicated members.

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[3] Zenzedi® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/zenzedi/. Last revised 5/1/15. Last accessed 5/15/15.
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[12] National Eating Disorders Association: Binge Eating Disorder, A New Diagnosis in the Diagnostic and Statistical Manual of Mental Disorders. Available online at: https://www.nationaleatingdisorders.org/sites/default/files/ResourceHandouts/MultiPageRGB.pdf. Last revised 2013. Last accessed 5/28/15.

Appendix J

Fiscal Year 2014 Annual Review of Otic Anti-Infectives and 30-Day Notice to Prior Authorize Xtoro™ (Finafloxacin)

Oklahoma Health Care Authority
June 2015

Current Prior Authorization Criteria

Otic Anti-Infectives		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	chloroxylenol/benzocaine/HC (Trioxin®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	chloroxylenol/pramoxine/zinc/ glycerin (Zinotic®, Zinotic® ES)	antipyrine/benzocaine/ glycerin/zinc (Neotic®)
neomycin/polymyxin B/ HC (Cortisporin®, Pediotic®)	ciprofloxacin (Cetraxal®)	
ofloxacin (Floxin® Otic)*	ciprofloxacin/HC (Cipro® HC)	
	neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S)	

Tier structure based on supplemental rebate participation.
HC = hydrocortisone
*Dexamethasone 0.1% ophthalmic solution is available without prior authorization for members who require concomitant steroid therapy.

Otic Anti-Infectives Tier-2 Approval Criteria:

1. Member must have an adequate 14-day trial of at least two Tier-1 medications; or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier-1 medications or infection by an organism not known to be covered by any of the Tier-1 medications.

Acetasol® HC, Vosol® HC, and Neotic® Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent (within 6 months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

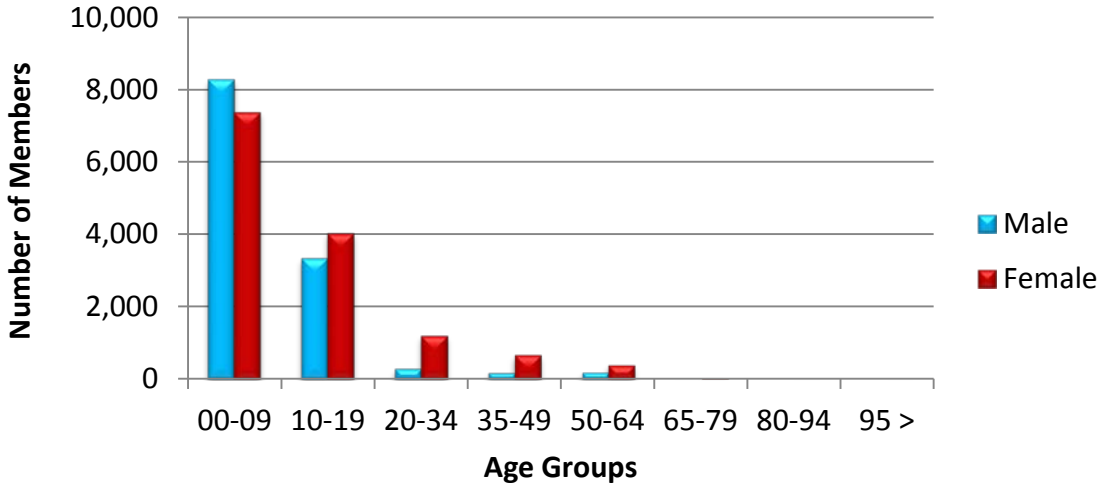
Utilization of Otic Anti-Infectives: Fiscal Year 2014

Comparison of Fiscal Years

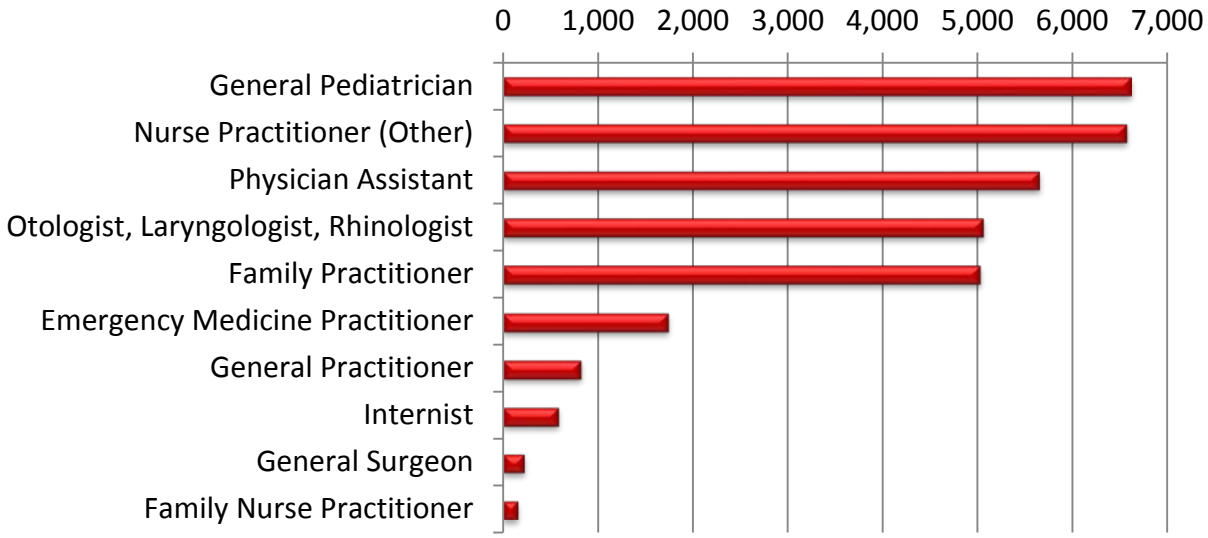
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	26,783	34,473	$699,480.54	$20.29	$2.05	292,329	340,989
2014	26,088	33,201	$868,508.97	$26.16	$2.58	281,129	337,224
% Change	**-2.60%**	**-3.70%**	**24.20%**	**28.90%**	**25.90%**	**-3.80%**	**-1.10%**
Change	**-695**	**-1,272**	**$169,028.43**	**$5.87**	**$0.53**	**-11,200**	**-3,765**

*Total number of unduplicated members.

Demographics of Members Utilizing Otic Anti-Infectives

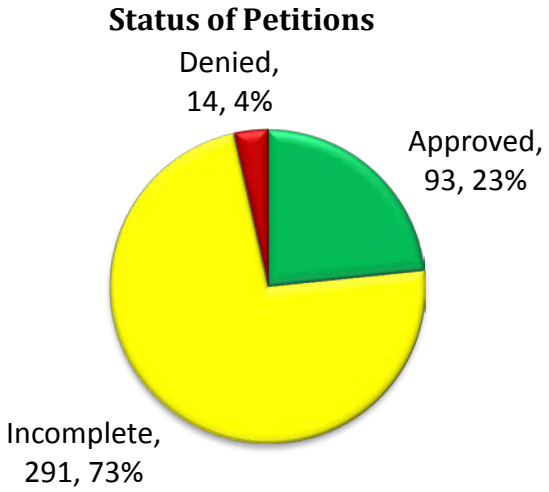


Top Prescriber Specialties of Otic Anti-Infectives by Number of Claims



Prior Authorization of Otic Anti-Infectives

There were 398 petitions submitted for the otic anti-infectives medication category during fiscal year 2014. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2]

Anticipated Patent Expirations:

- Cipro HC® (ciprofloxacin/hydrocortisone otic suspension): June 2015
- Ciprodex® (ciprofloxacin/dexamethasone otic suspension): June 2025

New FDA Approvals:

- In December 2014, the FDA approved Xtoro™ (finafloxacin otic suspension) for the treatment of acute otitis externa. Acute otitis externa is often referred to as swimmer's ear and is an infection in the outer ear and ear canal. Xtoro™ is not yet available on the market.

Xtoro™ (Finafloxacin Otic Suspension) Product Summary[3,45,6]

Indications: Xtoro™ (finafloxacin) is indicated for the treatment of acute otitis externa (AOE) with or without an otowick, caused by susceptible strains of *Pseudomonas aeruginosa* and *Staphylococcus aureus* in patients age one year and older.

Dosing:

- Xtoro™ is available as a 0.3% finafloxacin otic suspension.
- The recommended dosing of finafloxacin is to instill four drops in the affected ear(s) twice daily for seven days.
- The recommended dosing of finafloxacin for patients requiring use of an otowick is to instill eight drops in the affected ear(s) for the initial dose, followed by four drops in the affected ear(s) twice daily for seven days.

- The otic suspension should be warmed by holding the bottle in the hand for one or two minutes prior to dosing in order to avoid dizziness which may result from the instillation of a cold suspension. The bottle should be shaken well before each use.
- To instill the drops, the patient should lie with the affected ear upward, instill the drops, and maintain the position for 60 seconds to facilitate penetration of the drops into the ear canal, then repeat if necessary for the opposite ear.

Mechanism of Action: Finafloxacin is a fluoroquinolone antibacterial, which works by inhibiting bacterial type II topoisomerase enzymes, DNA gyrase, and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, and recombination. In both in vitro and clinical studies, finafloxacin has been shown to be active against most isolates of *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Contraindications: None

Safety:
- As with other antibacterial preparations, prolonged use of finafloxacin may lead to overgrowth of nonsusceptible organisms, including yeast and fungi. If this occurs, finafloxacin should be discontinued and alternative therapy instituted.
- Allergic reactions to finafloxacin may occur in patients with a history of hypersensitivity to finafloxacin, to other fluoroquinolones, or to any components of the medication. If this occurs, patients should discontinue use of finafloxacin and alternative therapy should be instituted.
- The safety and efficacy of finafloxacin in infants less than one year of age have not been established.

Adverse Reactions: The most common adverse reactions to finafloxacin reported in clinical trials, occurring at an incidence of 1%, include ear pruritus and nausea.

Efficacy:
- The safety and efficacy of finafloxacin as a treatment for acute otitis externa were established in two randomized, multicenter, vehicle-controlled studies in 1,234 patients between the ages of 6 months and 85 years.
- Among 560 patients (161 with an otowick) whose acute otitis externa was confirmed to be caused by *Pseudomonas aeruginosa* or *Staphylococcus aureus*, 71% of patients who received finafloxacin achieved clinical cure versus 37% of patients who received the vehicle. Finafloxacin was also superior to the vehicle for clearing the bacteria based on ear culture, and finafloxacin eased ear pain sooner than the vehicle.
- Among the total intent to treat (ITT) population (1,234 patients) who received the study treatment, clinical cures were 71% for finafloxacin compared to 50% for the vehicle.

Estimated Acquisition Cost: The estimated acquisition cost of Xtoro™ is not yet available.

Recommendations

The College of Pharmacy recommends placing Xtoro™ (finafloxacin) into Tier-2 of the Otic Anti-Infectives Product Based Prior Authorization (PBPA) category. The existing criteria for this category will apply.

Otic Anti-Infectives		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	chloroxylenol/benzocaine/HC (Trioxin®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	chloroxylenol/pramoxine/zinc/ glycerin (Zinotic®, Zinotic® ES)	antipyrine/benzocaine/ glycerin/zinc (Neotic®)
neomycin/polymyxin B/ HC (Cortisporin®, Pediotic®)	ciprofloxacin (Cetraxal®)	
ofloxacin (Floxin® Otic)*	ciprofloxacin/HC (Cipro® HC)	
	finafloxacin (Xtoro™)	
	neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S)	

Tier structure based on supplemental rebate participation.
HC = hydrocortisone
*Dexamethasone 0.1% ophthalmic solution is available without prior authorization for members who require concomitant steroid therapy.

