Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
February 8, 2017
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: Melissa Abbott, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – February 8, 2017

DATE: February 1, 2017

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 February 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/SoonerPsych Program Update – Appendix B

Action Item – Vote to Prior Authorize Syndros™ (Dronabinol), Sustol® (Granisetron), and Bonjesta® (Doxylamine/Pyridoxine) – Appendix C

Action Item – Vote to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir) – Appendix D

Action Item – Vote to Prior Authorize Exondys 51™ (Eteplirsen) – Appendix E

Action Item – Vote to Prior Authorize Otovel® (Ciprofloxacin/Fluocinolone Acetonide) – Appendix F

Action Item – Vote to Prior Authorize Cinqair® (Reslizumab) and Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate) – Appendix G

Action Item – Vote to Prior Authorize Fosrenol® (Lanthanum Carbonate), Velphoro® (Sucroferric Oxyhydroxide), and Auryxia™ (Ferric Citrate) – Appendix H

Action Item – Vote to Prior Authorize Defitelio® (Defibrotide Sodium) – Appendix I

Annual Review of Seizure Medications and 30-Day Notice to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection) – Appendix J

Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Nuplazid™ (Pimavanserin) – Appendix K

Annual Review of Hyperkalemia Medications and 30-Day Notice to Prior Authorize Veltassa® (Patiromer) – Appendix L

30-Day Notice to Prior Authorize Kanuma® (Sebelipase Alfa) – Appendix M

Annual Review of Solaraze® (Diclofenac Sodium 3% Gel) and 30-Day Notice to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel) – Appendix N

Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection) – Appendix O

Annual Review of Xuriden™ (Uridine Triacetate) – Appendix P

FDA and DEA Updates – Appendix Q

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – February 8, 2017 @ 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. Acknowledgement of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. December 14, 2016 DUR Minutes – Vote

B. December 14, 2016 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/SoonerPsych Program Update – See Appendix B

A. Medication Coverage Activity for December 2016

B. Pharmacy Help Desk Activity for December 2016

C. Medication Coverage Activity for January 2017

D. Pharmacy Help Desk Activity for January 2017

E. SoonerPsych Program Update

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

5. Action Item – Vote to Prior Authorize Syndros™ (Dronabinol), Sustol® (Granisetron), and Bonjesta® (Doxylamine/Pyridoxine) – See Appendix C

A. Introduction

B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir) – See Appendix D

A. Introduction

B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Exondys 51™ (Eteplirsen) – See Appendix E

A. Introduction

B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Otovel® (Ciprofloxacin/Fluocinolone Acetonide) – See Appendix F

A. Introduction

B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Cinqair® (Reslizumab) and Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Fosrenol® (Lanthanum Carbonate), Velphoro® (Sucroferric Oxyhydroxide), and Auryxia™ (Ferric Citrate) – See Appendix H

A. Introduction
B. Phosphate Binder Product Comparison
C. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Defitelio® (Defibrotide Sodium) – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

12. Annual Review of Seizure Medications and 30-Day Notice to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Seizure Medications
C. Prior Authorization of Seizure Medications
D. Market News and Updates
E. Briviact® (Brivaracetam) Product Summary
F. Fycompa™ (Perampanel Oral Suspension) Product Summary
G. Carnexiv™ (Carbamazepine Injection) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Seizure Medications

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

13. Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Nuplazid™ (Pimavanserin) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Parkinson's Disease Medications
C. Prior Authorization of Parkinson's Disease Medications
D. Market News and Updates
E. Nuplazid™ (Pimavanserin) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Parkinson's Disease Medications

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

14. Annual Review of Hyperkalemia Medications and 30-Day Notice to Prior Authorize Veltassa® (Patiromer) – See Appendix L

A. Chronic Hyperkalemia
B. Utilization of Potassium Binders
C. Market News and Updates
D. Veltassa® (Patiromer) Product Summary
E. College of Pharmacy Recommendations
F. Utilization Details of Potassium Binders

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

15. 30-Day Notice to Prior Authorize Kanuma® (Sebelipase Alfa) – See Appendix M

A. Lysosomal Acid Lipase Deficiency (LAL-D) Background Information
B. Kanuma® (Sebelipase Alfa) Product Summary
C. College of Pharmacy Recommendations