Utilization Details of Otic Anti-Infectives: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM	PERCENT COST
OFLOXACIN PRODUCTS						
OFLOXACIN DRO	20,969	16,471	$552,870.40	$2.70	$26.37	63.66%
SUBTOTAL	**20,969**	**16,471**	**$552,870.40**	**$2.70**	**$26.37**	**63.66%**
NEOMYCIN/POLYMYXIN B/HYDROCORTISONE PRODUCTS						
NEO/POLY/HC SUS 1%	6,593	6,161	$162,898.19	$2.42	$24.71	18.76%
NEO/POLY/HC SOL 1%	5,220	4,893	$125,155.72	$2.28	$23.98	14.41%
SUBTOTAL	**11,813**	**11,054**	**$288,053.91**	**$2.36**	**$24.38**	**33.17%**
ACETIC ACID PRODUCTS						
ACETIC ACID SOL 2% OTIC	294	265	$8,478.69	$0.94	$28.84	0.98%
SUBTOTAL	**294**	**265**	**$8,478.69**	**$0.94**	**$28.84**	**0.98%**
CIPROFLOXACIN/DEXAMETHASONE PRODUCTS						
CIPRODEX SUS 0.3-0.1%	105	89	$16,210.16	$13.30	$154.38	1.87%
SUBTOTAL	**105**	**89**	**$16,210.16**	**$13.30**	**$154.38**	**1.87%**
TIER-1 SUBTOTAL	**33,181**	**26,084***	**$865,613.16**	**$2.57**	**$26.09**	**99.67%**
CIPROFLOXACIN/HYDROCORTISONE PRODUCTS						
CIPRO HC SUS OTIC	13	11	$2,360.03	$8.91	$181.54	0.27%
SUBTOTAL	**13**	**11**	**$2,360.03**	**$8.91**	**$181.54**	**0.27%**
NEOMYCIN/COLISTIN/HYDROCORTISONE/THONZONIUM PRODUCTS						
CORTISPORIN SUS -TC	7	7	$535.78	$8.50	$76.54	0.06%
SUBTOTAL	**7**	**7**	**$535.78**	**$8.50**	**$76.54**	**0.06%**
TIER-2 SUBTOTAL	**20**	**18***	**$2,895.81**	**$8.83**	**$144.79**	**0.33%**
TOTAL	**33,201**	**26,088***	**$868,508.97**	**$2.58**	**$26.16**	**100.00%**

*Total number of unduplicated members

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 5/18/15. Last accessed 5/19/15.
[2] FDA News Release: FDA Approves Xtoro to treat swimmer's ear. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427274.htm. Last revised 12/17/14. Last accessed 5/20/15.
[3] Xtoro™ Prescribing Information, Alcon Laboratories, Inc. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206307s000lbl.pdf. Last revised 12/2014. Last accessed 5/20/15.
[4] Micromedex 2.0: Xtoro™ Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 1/30/15. Last accessed 5/20/15.
[5] Medscape: FDA Clears Finafloxacin Ear Drops (Xtoro) for Swimmer's Ear. Available online at: http://www.medscape.com/viewarticle/836771. Last revised 12/17/14. Last accessed 5/20/15.
[6] Mayo Clinic: Swimmer's Ear. Available online at: http://www.mayoclinic.org/diseases-conditions/swimmers-ear/basics/definition/con-20014723. Last revised 7/9/13. Last accessed 5/20/15.

Appendix K

Fiscal Year 2014 Annual Review of Insomnia Medications and 30-Day Notice to Prior Authorize Hetlioz® (Tasimelteon) and Belsomra® (Suvorexant)

Oklahoma Health Care Authority
June 2015

Current Prior Authorization Criteria

Insomnia Medications		
Tier-1	**Tier-2**	**Tier-3**
estazolam (ProSom®)	eszopiclone (Lunesta®)	doxepin (Silenor®)
flurazepam (Dalmane®)	zolpidem CR (Ambien CR®)	ramelteon (Rozerem®)
temazepam (Restoril® 15mg and 30mg)		temazepam (Restoril® 7.5mg and 22.5mg)
triazolam (Halcion®)		zolpidem SL Tablets (Edular®)
zaleplon (Sonata®)		zolpidem SL Tablets (Intermezzo®)
zolpidem (Ambien®)		zolpidem oral spray (Zolpimist®)

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

Insomnia Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A minimum of a 30-day trial with at least two Tier-1 products; and
3. Clinical documentation of attempts to correct any primary cause for insomnia; and
4. No concurrent anxiolytic benzodiazepine therapy greater than three times daily dosing.
5. Approvals will be granted for the duration of six months.

Insomnia Medications Tier- 3 Approval Criteria:

1. An FDA approved diagnosis; and
2. A minimum of a 30-day trial with at least two Tier-2 products; and
3. Clinical documentation of attempts to correct any primary cause for insomnia; and
4. No concurrent anxiolytic benzodiazepine therapy greater than three times daily dosing.
5. Approvals will be granted for the duration of six months.

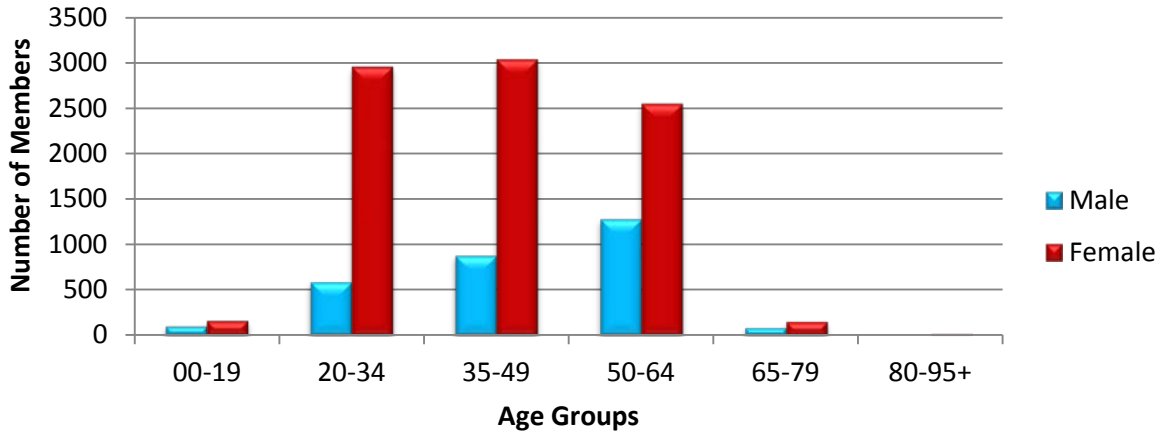
Utilization of Insomnia Medications: Fiscal Year 2014

Comparison of Fiscal Years

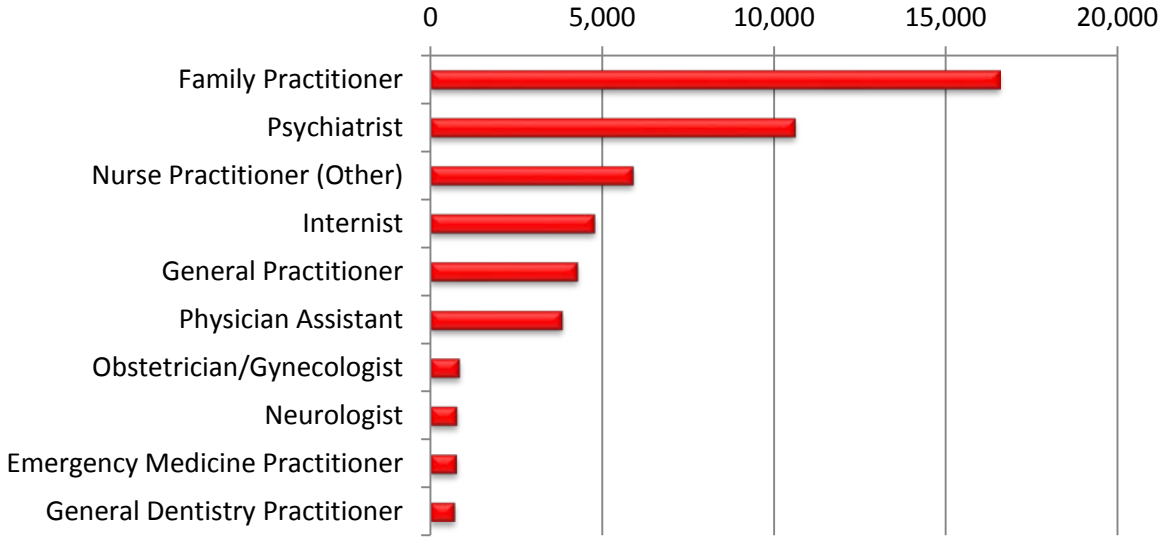
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	15,973	67,775	$825,426.58	$12.18	$0.42	1,961,470	1,960,441
2014	11,822	52,184	$652,402.72	$12.50	$0.43	1,503,110	1,504,438
% Change	**-26.00%**	**-23.00%**	**-21.00%**	**2.60%**	**2.40%**	**-23.40%**	**-23.30%**
Change	**-4,151**	**-15,591**	**-$173,023.86**	**$0.32**	**$0.01**	**-458,360**	**-456,003**

*Total number of unduplicated members.

Demographics of Members Utilizing Insomnia Medications

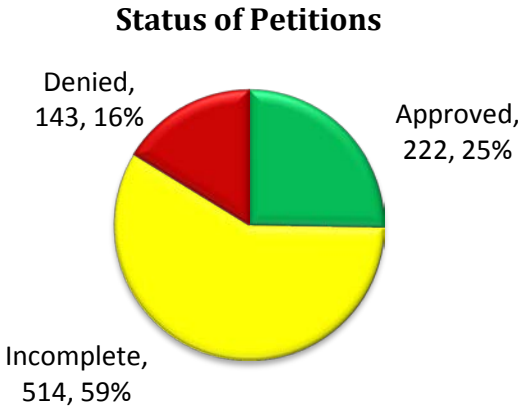


Top Prescriber Specialties of Insomnia Medications by Number of Claims



Prior Authorization of Insomnia Medications

There were 879 petitions submitted for the insomnia medications category during fiscal year 2014. Computer edits are in place to detect Tier-1 medications in members' 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]

Anticipated Patent Expirations:

- Rozerem® (ramelteon tablets): July 2019
- Intermezzo® (zolpidem sublingual tablets): August 2029
- Silenor® (doxepin tablets): April 2030

New FDA Approvals:

- Hetlioz® (tasimelteon): January 2014
- Belsomra® (suvorexant): August 2014

Hetlioz® (Tasimelteon) Product Summary[2]

Indications: Hetlioz® (tasimelteon) is a melatonin receptor agonist indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). Non-24 occurs almost exclusively in patients that are completely blind. Non-24 is a circadian rhythm disorder that causes problems with sleep timing.

Dosing:

- Tasimelteon is available as a 20mg capsule.
- The recommended dose is 20mg before bedtime, at the same time every night without food.
- Activities preparing for bed should be limited, as tasimelteon may cause somnolence and can impair the ability to complete tasks requiring mental alertness.
- Drug effect could take weeks or months to occur due to individual differences in circadian rhythms.

Mechanism of Action: Tasimelteon is an agonist of melatonin MT1 and MT2 receptors, which are thought to be involved in the control of circadian rhythms. The exact mechanism that tasimelteon exhibits its therapeutic effect on patients with Non-24 is unknown.

Contraindications: None.

Warnings and Precautions:

- Somnolence: Activities prior to bed should be limited, as tasimelteon has the potential to impair the performance of activities requiring mental alertness.

Adverse Reactions: The most common adverse reactions to tasimelteon (occurring in >5% and at least twice as much in patients on tasimelteon versus placebo) were:

- Headache
- Increase in alanine aminotransferase (ALT)
- Nightmare/abnormal dreams
- Upper respiratory tract infection
- Urinary tract infection

Use in Special Populations:

- Pregnancy: There are no adequate, well-controlled studies in pregnant women. Tasimelteon should only be used in pregnancy if the potential benefit outweighs the potential risk to the fetus.
- Nursing Mothers: It is not known whether or not tasimelteon is excreted in human breast milk. Caution should be used when tasimelteon is administered to a nursing woman.
- Pediatric Use: The safety and efficacy of tasimelteon have not been established in pediatric patients.
- Geriatric Use: Exposure to tasimelteon is increased approximately 2-fold in elderly patients (>65 years) compared with younger patients. Therefore, the risk of adverse reactions may be greater in geriatric patients.
- Hepatic Impairment: Dose adjustment is not necessary for mild or moderate hepatic impairment. Tasimelteon has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and is not recommended in those patients.
- Smokers: Tasimelteon exposure may be reduced in smokers. Tasimelteon is partly metabolized by the CYP1A2 isoenzyme, which is induced by smoking.
- Renal Impairment: Dose adjustments of tasimelteon in renal impairment are not necessary.

Clinical Studies: The effectiveness of tasimelteon for the treatment of Non-24 was established in two randomized double-masked, multicenter, placebo-controlled, parallel-group studies (Studies 1 and 2) in blind patients with Non-24-Hour Sleep-Wake Disorder. Efficacy endpoints were total nighttime sleep and daytime nap time. Treatment with tasimelteon compared with placebo, resulted in significant improvement in both endpoints in Study 1 and Study 2.

	Study 1		Study 2	
Change from Baseline	**Tasimelteon 20mg (N=42)**	**Placebo (N=42)**	**Tasimelteon 20mg (N=10)**	**Placebo (N=10)**
Nighttime sleep time on 25% most symptomatic nights (minutes)	50	22	-7	-74
Daytime nap time on 25% most symptomatic days (minutes)	-49	-22	-9	50

Belsomra® (Suvorexant) Product Summary[3]

Indications: Belsomra® (suvorexant) is an orexin receptor antagonist indicated for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Dosing:

- Suvorexant is available in four tablet strengths: 5mg, 10mg, 15mg, and 20mg tablets.
- The lowest effective dose of suvorexant should be used.
- The recommended dose of suvorexant is 10mg within 30 minutes of going to bed, with at least seven hours of planned sleep time.
- The dose of suvorexant can be increased up to a maximum of 20mg if the 10mg dose was well-tolerated, but ineffective.
- Suvorexant should only be taken once per night.
- Area under the curve (AUC) is not significantly changed when taken with a meal, however the T_{max} is delayed approximately 1.5 hours. For faster sleep onset, suvorexant should be administered on an empty stomach.
- Obese patients have increased exposure to suvorexant compared to non-obese patients. Exposure is also increased in women compared to men. In obese women, risk of increased exposure related adverse events should be carefully considered before dose increases.

Mechanism of Action:

- Suvorexant is thought to exert its therapeutic effect in insomnia by antagonism of orexin receptors. The orexin neuropeptide signaling system centrally promotes wakefulness. Blocking the attachment of wake-promoting neuropeptides orexin A and orexin B to receptors OX1R and OX2R is thought to suppress the wake drive.
- Blocking these orexin receptors may be the cause of potential adverse effects such as narcolepsy/cataplexy. Loss of orexin neurons has been reported in people who suffer from narcolepsy.
- Genetic mutations in the orexin neuropeptide signaling system in animals result in hereditary narcolepsy.

Contraindications:

- Suvorexant is contraindicated in patients with narcolepsy.

Warnings/Precautions:

- <u>CNS Depressant Effects and Daytime Impairment:</u>
    - Suvorexant is a central nervous system (CNS) depressant that can impair daytime wakefulness, even when taken exactly as prescribed. CNS depressant effects and somnolence should be monitored, however impairment can occur without the presence of symptoms and may not be reliably detected by ordinary clinical exam. Effects may persist in patients several days after discontinuation suvorexant.
    - Dosage adjustments may be necessary for co-administration of other CNS depressants because of the potential for additive side effects. Patients should be advised not to consume alcohol while taking suvorexant.

- Suvorexant can increase the risk of falling asleep while driving and impair driving skills. Dose decreases or discontinuation should be considered in patients who drive if daytime somnolence develops.
- Patients taking the maximum dose (20mg) should be cautioned against next day activities requiring full mental alertness. Risk of next-day impairment is increased if suvorexant is taken with less than a full night of rest remaining, if higher than recommended dose is taken, if used with other CNS depressants, or if co-administered with other drugs that increase blood levels of suvorexant.

- Evaluate for Co-Morbid Diagnoses: Treatment of insomnia should be initiated only after careful evaluation of the patient, as sleep disturbances may be the presenting manifestation of other physical or psychiatric disorders. If insomnia does not remit after 7 to 10 days of treatment, it may indicate the presence of a primary psychiatric or medical illness that should be evaluated. Emergence of new cognitive or behavioral abnormalities or worsening insomnia may be the result of an unrecognized, underlying psychiatric/medical disorder, and can emerge during treatment with hypnotic drugs, including suvorexant.
- Abnormal Thinking and Behavioral Changes: Multiple cognitive and behavioral changes (e.g., hallucinations, anxiety, and amnesia) have been reported during treatment with hypnotics such as suvorexant. Complex behaviors such as "sleep-driving" and others (e.g., preparing food, making phone calls, or having sex) with amnesia of the event, have been reported in association with the use of hypnotics. It can occur in hypnotic-naïve as well as hypnotic-experienced patients. Combination of hypnotics with alcohol or other CNS depressants may increase the risk of these behaviors. For patients who report any type of complex sleep behavior, discontinuation of suvorexant should be strongly considered.
- Worsening of Depression/Suicidal Ideation: A dose-dependent increase in suicidal ideation was observed in patients taking suvorexant as assessed by questionnaire in clinical studies. Patients with suicidal ideation or any new behavioral sign or symptom should be immediately evaluated. Worsening of depression and suicidal thoughts/actions have been reported in primarily depressed patients treated with sedative-hypnotics.
- Patients with Compromised Respiratory Function: Suvorexant has not been studied in patients with severe obstructive sleep apnea or severe chronic obstructive pulmonary disease. The effect of suvorexant on respiratory function should be considered when prescribed to patients with compromised respiratory function.
- Sleep Paralysis, Hypnagogic/Hypnopompic Hallucinations, Cataplexy-like Symptoms: Symptoms similar to mild cataplexy can occur, and increase with increased dose of suvorexant. Sleep paralysis, hypnagogic/hypnopompic hallucinations, including vivid, disturbing perceptions by the patient, can occur during treatment with suvorexant. The nature of these events should be explained to the patient by the prescriber.

Adverse reactions: The most common ($\geq$ 5% of patients and at least twice the placebo rate) adverse reaction reported with suvorexant was somnolence. Other reported adverse reactions include diarrhea, dry mouth, upper respiratory infection, headache, dizziness, abnormal dreams, and cough.

Use in Special Populations:

- Pregnancy: Suvorexant is Pregnancy Category C. Suvorexant should be used during pregnancy only if the potential risk to fetus is outweighed by potential benefit.
- Nursing Mothers: Suvorexant and its metabolite were excreted in rat milk at levels higher than that in maternal plasma. It is not known if suvorexant is secreted in human milk, but because many drugs are excreted in human breast milk, caution should be used when suvorexant is administered to nursing mothers.
- Renal Impairment: No dosage adjustment of suvorexant is recommended in patients with renal impairment.
- Hepatic Impairment: No dose adjustment of suvorexant is recommended for patients with mild-to-moderate hepatic impairment. Suvorexant has not been studied in patients with severe hepatic impairment and is not recommended for use in these patients.
- Geriatric patients: No clinically significant differences in safety and efficacy were observed between older patients (>65 years old) and younger patients at recommended doses of suvorexant.
- Compromised Respiratory Function: Suvorexant was studied in patients with mild-to-moderate obstructive sleep apnea (OSA) and mild-to-moderate chronic obstructive pulmonary disease (COPD). Patients with severe disease were not studied. The respiratory depressant effects of suvorexant on these patients were evaluated. There was a wide inter-individual and intra-individual variability such that clinically meaningful respiratory effects of suvorexant in OSA and COPD cannot be excluded and should be considered in patients with compromised respiratory function.

Efficacy:

- The safety and efficacy of suvorexant was evaluated in two randomized, double-blind, placebo-controlled, parallel-group studies in patients with insomnia characterized by both sleep onset and maintenance. Study 1 and 2 found suvorexant 15mg and 20mg to be superior to placebo for sleep latency and sleep maintenance. These endpoints were measured both objectively by polysomnography and subjectively by patient-estimated sleep latency/time.
- A third crossover study was done to evaluate higher doses of 30mg and 40mg. Higher doses were found to have similar efficacy, but a significantly higher incidence of adverse reactions.

Cost Comparison:

Medication Name	Cost/ Tablet	Cost/Month
Zolpidem 10mg Tablet	$0.09*	$2.70
Zolpidem CR 12.5mg Tablet	$2.21*	$66.30
Belsomra® 10mg Tablet	$9.26**	$277.80

*Based on state maximum allowable cost (SMAC)

**Estimated acquisition cost

Recommendations

The College of Pharmacy recommends the prior authorization of Hetlioz® (tasimelteon) with the following criteria:

Hetlioz® (Tasimelteon) Approval Criteria:

1. An FDA approved diagnosis of Non-24-Hour Sleep-Wake Disorder (Non-24); and
2. Member must be 18 years of age or older; and
3. Member must be totally blind; and
4. A failed trial of appropriately timed doses of melatonin.
5. Initial approvals will be for the duration of 12 weeks. For continuation, prescriber must include information regarding improved response/effectiveness of this medication.
6. A quantity limit of 30 capsules for 30 days will apply.

Additionally, the College of Pharmacy recommends the addition of Belsomra® (suvorexant) to Tier-3 of the Insomnia medications Product Based Prior Authorization (PBPA) category. The current criteria for this category will apply.

Lastly, the College of Pharmacy recommends moving Lunesta® (eszopiclone) to Tier-1 based on generic availability and state maximum allowable cost.

Insomnia Medications		
Tier-1	**Tier-2**	**Tier-3**
estazolam(ProSom®)	zolpidem CR (Ambien® CR)	doxepin (Silenor®)
eszopiclone (Lunesta®)		ramelteon (Rozerem®)
flurazepam (Dalmane®)		**suvorexant (Belsomra®)**
temazepam (Restoril® 15mg and 30mg)		**tasimelteon (Hetlioz®)***
triazolam (Halcion®)		temazepam (Restoril®) 7.5mg and 22.5mg
zaleplon (Sonata®)		zolpidem SL tablets (Edular®)
zolpidem (Ambien®)		zolpidem SL tablets (Intermezzo®)
		zopidem oral spray (Zopimist®)

*Hetlioz® (tasimelteon): Special prior authorization approval criteria. Tier-3 criteria doesn't apply.

Utilization Details of Insomnia Medications: Fiscal Year 2014

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
ZOLPIDEM PRODUCTS					
ZOLPIDEM TARTRATE 10MG TABLET	29,506	6,760	$148,469.48	$0.17	$5.03
ZOLPIDEM TARTRATE 5MG TABLET	6,303	2,354	$33,359.06	$0.19	$5.29
SUBTOTAL	**35,809**	**9,114**	**$181,828.54**	**$0.18**	**$5.16**
TEMAZEPAM PRODUCTS					
TEMAZEPAM 30MG CAPSULE	7,414	1,747	$53,416.69	$0.24	$7.20
TEMAZEPAM 15MG CAPSULE	3,686	1,323	$25,180.79	$0.24	$6.83
SUBTOTAL	**11,100**	**3,070**	**$78,597.48**	**$0.24**	**$7.02**
TRIAZOLAM PRODUCTS					
TRIAZOLAM 0.25MG TABLET	1,262	616	$15,306.10	$0.64	$12.13
TRIAZOLAM 0.125MG TABLET	49	23	$811.41	$0.72	$16.56
SUBTOTAL	**1,311**	**639**	**$16,117.51**	**$0.68**	**$14.35**
ZALEPLON PRODUCTS					
ZALEPLON 10MG CAPSULE	869	305	$16,185.19	$0.63	$18.63
ZALEPLON 5MG CAPSULE	195	119	$3,185.00	$0.64	$16.33
SUBTOTAL	**1,064**	**424**	**$19,370.19**	**$0.64**	**$17.48**
FLURAZEPAM PRODUCTS					
FLURAZEPAM 30MG CAPSULE	231	47	$1,479.39	$0.22	$6.40
FLURAZEPAM 15MG CAPSULE	51	13	$324.55	$0.21	$6.36
SUBTOTAL	**281**	**60**	**$1,803.94**	**$0.22**	**$12.76**
ESTAZOLAM PRODUCTS					
ESTAZOLAM 2MG TABLET	108	24	$1,220.27	$0.40	$11.30
ESTAZOLAM 1MG TABLET	13	5	$142.10	$0.36	$10.93
SUBTOTAL	**131**	**29**	**$1362.37**	**$0.38**	**$11.12**
TIER-1 SUBTOTAL	**49,687**	**13,336**	**$299,080.03**	**$0.39**	**$10.25**
TIER-2 PRODUCTS					
ZOLPIDEM PRODUCTS					
ZOLPIDEM CR 12.5MG TABLET	1,443	266	$126,376.63	$2.95	$87.58
ZOLPIDEM CR 6.25MG TABLET	152	43	$13,972.68	$3.08	$91.93
AMBIEN CR 12.5MG TABLET	13	1	$3,920.52	$10.05	$301.52
SUBTOTAL	**1,608**	**310**	**$144,269.83**	**$5.36**	**$160.33**
ESZOPICLONE PRODUCTS					
LUNESTA 3MG TABLET	436	76	$128,454.06	$9.90	$294.62
ESZOPICLONE 3MG TABLET	96	57	$2,412.66	$0.84	$25.13
LUNESTA 2MG TABLET	92	23	$26,773.35	$9.97	$291.01
ESZOPICLONE 2MG TABLET	22	18	$554.23	$0.84	$25.19
LUNESTA 1MG TABLET	8	3	$2,400.44	$10.00	$300.06
ESZOPICLONE 1MG TABLET	6	5	$190.61	$0.91	$31.77
SUBTOTAL	**660**	**209**	**$160,785.35**	**$5.41**	**$161.30**
TIER-2 SUBTOTAL	**2,268**	**519**	**$305,055.18**	**$5.39**	**$160.98**
TIER-3 PRODUCTS					
RAMELTEON PRODUCTS					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ROZEREM 8MG TABLET	193	27	$43,104.15	$7.46	$223.34
SUBTOTAL	**193**	**27**	**$43,104.15**	**$7.46**	**$223.34**
TEMAZEPAM PRODUCTS					
TEMAZEPAM 7.5MG CAPSULE	24	5	$2,314.48	$4.51	$96.44
SUBTOTAL	**24**	**5**	**$2,314.48**	**$4.51**	**$96.44**
ZOLPIDEM PRODUCTS					
INTERMEZZO 3.5MG SL TABLET	6	2	$1,314.96	$7.31	$219.16
EDLUAR 10MG SL TABLET	2	1	$307.60	$5.13	$153.80
INTERMEZZO 1.75MG SL TABLET	1	1	$241.03	$8.03	$241.03
SUBTOTAL	**9**	**4**	**$1,863.59**	**$6.82**	**$204.66**
DOXEPIN PRODUCTS					
SILENOR 3MG TABLET	2	2	$651.51	$10.86	$325.76
SILENOR 6MG TABLET	1	1	$333.78	$11.13	$333.78
SUBTOTAL	**3**	**3**	**$985.29**	**$11.00**	**$329.77**
TIER-3 SUBTOTAL	**229**	**39**	**$48,267.51**	**$7.13**	**$227.62**
TOTAL	**52,184**	**11,822***	**$652,402.72**	**$0.43**	**$12.50**

*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 5/18/15. Last accessed 5/19/15.