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

16. Annual Review of Solaraze® (Diclofenac Sodium 3% Gel) and 30-Day Notice to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Solaraze® (Diclofenac 3% Gel)
C. Prior Authorization of Solaraze® (Diclofenac 3% Gel)
D. Market News and Updates
E. Picato® (Ingenol Mebutate Gel) Product Summary
F. College of Pharmacy Recommendations

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

17. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) and Zembrace™ SymTouch™ (Sumatriptan Injection) – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Onzetra® Xsail® (Sumatriptan Nasal Powder) Product Summary
F. Zembrace™ SymTouch™ (Sumatriptan Injection) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Anti-Migraine Medications

Non-presentation; questions only:

18. Annual Review of Xuriden™ (Uridine Triacetate) – See Appendix P

A. Hereditary Orotic Aciduria Overview
B. Current Prior Authorization Criteria
C. Utilization of Xuriden™ (Uridine Triacetate)
D. Prior Authorization of Xuriden™ (Uridine Triacetate)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

19. FDA and DEA Updates – See Appendix Q

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

20. Future Business* (Upcoming Product and Class Reviews)

A. Multiple Sclerosis Medications
B. Zinplava™ (Bezlotoxumab)
C. Pulmonary Arterial Hypertension Medications
D. Ulcerative Colitis and Crohn's Disease Medications
E. Naloxone Medications
F. Gaucher Disease Medications
G. Makena® (Hydroxyprogesterone Caproate) and Vaginal Progesterone Products

**Future business subject to change.*

21. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF DECEMBER 14, 2016

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.		x
Anetta Harrell, Pharm.D.		x
Ashley Huddleston, Pharm.D., BCOP		x
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, Pharm.D.	x	
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA; Vice Chairman	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	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, 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	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Graduate Students: Christina Bulkley, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Visiting Pharmacy Student(s): N/A		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Marlene Asmussen, R.N.; Population Care Management Director		x
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm	x	
Kelli Brodersen, Marketing Coordinator	x	
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director; CEO	x	
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Garth Splinter, M.D.; M.B.A.; Deputy Chief Executive Officer	x	
Joseph Young, Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Pratik Parikh, Sarepta	Cheryl Donahue, Sarepta	Patrick Harvey, Walgreens
Brandon Ross, Merck	Mark DeClerk, Lilly	Deron Grothe, Teva
Torey Batts, Teva	Ty Griffin, Medco	Michele Puyear, Gilead
Jeff Knappen, Allergan	Jason Schwier, Amgen	Corinne Copeland, Eisai
Lee Stout, Chiesi	Jim Dunlap, PhRMA	Tyler Craddock, Medco
Bobby White, UCB	Gay Thomas, BMS	Sean Seago, Merck
Kari Suttee, Novartis	Jim Chapman, Abbvie	Brian Maves, Pfizer
Eric Gardner, Vortex Pharma	Marc Parker, Sunovion	Terry McCurren, Otsuka
Jim Fowler, Astra Zeneca	Jeff C., Eisai	

PRESENT FOR PUBLIC COMMENT:	
Michele Puyear	Gilead Sciences
Pratik Parikh	Sarepta Therapeutics
Torey Batts	Teva Pharmaceuticals

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. 10 SPEAKER: MICHELE PUYEAR

2B: AGENDA NO. 11 SPEAKER: PRATIK PARIKH

2C: AGENDA NO. 13 SPEAKER: TOREY BATTS

ACTION: NONE REQUIRED

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

3A: NOVEMBER 9, 2016 DUR MINUTES – VOTE

3B: NOVEMBER 9, 2016 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2016

4B: PHARMACY HELP DESK ACTIVITY FOR NOVEMBER 2016

4C: CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **PROPOSED EXECUTIVE SESSION AS RECOMMENDED BY THE OFFICE OF LEGAL SERVICES AND AUTHORIZED BY THE OPEN MEETINGS ACT, 25 O.S. § 307(B)(4) – DISCUSSION OF PENDING AND POTENTIAL LITIGATION/CLAIMS**