[2] Hetlioz® Product Information. Vanda Pharmaceuticals, Inc. Available online at http://www.hetliozpro.com. Last revised 2/2015. Last accessed 5/19/15.

[3] Belsomra® Prescribing information. Merk & Co., Inc. Available online at http://www.belsomra.com. Last revised 8/2014. Last accessed 5/19/15.

Appendix L

Calendar Year 2014 Annual Review of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations and 30-Day Notice to Prior Authorize Avycaz™ (Ceftazidime/Avibactam) and Zerbaxa™ (Ceftolozane/Tazobactam)

Oklahoma Health Care Authority
June 2015

Introduction

Suprax® (cefixime), Cedax® (ceftibuten), and Spectracef® (cefditoren) were voted to be prior authorized by the drug utilization review (DUR) board in February 2014. After several educational interventions were executed, the prior authorization of the aforementioned antibiotics was implemented July 1, 2014. The prior authorization of Sivextro™ (tedizolid phosphate), Dalvance™ (dalbavancin), and Orbactiv™ (oritavancin) was voted on in November 2014 and implemented January 1, 2014.

Current Prior Authorization Criteria

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

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

Oral Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient specific, clinically significant reason why the immediate release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.

Sivextro™ (Tedizolid Phosphate) Tablet Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; 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 resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; 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 resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; 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.

Utilization of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations: Calendar Year 2014

Comparison of Calendar Years: Cephalosporin Antibiotics

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	103,343	138,955	$10,022,365.71	$72.13	$7.54	9,987,844	1,329,872
2014	100,751	137,495	$8,100,640.97	$58.92	$6.15	10,325,492	1,317,837
% Change	**-2.50%**	**-1.10%**	**-19.20%**	**-18.30%**	**-18.40%**	**3.40%**	**-0.90%**
Change	**-2,592**	**-1,460**	**-$1,921,724.74**	**-$13.21**	**-$1.39**	**337,648**	**-12,035**

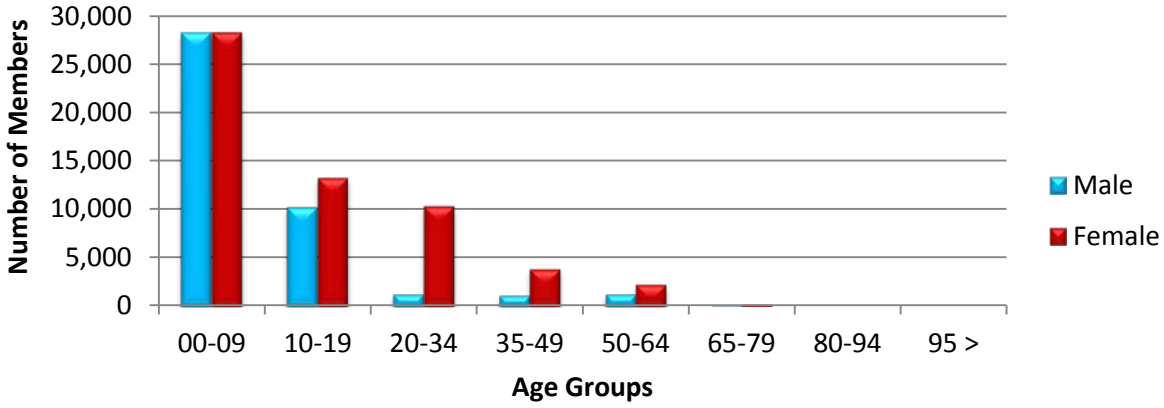
*Total number of unduplicated members.

Comparison of Calendar Years: Systemic Antibiotic Special Formulations

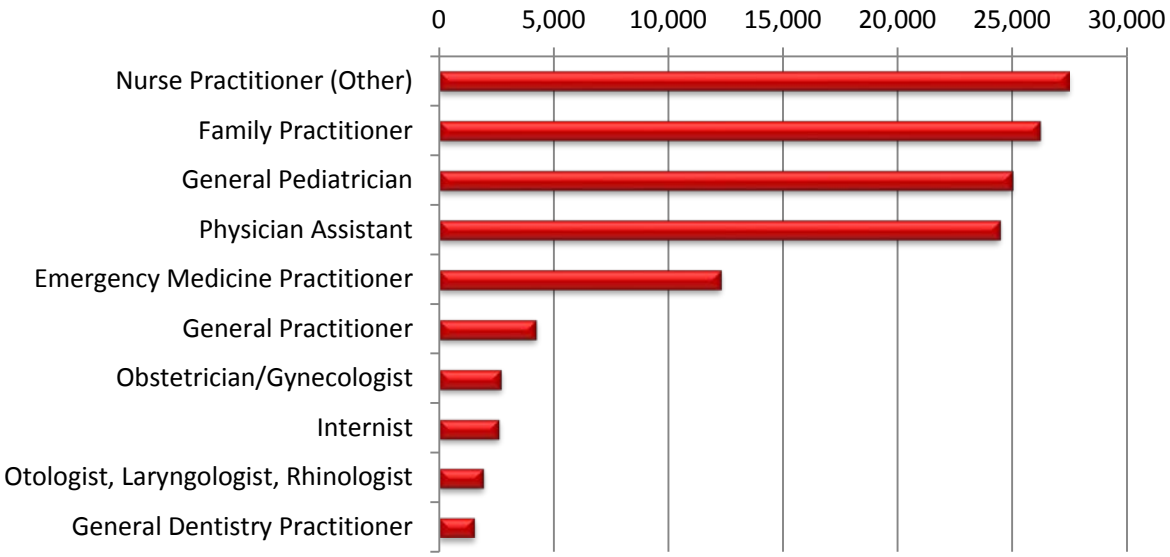
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	232	362	$28,151.78	$77.77	$3.45	27,303	8,171
2014	294	424	$44,885.06	$105.86	$4.72	38,408	9,513
% Change	**26.70%**	**17.10%**	**59.40%**	**36.10%**	**36.80%**	**40.70%**	**16.40%**
Change	**62**	**62**	**$16,733.28**	**$28.09**	**$1.27**	**11,105**	**1,342**

*Total number of unduplicated members.

Demographics of Members Utilizing Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations

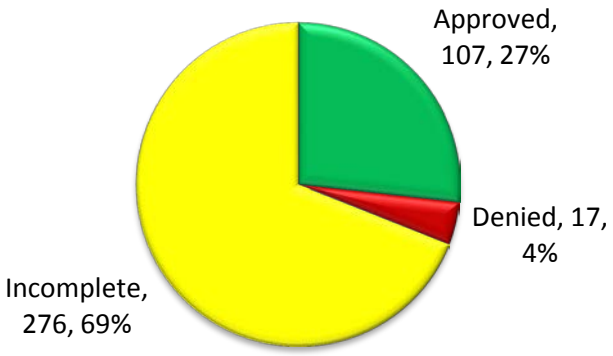


Top Prescriber Specialties of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations by Number of Claims

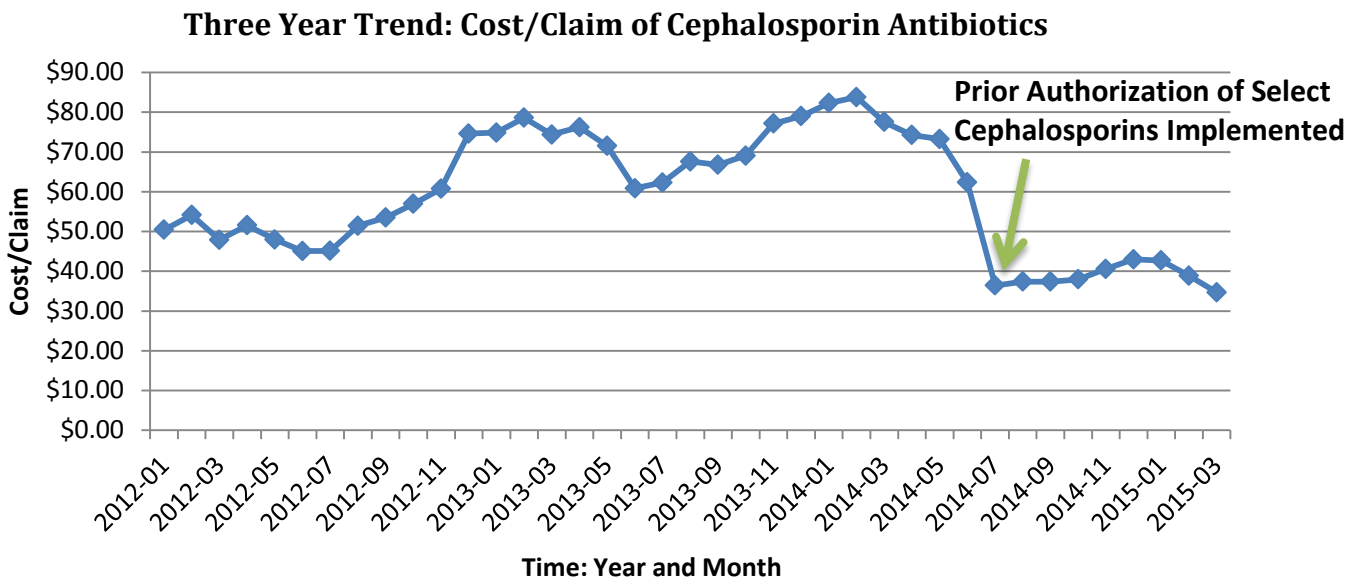


Prior Authorization of Cephalosporin Antibiotics & Systemic Antibiotic Special Formulations

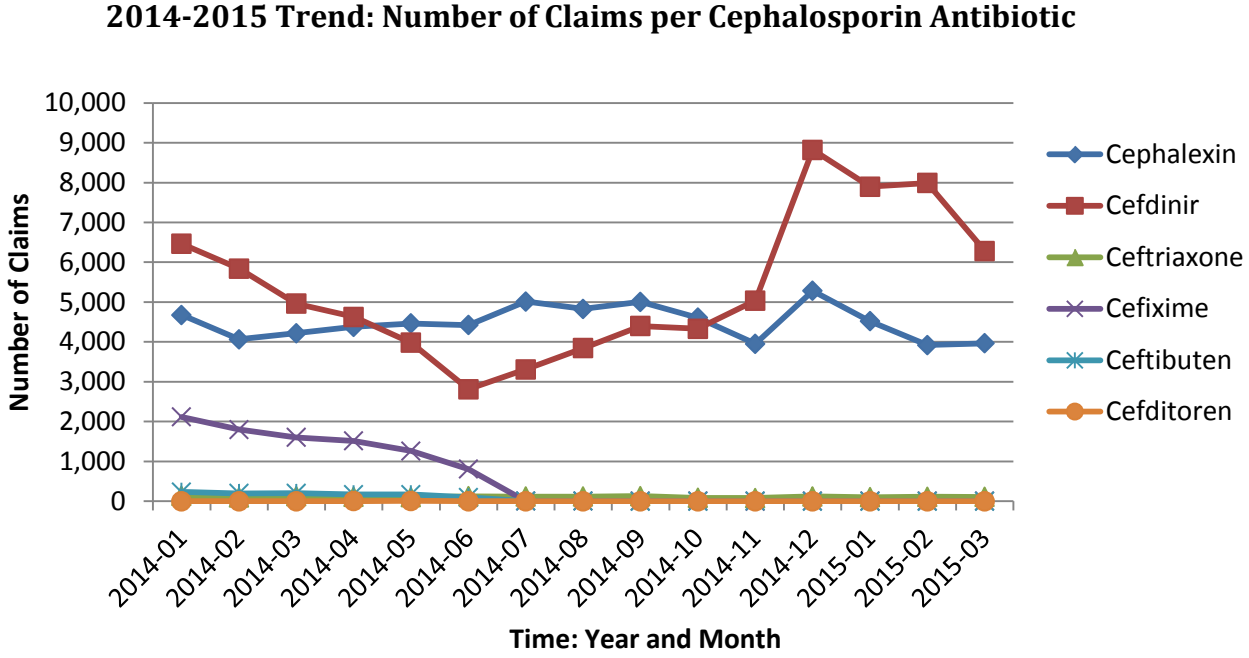
There were 400 petitions submitted for cephalosporin antibiotics and systemic antibiotic special formulations during calendar year 2014. The following chart shows the status of the submitted petitions.



Cephalosporin Utilization Evaluation



The trend in cost/claim for the cephalosporin antibiotics increased over the past two years until implementation of a prior authorization on select cephalosporins on July 1, 2014. The cost/claim price post prior authorization has averaged $41.37 compared to an average cost of $65.04 before prior authorization implementation.



A review of other commonly used cephalosporin antibiotics was conducted to analyze the shift in cephalosporin usage post prior authorization. An increase in cefdinir utilization indicates usage may have shifted from cefixime, cefditoren, and ceftibuten to cefdinir.

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

Anticipated Patent Expirations:

- Dalvance™ (dalbavancin): December 2023
- Orbactiv™ (oritavancin): August 2029
- Sivextro™ (tedizolid phosphate) oral tablets: December 2030

New FDA Approvals:

- December 2014: The FDA approved Zerbaxa™ (ceftolozane/tazobactam), a new antibacterial drug product to treat adults with complicated intra-abdominal infections (cIAI), in combination with metronidazole, and complicated urinary tract infections (cUTI), including kidney infections (Pyelonephritis).
- February 2015: The FDA approved Avycaz™ (ceftazidime/avibactam) to treat adults with cIAI, in combination with metronidazole, and cUTI, including Pyelonephritis, who have limited or no alternative treatment options.
- April 2015: The FDA approved Aurobindo Pharma to manufacture and sell the generic version of Suprax® (cefixime) oral suspension in the 100mg and 200mg dosage strengths. The generic price remains comparable to the branded formulation at this time.

Safety Updates:

- May 2015: The FDA warned health care professionals about the risk for dosing errors with Zerbaxa™ (ceftolozane/tazobactam) due to confusion about the drug strength displayed on the vial. The vial label initially showed a strength that reflects each individual active ingredient (e.g. 1 g/0.5 grams); however, the product is dosed based on the sum of these ingredients (e.g. 1.5 grams). The strength on the drug labeling has been revised to reflect the sum of the two active ingredients.

Avycaz™ (Ceftazidime/Avibactam) Product Summary[6]

Indications: Avycaz™ (ceftazidime/avibactam) is a combination of a cephalosporin and a beta-lactamase inhibitor indicated for the treatment of patients 18 years or older with the following infections caused by designated susceptible organisms:

- Complicated Intra-abdominal Infections (cIAI), used in combination with metronidazole
- Complicated Urinary Tract Infections (cUTI), including Pyelonephritis

Limitations of Use: As only limited clinical safety and efficacy data for ceftazidime/avibactam are currently available, ceftazidime/avibactam should be reserved for use in patients who have limited or no alternative treatment options. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftazidime/avibactam and other antibacterial drugs, ceftazidime/avibactam should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

Microbiology: Ceftazidime/avibactam has been shown to be active against most isolates of the following bacteria:

- Complicated Intra-abdominal Infections: *Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis, Providencia stuartii, and Pseudomonas aeruginosa*
- Complicated Urinary Tract Infections, including Pyelonephritis: *Citrobacter freundii, Citrobacter koseri, Escherichia coli, Pseudomonas aeruginosa, Enterobacter aerogenes, Enterobacter cloacae, Proteus spp, and Klebsiella pneumoniae*

Dosing:

- Ceftazidime/avibactam is available for injection in single use vials containing 2 grams ceftazidime and 0.5 grams avibactam.
- The recommended dosing of ceftazidime/avibactam is 2.5 grams (2 grams ceftazidime and 0.5 grams avibactam) administered every eight hours by intravenous (IV) infusion over two hours.
- The recommended duration of total antimicrobial treatment is from five to fourteen days for cIAI and seven to fourteen days for cUTI.
- Dosage adjustments are recommended in patients with varying degrees of renal function. Specific dosage adjustments are outlined in the table below.

Estimated Creatinine Clearance (mL/minute)[a]	Recommended Dosage Regimen for Ceftazidime/Avibactam
>50 mL/min	2.5 grams IV every 8 hours
31 to 50 mL/min	1.25 grams IV every 8 hours
16 to 30 mL/min	0.94 grams IV every 12 hours
6 to 15 mL/min[b]	0.94 grams IV every 24 hours
≤5 mL/min[b]	0.94 grams IV every 48 hours

a: As calculated using the Cockcroft-Gault formula.
b: Both ceftazidime and avibactam are hemodialyzable; thus ceftazidime/avibactam should be administered after hemodialysis on hemodialysis days.

Mechanism of Action: The ceftazidime component is a cephalosporin antibacterial drug with *in vitro* activity against certain gram-negative and gram-positive bacteria. The bactericidal action of ceftazidime is mediated through binding to essential penicillin-binding proteins (PBPs). The avibactam component is a beta lactamase inhibitor that inactivates some beta-lactamases and protects ceftazidime from degradation by certain beta-lactamases.

Contraindications:

- Ceftazidime/avibactam is contraindicated in patients with known serious hypersensitivity to avibactam, ceftazidime, other members of the cephalosporin class, or any of the product components.

Warnings and Precautions:

- Decreased Clinical Response in Patients with Baseline Creatinine Clearance of 30 to 50mL/min: In a phase III trial, clinical cure rates were lower in a subgroup of patients with baseline CrCL of 30 to 50mL/min compared to those with CrCL greater than 50mL/min.

- Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivitiy (anaphylactic) reactions and serious skin reactions have been reported in patients receiving beta-lactam antibacterial drugs. Caution should be used if this product is to be given to a penicillin or other beta-lactam allergic patient because cross sensitivity among beta-lactam antibacterial drugs has been established.
- *Clostridium difficile*-Associated Diarrhea: *Clostridium difficile*-associated diarrhea has been reported in patients using ceftazidime/avibactam and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial drugs alters the normal flora of the colon and may permit overgrowth of *C. difficile*.
- Central Nervous System Reactions: Seizures, nonconvulsive status epilepticus, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia have been reported in patients treated with ceftazidime, particularly in the setting of renal impairment.
- Development of Drug-Resistant Bacteria: Prescribing ceftazidime/avibactam in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions: The most common adverse reactions reported (≥5%) with ceftazidime/ avibactam during clinical trials were vomiting, nausea, constipation, abdominal pain, upper abdominal pain, increased blood alkaline phosphate, increased alanine aminotransferase, dizziness, and anxiety.

Use in Special Populations:

- Pregnancy: Ceftazidime/avibactam is pregnancy category B. There are no adequate and well controlled studies of ceftazidime/avibactam in pregnant women. Ceftazidime/ avibactam should only be used if the potential benefit justifies the potential risk.
- Nursing Mothers: Ceftazidime is excreted in human milk in low concentrations. It is not known whether avibactam is excreted into human milk.
- Pediatric Use: The safety and effectiveness of ceftazidime/avibactam in patients less than 18 years of age has not been established.
- Geriatric Use: Of the 169 patients treated with ceftazidime/avibactam in phase II trials, 18 were 65 years and older. Because of limited data, differences in outcomes or specific risks with ceftazidime/avibactam cannot be ruled out for patients 65 years of age and older.
- Renal Impairment: Dosage adjustment is required in patients with moderately or severely impaired renal function. For patients with changing renal function, CrCL should be monitored daily and the dosage should be adjusted accordingly.

Efficacy: The determination of efficacy of ceftazidime/avibactam was based on the previous findings of the efficacy and safety of ceftazidime for the treatment of cIAI and cUTI. The contribution of avibactam to ceftazidime/avibactam was primarily established *in vitro* and in animal models of infection. Ceftazidime/avibactam was studied in two phase II randomized, blinded, active-controlled trials, one each in cIAI and cUTI, including Pyelonephritis. These trials were not designed with any formal hypothesis for inferential testing against the active comparators.

Zerbaxa™ (Ceftolozane/Tazobactam) Product Summary[7]

Indications: Zerbaxa™ (ceftolozane/tazobactam) is a combination of a cephalosporin and a beta-lactamase inhibitor indicated for the treatment of patients 18 years or older with the following infections caused by designated susceptible organisms:

- Complicated Intra-abdominal Infections (cIAI), used in combination with metronidazole
- Complicated Urinary Tract Infections (cUTI), including Pyelonephritis

Limitations of Use: To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftolozane/tazobactam and other antibacterial drugs, ceftolozane/tazobactam should only be used to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

Microbiology: Ceftolozane/tazobactam has been shown to be active against the following bacteria:

- Complicated Intra-abdominal Infections: *Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis, Pseudomonas aeruginosa, Streptococcus anginosus, Streptococcus constellatus, Streptococcus salivarius, and Bacteroides fragilis*
- Complicated Urinary Tract Infections, including Pyelonephritis: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Pseudomonas aeruginosa*

Dosing:

- Ceftolozane/tazobactam is available for injection in single-dose vials containing 1 gram ceftolozane and 0.5 grams tazobactam.
- The recommended dosing of ceftolozane/tazobactam is 1.5 grams (1 gram ceftolozane and 0.5 grams tazobactam) administered every eight hours by IV infusion over one hour.
- The recommended duration of therapy should be guided by the severity and site of infection and the patient's clinical and bacteriological progress. The duration of antimicrobial treatment ranges from four to fourteen days for cIAI and seven days for cUTI.
- Dosage adjustments are recommended in patients with varying degrees of renal function. Specific dosage adjustments are outlined in the table below.

Estimated Creatinine Clearance (mL/minute)[a]	Recommended Dosage Regimen for Ceftolozane/Tazobactam
30-50 mL/min	750mg IV every 8 hours
15 to 29 mL/min	375mg IV every 8 hours
End-Stage Renal Disease on hemodialysis[b]	Single loading dose of 750mg followed by 150mg maintenance dose administered every 8 hours

a: As calculated using the Cockcroft-Gault formula.
b: Should be administered after hemodialysis on hemodialysis days.

Mechanism of Action: The bactericidal action of ceftolozane results from inhibition of cell wall biosynthesis, and is mediated through binding to PBPs. The tazobactam component has little clinically relevant *in vitro* activity against bacteria due to its reduced affinity to PBPs. It is an irreversible inhibitor of some beta-lactamases, and can bind covalently to some chromosomal and plasmid mediated bacterial beta-lactamases.

Contraindications:

- Ceftolozane/tazobactam is contraindicated in patients with known serious hypersensitivity to ceftolozane/tazobactam, piperacillin/tazobactam, or other members of the beta-lactam class.

Warnings and Precautions:

- Decreased Efficacy in Patients with Baseline Creatinine Clearance of 30 to 50mL/min: In a subgroup analysis of a phase III trial, clinical cure rates were lower in patients with baseline CrCL of 30 to 50mL/min compared to those with CrCL greater than 50mL/min.
- Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivitiy (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterial drugs. Caution should be used if this product is to be given to a penicillin or other beta-lactam allergic patient because cross sensitivity among beta-lactam antibacterial drugs has been established.
- *Clostridium difficile*-Associated Diarrhea: *Clostridium difficile*-associated diarrhea has been reported in patients using ceftolozane/tazobactam and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial drugs alters the normal flora of the colon and may permit overgrowth of *C. difficile*.
- Development of Drug-Resistant Bacteria: Prescribing ceftolozane/tazobactam in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Adverse Reactions: The most common adverse reactions reported (≥5%) with ceftolozane/tazobactam during clinical trials were nausea, diarrhea, headache, and pyrexia.

Use in Special Populations:

- Pregnancy: Ceftolozane/tazobactam is pregnancy category B. There are no adequate and well controlled studies of ceftolozane/tazobactam in pregnant women. Ceftolozane/tazobactam should only be used if the potential benefit justifies the potential risk to fetus.
- Nursing Mothers: It is not known whether ceftolozane or tazobactam is excreted in human milk.
- Pediatric Use: The safety and effectiveness of ceftolozane/tazobactam in patients less than 18 years of age has not been established.
- Geriatric Use: Of the 1,015 patients treated with ceftolozane/tazobactam in phase III trials, 250 were 65 years and older. The incidence of adverse events in both treatment groups was higher in older subjects (65 years and older) in the trials for both indications.
- Renal Impairment: Dosage adjustment is required in patients with moderately or severely impaired renal function.

Efficacy: The efficacy of ceftolozane/tazobactam for the treatment of cIAI and cUTI was established in two randomized, multinational, double-blind studies comparing ceftolozane/tazobactam to an active comparator.

- cIAI: A total of 979 hospitalized adults with cIAI were randomized to receive ceftolozane/tazobactam (1.5 grams every eight hours plus metronidazole) or meropenem (1 gram every eight hours) for four to fourteen days of therapy.
    - The primary efficacy endpoint was clinical response, defined as complete resolution or significant improvement in signs and symptoms of the index infection at the test-of-cure (TOC) visit which occurred 24 to 32 days after the first dose of the study drug.
    - Ceftolozane/tazobactam plus metronidazole was non-inferior to meropenem with regard to clinical cure rates at the TOC visit (ceftolozane/tazobactam 83% versus meropenem 87.3%).
- cUTI: A total of 1,068 hospitalized adults with cUTI were randomized to receive ceftolozane/tazobactam (1.5 grams every eight hours) or levofloxacin (750mg IV once daily) for seven days of therapy.
    - The primary efficacy endpoint was defined as complete resolution or marked improvement of the clinical symptoms and microbiological eradication at the TOC visit seven days after the last dose of the study drug.
    - Ceftolozane/tazobactam demonstrated efficacy with regard to the composite endpoint of microbiological and clinical cure at the TOC visit (ceftolozane/tazobactam 76.9% versus levofloxacin 68.4%).
    - Although a statistically significant difference was observed in the ceftolozane/tazobactam arm compared to the levofloxacin arm with respect to the primary endpoint, it was likely attributable to the 26.5% of patients with baseline organisms non-susceptible to levofloxacin. Among patients infected with a levofloxacin-susceptible organism at baseline, the response rates were similar.

Cost Comparison

Medication Name	Strength	Cost/ Dose	Cost/ Day**	Cost/14-Day Treatment**
Avycaz™ (ceftazidime/avibactam)	2.5 grams	$300.96+	$902.88	$12,640.32
Zerbaxa™ (ceftolozane/tazobactam)	1.5 grams	$87.64+	$262.92	$3,680.88
ceftazidime	2 grams	$14.65*	$43.95	$615.30
piperacillin/tazobactam	3.375 grams	$5.32+	$21.28	$297.92
meropenem	1 gram	$11.31+	$33.93	$475.02
levofloxacin	750mg	$38.00*	$38.00	$532.00

+ Estimated acquisition cost per vial.
*State maximum allowable cost per vial.
**Dosing based on normal renal function.

Recommendations

The College of Pharmacy recommends the prior authorization of Avycaz™ (ceftazidime/avibactam) and Zerbaxa™ (ceftolozane/tazobactam) with the following criteria:

Avycaz™ (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
    b. Complicated urinary tract infections (cUTI), including Pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Avycaz™ must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Zerbaxa™ (Ceftolozane/Tazobactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
    a. Complicated intra-abdominal infections (cIAI) used in combination with metronidazole; or
    b. Complicated urinary tract infections (cUTI), including Pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Zerbaxa™ must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Utilization Details of Cephalosporins: Calendar Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Cephalexin Products					
CEPHALEXIN CAP 500MG	32,182	26,798	$229,598.98	$0.80	$7.13
CEPHALEXIN SUS 250/5ML	17,446	15,344	$562,341.75	$3.39	$32.23
CEPHALEXIN CAP 250MG	3,193	2,825	$23,063.74	$0.76	$7.22
CEPHALEXIN SUS 125/5ML	2,090	1,886	$50,900.62	$2.61	$24.35
CEPHALEXIN TAB 250MG	3	3	$38.89	$1.44	$12.96
KEFLEX CAP 750MG	1	1	$7.65	$0.77	$7.65
Subtotal	**54,915**	**46,018**	**$865,951.63**	**$1.72**	**$15.77**
Cefdinir Products					
CEFDINIR SUS 250/5ML	28,717	22,911	$1,869,484.42	$6.44	$65.10
CEFDINIR SUS 125/5ML	18,901	14,908	$1,024,215.56	$5.44	$54.19
CEFDINIR CAP 300MG	10,816	9,276	$311,808.26	$2.97	$28.83
Subtotal	**58,434**	**44,720**	**$3,205,508.24**	**$5.49**	**$54.86**
Cefixime Products					
SUPRAX SUS 200/5ML	5,350	4,746	$1,920,996.68	$35.05	$359.06
SUPRAX SUS 100/5ML	2,222	1,972	$419,609.44	$18.77	$188.84
SUPRAX TAB 400MG	1,029	976	$176,468.15	$18.39	$171.49
SUPRAX CHW 200MG	256	237	$93,003.60	$36.62	$363.30
SUPRAX CAP 400MG	192	188	$34,648.60	$18.46	$180.46
SUPRAX CHW 100MG	38	34	$10,263.13	$27.22	$270.08
SUPRAX SUS 500/5ML	30	30	$15,551.52	$55.74	$518.38
Subtotal	**9,117**	**7,920**	**$2,670,541.12**	**$29.08**	**$292.92**
Cefprozil Products					
CEFPROZIL SUS 250/5ML	4,335	3,563	$276,109.73	$6.41	$63.69
CEFPROZIL SUS 125/5ML	972	840	$36,846.01	$3.84	$37.91
CEFPROZIL TAB 500MG	653	588	$29,477.80	$4.59	$45.14
CEFPROZIL TAB 250MG	605	521	$20,346.30	$3.54	$33.63
Subtotal	**6,565**	**5,394**	**$362,779.84**	**$5.59**	**$55.26**
Cefuroxime Products					
CEFUROXIME TAB 500MG	1,482	1,284	$68,062.52	$4.89	$45.93
CEFUROXIME TAB 250MG	1,248	1,099	$28,740.60	$2.43	$23.03
CEFTIN SUS 250/5ML	859	768	$141,645.24	$16.60	$164.90
CEFTIN SUS 125/5ML	158	151	$17,223.66	$11.24	$109.01
Subtotal	**3,747**	**3,243**	**$255,672.02**	**$7.15**	**$68.23**
Ceftriaxone Products					
CEFTRIAXONE INJ 1GM	918	680	$11,964.55	$3.52	$13.03
CEFTRIAXONE INJ 10GM	141	64	$6,301.08	$5.05	$44.69
CEFTRIAXONE INJ 250MG	90	76	$415.48	$1.58	$4.62
CEFTRIAXONE INJ 500MG	82	74	$486.45	$2.69	$5.93
CEFTRIAXONE INJ 2GM	81	47	$3,329.43	$5.19	$41.10
CEFTRIAXONE/ INJ DEX 1GM	5	3	$65.71	$5.48	$13.14
ROCEPHIN INJ 1GM	3	3	$9.18	$3.06	$3.06
Subtotal	**1,320**	**933**	**$22,571.88**	**$3.93**	**$17.10**
Cefadroxil Products					
CEFADROXIL CAP 500MG	750	668	$8,576.47	$1.17	$11.44
CEFADROXIL SUS 250/5ML	443	408	$22,305.72	$4.87	$50.35

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
CEFADROXIL SUS 500/5ML	260	227	$14,699.05	$4.89	$56.53
CEFADROXIL TAB 1GM	3	3	$179.94	$4.61	$59.98
Subtotal	**1,456**	**1,287**	**$45,761.18**	**$3.06**	**$31.43**
Ceftibuten Products					
CEDAX SUS 180/5ML	675	601	$405,969.26	$57.16	$601.44
CEFTIBUTEN SUS 180/5ML	318	294	$134,358.58	$40.80	$422.51
CEDAX CAP 400MG	61	59	$20,476.93	$33.96	$335.69
CEFTIBUTEN CAP 400MG	6	6	$1,428.10	$23.80	$238.02
Subtotal	**1,060**	**934**	**$562,232.87**	**$50.84**	**$530.41**
Cefpodoxime Products					
CEFPODOXIME TAB 200MG	183	152	$23,466.14	$14.00	$128.23
CEFPODOXIME TAB 100MG	90	60	$11,110.94	$12.80	$123.45
CEFPODO PROX SUS 100/5ML	16	14	$2,503.09	$15.64	$156.44
CEFPODO PROX SUS 50MG/5ML	5	5	$288.21	$6.40	$57.64
Subtotal	**294**	**226**	**$37,368.38**	**$13.59**	**$127.10**
Cefazolin Products					
CEFAZOLIN INJ 10GM	97	52	$7,493.91	$5.25	$77.26
CEFAZOLIN INJ 1GM	73	29	$3,564.63	$5.86	$48.83
CEFAZOLIN INJ 1GM/50ML	3	1	$466.23	$29.14	$155.41
CEFAZOLIN SOD 10G VIAL	1	1	$134.81	$4.81	$134.81
CEFAZOLIN INJ 500MG	1	1	$6.38	$2.13	$6.38
Subtotal	**175**	**75**	**$11,665.96**	**$5.60**	**$66.66**
Cefepime Products					
CEFEPIME INJ 2GM	81	45	$12,834.08	$17.78	$158.45
CEFEPIME INJ 1GM	41	25	$2,854.22	$15.60	$69.62
Subtotal	**122**	**65**	**$15,688.30**	**$17.34**	**$128.59**
Ceftazidime Products					
CEFTAZIDIME INJ 1GM	60	22	$5,220.21	$20.39	$87.00
CEFTAZIDIME INJ 6GM	25	12	$4,574.72	$20.79	$182.99
CEFTAZIDIME INJ 2GM	23	9	$2,863.43	$13.97	$124.50
TAZICEF INJ 6GM	7	1	$683.05	$16.66	$97.58
TAZICEF INJ 1GM	3	3	$232.04	$10.55	$77.35
Subtotal	**118**	**45**	**$13,573.45**	**$18.24**	**$115.03**
Cefaclor Products					
CEFACLOR CAP 500MG	52	32	$2,453.48	$5.30	$47.18
CEFACLOR SUS 250/5ML	46	46	$12,026.81	$24.20	$261.45
CEFACLOR CAP 250MG	36	27	$1,758.45	$5.60	$48.85
CEFACLOR SUS 125/5ML	21	21	$2,799.69	$12.44	$133.32
CEFACLOR SUS 375/5ML	4	4	$1,003.54	$28.67	$250.89
Subtotal	**159**	**129**	**$20,041.97**	**$13.07**	**$126.05**
Ceftaroline Products					
TEFLARO INJ 600MG	4	4	$10,223.00	$126.21	$2,555.75
Subtotal	**4**	**4**	**$10,223.00**	**$126.21**	**$2,555.75**
Cefditoren Products					
SPECTRACEF TAB 400MG	3	3	$483.42	$16.11	$161.14
CEFDITOREN TAB 400MG	3	3	$394.22	$13.14	$131.41
Subtotal	**6**	**6**	**$877.64**	**$14.63**	**$146.27**
Cefotaxime Products					

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
CEFOTAXIME INJ 2GM	2	1	$143.81	$7.99	$71.91
CLAFORAN INJ 1GM	2	2	$21.29	$2.37	$10.65
CLAFORAN INJ 2GM	1	1	$76.60	$12.77	$76.60
Subtotal	**5**	**3**	**$241.70**	**$7.32**	**$48.34**
Cefoxitin Products					
CEFOXITIN INJ 2GM	2	2	$114.16	$7.14	$57.08
Subtotal	**2**	**2**	**$114.16**	**$7.14**	**$57.08**
Cefotetan Products					
CEFOTETAN INJ 1GM/10ML	1	1	$50.56	$16.85	$50.56
Subtotal	**1**	**1**	**$50.56**	**$16.85**	**$50.56**
Total	**137,500**	**100,755***	**$8,100,863.90**	**$6.15**	**$58.92**

*Total number of unduplicated members.

Utilization Details of Systemic Antibiotic Special Formulations: Calendar Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Minocycline Products					
MINOCYCLINE TAB 100MG	166	102	$23,396.19	$4.66	$140.94
MINOCYCLINE TAB 50MG	64	31	$5,427.65	$2.85	$84.81
MINOCYCLINE TAB 45MG ER	6	1	$562.49	$3.12	$93.75
MINOCYCLINE TAB 75MG	5	5	$486.18	$2.49	$97.24
Subtotal	**241**	**139**	**$29,872.51**	**$4.09**	**$123.95**
Doxycycline Products					
DOXYCYCLINE SUS 25MG/5ML	133	117	$8,214.26	$5.80	$61.76
VIBRAMYCIN SUS 25MG/5ML	16	16	$1,038.24	$7.16	$64.89
DOXYCYC MONO CAP 100MG	13	13	$219.20	$1.32	$16.86
DOXYCYC MONO TAB 50MG	11	1	$240.32	$0.73	$21.85
DOXYCYCL HYC TAB 150MG DR	2	1	$893.12	$14.89	$446.56
DOXYCYC MONO TAB 100MG	1	1	$12.69	$0.91	$12.69
DOXYCYC MONO CAP 50MG	1	1	$6.32	$0.79	$6.32
Subtotal	**177**	**150**	**$10,624.15**	**$4.97**	**$60.02**
Amoxicillin & K Clavulanate Extended-Release Products					
AMOX-POT CLA TAB ER	4	4	$642.74	$11.69	$160.69
Subtotal	**4**	**4**	**$642.74**	**$11.69**	**$160.69**
Tedizolid Products					
SIVEXTRO TAB 200MG	2	2	$3,745.66	$312.14	$1,872.83
Subtotal	**2**	**2**	**$3,745.66**	**$312.14**	**$1,872.83**
Total	**424**	**294***	**$44,885.06**	**$4.72**	**$105.86**

*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 3/27/15. Last accessed 05/26/15.
[2] FDA: FDA Approves New Antibacterial Drug Zerbaxa. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427534.htm. Last revised 12/22/14. Last accessed 05/28/15.
[3] FDA: FDA Approves New Antibacterial Drug Avycaz. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm435629.htm . Last revised 02/26/15. Last accessed 05/28/15.
[4] Drug Store News: Aurobindo Pharma Approved for Generic Cefixime. Available online at: http://www.drugstorenews.com/article/aurobindo-pharma-approved-generic-cefixime. Last revised 04/20/15. Last accessed 05/26/15.
[5] FDA: FDA Drug Safety Communication: FDA Cautions About Dose Confusion and Medication Errors for Antibacterial Drug Zerbaxa (Ceftolozane and Tazobactam). Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm445919.htm. Last revised 05/21/2015. Last accessed 05/28/15.
[6] Avycaz Product Information. Actavis, Inc. Available online at: http://pi.actavis.com/data_stream.asp?product_group=1957&p=pi&language=E. Last revised 02/2015. Last accessed 05/28/2015.
[7] Zerbaxa Product Information. Cubist Pharmaceuticals. Available online at: http://www.zerbaxa.com/pdf/PrescribingInformation.pdf. Last revised 05/2015. Last accessed 05/28/2015.

Appendix M

30-Day Notice to Prior Authorize
Copaxone® (Glatiramer Acetate) 40mg/mL

Oklahoma Health Care Authority
June 2015

Introduction[1]

On January 26, 2014, Teva Pharmaceutical Industries Ltd. announced the FDA approval of the company's supplemental new drug application for three-times-a-week Copaxone® (glatiramer acetate) 40mg/mL. The 40mg/mL strength is a new dose of Copaxone® with less frequent administration. In addition to the newly approved 40mg/mL strength dosed three-times-weekly, the 20mg/mL strength dosed daily remains available.

Current Prior Authorization Criteria

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing, remitting Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Compliance will be checked for continued approval every six months.

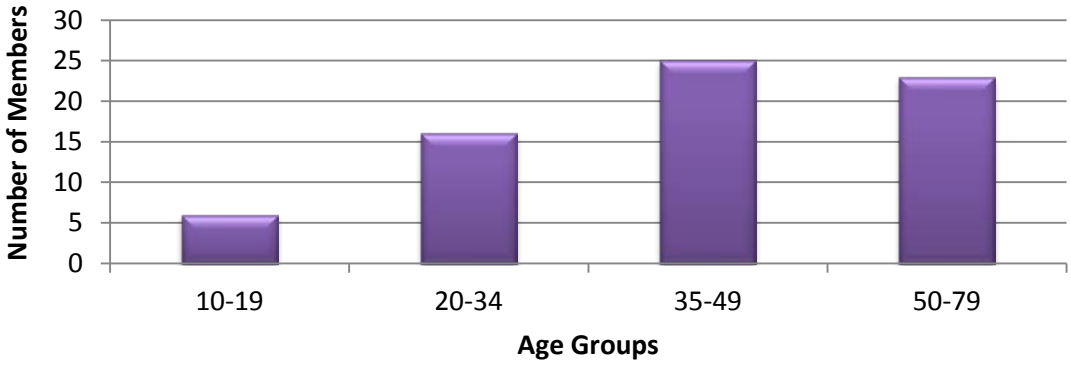
Copaxone® (Glatiramer Acetate) Utilization: Calendar Year 2014

Comparison of Calendar Years

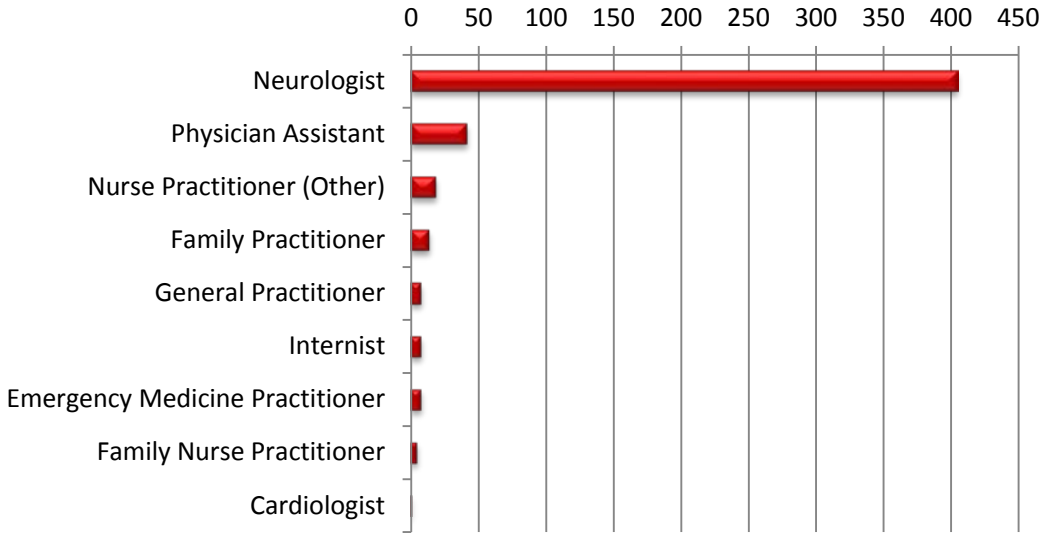
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2013	91	527	$2,553,542.18	$4,845.43	$161.51	527	15,810
2014	70	510	$2,595,623.64	$5,089.46	$174.82	4,553	14,847
% Change	**-23.10%**	**-3.20%**	**1.60%**	**5.00%**	**8.20%**	**763.90%**	**-6.10%**
Change	**-21**	**-17**	**$42,081.46**	**$244.03**	**$13.31**	**4,026**	**-963**

*Total number of unduplicated members.

Demographics of Members Utilizing Copaxone® (Glatiramer Acetate)



Top Prescriber Specialties of Copaxone® (Glatiramer Acetate) by Number of Claims



Market News and Updates[2, 3, 4]

- April 2015: The FDA approved the first generic version of Copaxone® (glatiramer acetate). Sandoz has received FDA approval to market generic glatiramer acetate in a 20mg/1mL daily injection.
    - Teva, the makers of the brand formulation of Copaxone® (glatiramer acetate), have filed several citizen's petitions with the FDA stating that glatiramer acetate is a complex product and not easy to duplicate. Teva commented that subtle differences might harm patients. Glatiramer acetate is made of four different amino acids linked in chains of various size and sequence.
    - The FDA posted a response to Teva's arguments: "*The FDA applies the same rigorous and reliable standards to evaluate all generic drug products. As needed, the agency requires appropriate information to demonstrate sameness for complex active ingredients, such as glatiramer acetate. For this approval, FDA*

scientists established a thorough scientific approach for demonstrating active ingredient sameness that takes into consideration the complexity of glatiramer acetate."

- Despite the approval of the generic product, an ongoing patent lawsuit will likely delay availability. The generic formulation is not yet available for patients.

Price Comparison

Despite the estimated acquisition for the 20mg appearing greater for 28 days of therapy than the 40mg, the prices do not reflect net cost. The federal and supplemental rebates represent a significant price difference resulting in the Copaxone® 20mg being much less costly than the 40mg.

Product	Dosing	Price Per 28 Days*
Copaxone® 20mg	20mg once daily	$6,022.52
Copaxone® 40mg	40mg three times weekly	$5,288.40

*Estimated acquisition cost. Price does not reflect supplemental rebates.

Discussion[5]

Evidence supporting the effectiveness of Copaxone® derives from five placebo-controlled trials, four of which used a Copaxone® dose of 20mg/mL per day and one of which used a Copaxone® dose of 40mg/mL three times per week. Limited clinical comparison data is available in determining superior efficacy or tolerability in either dosage strength since all efficacy data is based on placebo-controlled trials.

If the majority of members switched to the 20mg strength in place of the 40mg strength a significant savings could be anticipated. Additionally, when the generic 20mg strength becomes available at a competitive price it is likely that the generic formulation would become the preferred option. A transition to preferring the 20mg strength at this time could make the transition to the generic formulation in the future a smoother process.

Recommendations

Based on supplemental rebate pricing and potential generic availability, the College of Pharmacy recommends the prior authorization of Copaxone® (glatiramer acetate) 40mg with the criteria presented below. A pre-emptive educational initiative will be sent to prescriber and pharmacy providers before these prior authorizations become effective.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing, remitting Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
4. Compliance will be checked for continued approval every six months.

Utilization Details of Copaxone® (Glatiramer Acetate): Calendar Year 2014

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Glatiramer Acetate 40 MG/ML					
COPAXONE INJ 40MG/ML	270	48	$1,318,792.01	$172.53	$4,884.41
Subtotal	**270**	**48**	**$1,318,792.01**	**$172.53**	**$4,884.41**
Glatiramer Acetate 20 MG/ML					
COPAXONE INJ 20MG/ML	240	53	$1,276,831.63	$177.26	$5,320.13
Subtotal	**240**	**53**	**$1,276,831.63**	**$177.26**	**$5,320.13**
Total	**510**	**70***	**$2,595,623.64**	**$174.82**	**$5,089.46**

*Total number of unduplicated members.

[1] Drugs.com: Teva Announces U.S. FDA Approval of Three-Times-a-Week Copaxone (glatiramir acetate injection) 40mg/mL. Available online at: http://www.drugs.com/newdrugs/teva-announces-u-s-fda-approval-three-times-week-copaxone-glatiramer-acetate-40mg-ml-4004.html. Last revised 01/2014. Last accessed 05/28/15.

[2] FDA: FDA Approves First Generic Copaxone to Treat Multiple Sclerosis. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm443143.htm. Last revised 04/16/15. Last accessed 05/28/15.

[3] Pollack, Andrew. Generic Version of Copaxone, Multiple Sclerosis Drug, Is Approved. *New York Times.* Available online at: http://www.nytimes.com/2015/04/17/business/generic-version-of-copaxone-multiple-sclerosis-drug-is-approved.html?_r=0. Last revised 04/18/15. Last accessed 05/28/15.

[4] Silverman, Ed. FDA Approves Generic Copaxone, but When Will it Become Available? *Wall Street Journal.* Available online at: http://blogs.wsj.com/pharmalot/2015/04/16/fda-approves-generic-copaxone-but-when-will-it-become-available/. Last revised 04/16/15. Last accessed 05/28/15.

[5] Copaxone Prescribing Information. Teva Pharmaceuticals USA, Inc. Available online at: https://www.copaxone.com/resources/pdfs/prescribinginformation.pdf. Last revised 01/2014. Last accessed 05/28/15.

Appendix N

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

FDA NEWS RELEASE

For Immediate Release: April 28th, 2015

FDA approves first generic Abilify to treat mental illnesses

The U.S. Food and Drug Administration approved the first generic versions of Abilify (aripiprazole). Generic aripiprazole is an atypical antipsychotic drug approved to treat schizophrenia and bipolar disorder. Alembic Pharmaceuticals Ltd., Hetero Labs Ltd., Teva Pharmaceuticals and Torrent Pharmaceuticals Ltd. have received FDA approval to market generic aripiprazole in multiple strengths and dosage forms.

Schizophrenia is a chronic, severe and disabling brain disorder. About one percent of Americans have this illness. Typically, symptoms are first seen in adults younger than 30 years of age. Symptoms of schizophrenia include hearing voices, believing other people are reading their minds or controlling thoughts and being suspicious or withdrawn.

Bipolar disorder, also known as manic-depressive illness, is another brain disorder that causes unusual shifts in mood, energy, activity levels and the ability to carry out day-to-day tasks. The symptoms of bipolar disorder include alternating periods of depression and high or irritable mood, increased activity and restlessness, racing thoughts, talking fast, impulsive behavior and a decreased need for sleep.

All atypical antipsychotics contain a Boxed Warning alerting health care professionals about an increased risk of death associated with the off-label use of these drugs to treat behavioral problems in older people with dementia-related psychosis. No drug in this class is approved to treat patients with dementia-related psychosis.

Aripiprazole's Boxed Warning also warns about an increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. Patients should be monitored for worsening and emergence of suicidal thoughts and behaviors. Aripiprazole must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

In the clinical trials for Abilify, the most common side effects reported by adults taking Abilify were nausea, vomiting, constipation, headache, dizziness, uncontrollable limb and body movements (akathisia), anxiety, insomnia, and restlessness.

Generic prescription drugs approved by the FDA have the same high quality and strength as brand-name drugs. Generic prescription drug manufacturing and packaging sites must pass the same quality standards as those of brand-name drugs.

FDA NEWS RELEASE

For Immediate Release: April 29th, 2015

FDA approves treatment for fat below the chin

The U.S. Food and Drug Administration approved Kybella (deoxycholic acid), a treatment for adults with moderate-to-severe fat below the chin, known as submental fat. Using Kybella for the treatment of fat outside of the submental area is not approved and is not recommended.

Kybella is identical to the deoxycholic acid that is produced in the body. Deoxycholic acid produced in the body helps the body absorb fats. Kybella is a cytolytic drug, which when injected into tissue physically destroys the cell membrane. When properly injected into submental fat, the drug destroys fat cells; however, it can also destroy other types of cells, such as skin cells, if it is inadvertently injected into the skin.

Kybella is administered as an injection into the fat tissue in the submental area. Patients may receive up to 50 injections in a single treatment, with up to six single treatments administered no less than one month apart. Kybella is being provided in single patient use vials and should not be diluted or mixed with any other compounds.

The safety and effectiveness of Kybella for treatment of submental fat were established in two clinical trials which enrolled 1,022 adult participants with moderate or severe submental fat. Participants were randomly assigned to receive Kybella or a placebo for up to six treatments. The results showed that reductions in submental fat were observed more frequently in participants who received Kybella versus placebo.

Kybella can cause serious side effects, including nerve injury in the jaw that can cause an uneven smile or facial muscle weakness, and trouble swallowing. The most common side effects of Kybella include swelling, bruising, pain, numbness, redness and areas of hardness in the treatment area.
Kybella should not be used outside of the submental area, and it should not be used if there is an infection at the injection site. Caution should also be used in patients who have had prior surgical or aesthetic treatment of the submental area.
Kybella is being distributed in a dispensing pack that has a unique hologram on the vial label. If there is no hologram, do not use the product.
Consumers and health care professionals are encouraged to report adverse reactions from the use of Kybella to the FDA's MedWatch Adverse Event Reporting program at www.fda.gov/MedWatch or by calling 800-FDA-1088.
Kybella is manufactured by Kythera Biopharmaceuticals Inc. based in Westlake Village, California.

FDA NEWS RELEASE

For Immediate Release: May 8th, 2015

FDA approves additional antibacterial treatment for plague

The U.S. Food and Drug Administration approved Avelox (moxifloxacin) to treat patients with plague, a rare and potentially fatal bacterial infection. The agency approval for plague includes use of the drug for the treatment of pneumonic plague (infection of the lungs), and septicemic plague (infection of the blood). Avelox is also approved for prevention of plague in adult patients.
Plague is extremely rare in most parts of the world, including the United States, with 1,000 to 2,000 cases worldwide each year. The three most common forms of plague are bubonic plague (infection of the lymph nodes), pneumonic plague and septicemic plague.
Plague can be spread to humans through bites from infected fleas, contact with infected animals or humans, or laboratory exposure. The bacteria that causes plague, Yersinia pestis, is considered a biological threat agent that could potentially be used as a bioterrorism agent.
The FDA approved Avelox for plague under the agency's Animal Efficacy Rule, which allows efficacy findings from adequate and well-controlled animal studies to be used in cases where it is not feasible or ethical to conduct trials in humans. Because plague is such a rare disease, it would not be possible to conduct adequate efficacy trials in humans.
Avelox's approval was based on an efficacy study conducted in African green monkeys that were infected with Yersinia pestis in a laboratory setting. Animals were randomly selected to receive a 10-day regimen of Avelox or placebo at least four hours after the onset of fever following exposure to Yersinia pestis. The primary endpoint was survival at the end of the study. All 10 monkeys treated with Avelox survived. None of the 10 monkeys treated with placebo survived.
Avelox's safety has been characterized in clinical studies and post-marketing information for the drug's existing clinical uses. Common side effects are nausea, diarrhea, headache and dizziness.
Avelox carries a Boxed Warning regarding an increased risk of tendinitis and tendon rupture and worsening of muscle weakness in people with the neuromuscular disorder myasthenia gravis. Other side effects include allergic reactions, liver damage, abnormalities of the blood, effects on the nervous system and abnormal heart rhythm. However, given that plague is a very serious and often deadly condition, the benefit of Avelox for treating plague outweighs these potential risks. Avelox is manufactured by Whippany, New Jersey-based Bayer HealthCare Pharmaceuticals.

FDA NEWS RELEASE

For Immediate Release: May 27th, 2015

FDA approves two therapies to treat IBS-D

The U.S. Food and Drug Administration approved Viberzi (eluxadoline) and Xifaxan (rifaximin), two new treatments, manufactured by two different companies, for irritable bowel syndrome with diarrhea (IBS-D) in adult men and women.
According to the National Institutes of Health, patients with irritable bowel syndrome (IBS) experience a number of signs and symptoms, including pain or discomfort in the abdomen and changes in bowel movement patterns. Studies estimate that IBS affects 10 to 15 percent of adults in the United States. IBS-D is a subtype characterized mainly by loose or watery stools at least 25 percent of the time.

Viberzi, which contains a new active ingredient, is taken orally twice daily with food. Viberzi activates receptors in the nervous system that can lessen bowel contractions. Viberzi is intended to treat adults with IBS-D.
Xifaxan can be taken orally three times a day for 14 days, for the treatment of abdominal pain and diarrhea in patients with IBS-D. Patients who experience a recurrence of symptoms can be retreated with a 14 day treatment course, up to two times. Xifaxan, an antibiotic derived from rifampin, was previously approved as treatment for travelers' diarrhea caused by E. coli and for reduction of the risk in adult patients of recurring overt hepatic encephalopathy, the changes in brain function that occur when the liver is unable to remove toxins from the blood. The exact mechanism of action of Xifaxan for treatment of IBS-D is not known, but is thought to be related to changes in the bacterial content in the gastrointestinal tract.
The safety and effectiveness of Viberzi for treatment of IBS-D were established in two double-blind, placebo-controlled clinical trials in which 2,425 patients were randomly assigned to receive Viberzi or placebo. Results showed Viberzi was more effective in simultaneously reducing abdominal pain and improving stool consistency than placebo over 26 weeks of treatment.
The safety and effectiveness of Xifaxan for treatment of IBS-D were established in three double-blind, placebo-controlled trials. In the first two trials, 1,258 patients were randomly assigned to receive Xifaxan or placebo for 14 days, and then followed for a 10-week treatment-free period. More Xifaxan-treated patients reported improvements in abdominal pain and stool consistency than those on placebo. A third trial evaluated repeat courses of Xifaxan, because patients with IBS-D can develop recurrent signs and symptoms after a single treatment course of Xifaxan. A total of 636 patients with recurrence were randomized to receive either Xifaxan or placebo for two additional 14-day courses separated by 10 weeks. More patients treated with Xifaxan than placebo were responders in abdominal pain and stool consistency in this phase of the study.
The most common side effects in patients treated with Viberzi include constipation, nausea and abdominal pain. The most serious known risk associated with Viberzi is the risk of spasm in the sphincter of Oddi, the smooth muscle that surrounds the end portion of the common bile and pancreatic ducts, which can result in pancreatitis. Viberzi should not be used in patients with a history of bile duct obstruction, pancreatitis, severe liver impairment, or severe constipation, and in patients who drink more than three alcoholic beverages per day.
The most common side effects in patients treated with Xifaxan for IBS-D include nausea and an increase in alanine aminotransferase (ALT). If diarrhea does not improve or worsens after treatment with Xifaxan, then evaluation for development of C. difficile enterocolitis, should be performed. Caution should be used when using Xifaxan in patients with severe liver impairment or when combined with certain other drugs.
Viberzi is manufactured by Patheon Pharmaceuticals, Inc. based in Cincinnati, Ohio and distributed by Forest Pharmaceuticals, Inc. a subsidiary of Forest Laboratories, LLC, based in Cincinnati, Ohio.
Xifaxan is marketed by Salix Pharmaceuticals, Inc. based in Raleigh, North Carolina.

FDA NEWS RELEASE

For Immediate Release: May 28th, 2015

FDA approves Rapamune to treat LAM, a very rare lung disease

The U.S. Food and Drug Administration approved Rapamune (sirolimus), to treat lymphangioleiomyomatosis (LAM), a rare, progressive lung disease that primarily affects women of childbearing age. This is the first drug approved to treat the disease.
LAM is characterized by an abnormal growth of smooth muscle cells that invade lung tissues, including the airways, and blood/lymph vessels that cause destruction of the lung, resulting in airflow obstruction, and limiting the delivery of oxygen to the body. LAM is a very rare disease. According to the U.S. National Library of Medicine, only between two and five women per million women worldwide are known to have the disease.
Rapamune, which is available as both a tablet and an oral solution, was originally approved in 1999 as an immunosuppressive agent to help prevent organ rejection in patients 13 years and older receiving kidney transplants. Because Rapamune's sponsor demonstrated that the drug may offer a substantial improvement over available therapies, it received breakthrough therapy designation. It also received a priority review, which provides for an expedited review of drugs that have the potential to provide a significant improvement in safety or effectiveness in the treatment of a serious disease or condition. Rapamune also received orphan product designation for this indication because LAM is a rare disease or condition. Development of

this drug was also supported in part by the FDA Orphan Products Grants Program which provides grants for clinical studies on safety and/or effectiveness of products for use in rare diseases or conditions.
The safety and efficacy of Rapamune for treatment of LAM were studied in a clinical trial that compared Rapamune with placebo in 89 patients for a 12-month treatment period, followed by a 12-month observation period. The primary endpoint was the difference between the groups in the rate of change in how much air a person can exhale during a forced breath in one second (forced expiratory volume in one second or FEV1). The difference in the average decrease in FEV1 during the 12-month treatment period was approximately 153 mL. After discontinuation of Rapamune, the decline in lung function resumed at a rate similar to the placebo group.
The most commonly reported side effects associated with Rapamune for the treatment of LAM were mouth and lip ulcers, diarrhea, abdominal pain, nausea, sore throat, acne, chest pain, leg swelling, upper respiratory tract infection, headache, dizziness, muscle pain and elevated cholesterol. Serious side effects including hypersensitivity and edema have been observed in renal transplant patients.
Rapamune is made by Wyeth Pharmaceuticals, Inc., a subsidiary of Pfizer, Inc., Philadelphia, Pennsylvania.

Safety Announcements

FDA Drug Safety Communication: FDA warns that SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood

[May 15th, 2015] The FDA is warning that the type 2 diabetes medicines canagliflozin, dapagliflozin, and empagliflozin may lead to ketoacidosis, a serious condition where the body produces high levels ketones that may require hospitalization. We are continuing to investigate this safety issue and will determine whether changes are needed in the prescribing information for this class of drugs, called sodium-glucose cotransporter-2 (SGLT2) inhibitors.
Patients should pay close attention for any signs of ketoacidosis and seek medical attention immediately if they experience symptoms such as difficulty breathing, nausea, vomiting, abdominal pain, confusion, and unusual fatigue or sleepiness. Do not stop or change your diabetes medicines without first talking to your prescriber. Health care professionals should evaluate for the presence of acidosis, including ketoacidosis, in patients experiencing these signs or symptoms; discontinue SGLT2 inhibitors if acidosis is confirmed; and take appropriate measures to correct the acidosis and monitor sugar levels.
SGLT2 inhibitors are FDA-approved for use with diet and exercise to lower blood sugar in adults with type 2 diabetes. When untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. SGLT2 inhibitors lower blood sugar by causing the kidneys to remove sugar from the body through the urine. These medicines are available as single-ingredient products and also in combination with other diabetes medicines such as metformin. The safety and efficacy of SGLT2 inhibitors have not been established in patients with type 1 diabetes, and FDA has not approved them for use in these patients.
A search of the FDA Adverse Event Reporting System (FAERS) database identified 20 cases of acidosis reported as diabetic ketoacidosis (DKA), ketoacidosis, or ketosis in patients treated with SGLT2 inhibitors from March 2013 to June 6, 2014. All patients required emergency room visits or hospitalization to treat the ketoacidosis. Since June 2014, we have continued to receive additional FAERS reports for DKA and ketoacidosis in patients treated with SGLT2 inhibitors.
DKA, a subset of ketoacidosis or ketosis in diabetic patients, is a type of acidosis that usually develops when insulin levels are too low or during prolonged fasting. DKA most commonly occurs in patients with type 1 diabetes and is usually accompanied by high blood sugar levels. The FAERS cases were not typical for DKA because most of the patients had type 2 diabetes and their blood sugar levels, when reported, were only slightly increased compared to typical cases of DKA. Factors identified in some reports as having potentially triggered the ketoacidosis included major illness, reduced food and fluid intake, and reduced insulin dose.
We urge health care professionals and patients to report side effects involving SGLT2 inhibitors to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA cautions about dose confusion and medication errors for antibacterial drug Zerbaxa (ceftolozane and tazobactam)

[May 20th, 2015] The U.S. Food and Drug Administration (FDA) is warning health care professionals about the risk for dosing errors with the antibacterial drug Zerbaxa (ceftolozane and tazobactam) due to confusion about the drug strength displayed on the vial and carton labeling. Zerbaxa's vial label was initially approved with a strength that reflects each individual active ingredient (e.g. 1 g/0.5 g); however, the product is dosed based on the sum of these ingredients (e.g. 1.5 g). To prevent future medication errors, the strength on the drug labeling has been revised to reflect the sum of the two active ingredients. Thus, one vial of Zerbaxa will now list the strength as 1.5 grams equivalent to ceftolozane 1 gram and tazobactam 0.5 gram.

Zerbaxa is used to treat complicated infections in the urinary tract, or in combination with the antibacterial drug metronidazole to treat complicated infections in the abdomen.

We evaluated seven reported cases of medication error that occurred during preparation of the dose in the pharmacy due to confusion with the display of the strength of individual ingredients on Zerbaxa's vial label and carton labeling. Listing the individual drug strengths led to confusion because it was different from labeling for other beta-lactam/beta-lactamase antibacterial drugs that express strength as the sum of the two active ingredients. In some cases, this led to administration of 50% more drug than was prescribed. No adverse events were reported among these seven cases.

We urge health care professionals and patients to report side effects and medication errors involving Zerbaxa to the FDA MedWatch program.

Current Drug Shortages Index (as of May 31st, 2015):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azathioprine Tablet	***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 Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Ephedrine Sulfate Injection	***Currently in Shortage***
Epinephrine 1mg/mL (Preservative Free)[13]	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluoxymesterone (Androxy) Tablets, USP	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Haloperidol Lactate Injection	***Currently in Shortage***

Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigo Carmine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***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***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylin Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride ER Capsules/Tablets[14]	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Nebivolol (BYSTOLIC) Tablets	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Pancuronium Bromide Injection	***Currently in Shortage***
Papaverine Hydrochloride Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Phosphate (Glycophos) Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Quazepam (Doral) Tablets	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Secretin Synthetic Human (ChiRhoStim) Injection	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thiotepa (Thioplex) for Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trace Elements	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***