Presented by Joseph Young

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 6:</u> **VOTE TO PRIOR AUTHORIZE ACTICLATE® (DOXYCYCLINE HYCLATE)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 7:</u> **VOTE TO PRIOR AUTHORIZE JADENU™ (DEFERASIROX) AND FERRIPROX® (DEFERIPRONE)**

7A: INTRODUCTION: ORAL IRON CHELATING AGENTS

7B: ESTIMATED COST SAVINGS: ORAL IRON CHELATING AGENTS

7C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 8:</u> **VOTE TO PRIOR AUTHORIZE PANCREAZE® (PANCRELIPASE), PERTZYE® (PANCRELIPASE), AND VIOKACE® (PANCRELIPASE)**

8A: INTRODUCTION

8B: PANCREATIC ENZYME PRODUCT SUMMARIES

8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 9:</u> **VOTE TO PRIOR AUTHORIZE BROMSITE™ (BROMFENAC 0.075% OPHTHALMIC SOLUTION)**

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

Dr. Preslar moved to approve; seconded Dr. Garton

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 10:</u> **ANNUAL REVIEW OF HEPATITIS C MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VIEKIRA XR™ (DASABUVIR/OMBITASVIR/PARITAPREVIR/RITONAVIR) AND EPCLUSA® (SOFOSBUVIR/VELPATASVIR)**

10A: INTRODUCTION

10B: CURRENT PRIOR AUTHORIZATION CRITERIA

10C: UTILIZATION OF HEPATITIS C MEDICATIONS

10D: PRIOR AUTHORIZATION OF HEPATITIS C MEDICATIONS

10E: MARKET NEWS AND UPDATES

10F: REGIMEN COMPARISON

10G: VIEKIRA XR™ (DASABUVIR/OMBITASVIR/PARITAPREVIR/RITONAVIR) PRODUCT SUMMARY

10H: EPCLUSA® (SOFOSBUVIR/VELPATASVIR) PRODUCT SUMMARY

10I: COLLEGE OF PHARMACY RECOMMENDATIONS

10J: UTILIZATION DETAILS OF HEPATITIS C MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 11:</u> **30-DAY NOTICE TO PRIOR AUTHORIZE EXONDYS 51™ (ETEPLIRSEN)**

11A: DUCHENNE MUSCULAR DYSTROPHY
11B: EXONDYS 51™ (ETEPLIRSEN) PRODUCT SUMMARY
11C: MARKET NEWS AND UPDATES
11D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 12:</u> **ANNUAL REVIEW OF OTIC ANTI-INFECTIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OTOVEL® (CIPROFLOXACIN/FLUOCINOLONE ACETONIDE)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF OTIC ANTI-INFECTIVE MEDICATIONS
12C: PRIOR AUTHORIZATION OF OTIC ANTI-INFECTIVE MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: OTOVEL® (CIPROFLOXACIN/FLUOCINOLONE ACETONIDE) PRODUCT SUMMARY
12F: COLLEGE OF PHARMACY RECOMMENDATIONS
12G: UTILIZATION DETAILS OF OTIC ANTI-INFECTIVE MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 13:</u> **ANNUAL REVIEW OF MAINTENANCE ASTHMA & CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS & 30-DAY NOTICE TO PRIOR AUTHORIZE CINQAIR® (RESLIZUMAB) AND BEVESPI AEROSPHERE® (GLYCOPYRROLATE/FORMOTEROL FUMARATE)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
13C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: CINQAIR® (RESLIZUMAB) PRODUCT SUMMARY
13F: BEVESPI AEROSPHERE® (GLYCOPYRROLATE/FORMOTEROL FUMARATE) PRODUCT SUMMARY
13G: COLLEGE OF PHARMACY RECOMMENDATIONS
13H: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 14:</u> **ANNUAL REVIEW OF ANTI-EMETIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE SYNDROS™ (DRONABINOL), SUSTOL® (GRANISETRON), AND BONJESTA® (DOXYLAMINE/PYRIDOXINE)**

14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF ANTI-EMETIC MEDICATIONS
14C: PRIOR AUTHORIZATION OF ANTI-EMETIC MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: SYNDROS™ (DRONABINOL) PRODUCT SUMMARY
14F: SUSTOL® (GRANISETRON) PRODUCT SUMMARY
14G: BONJESTA® (DOXYLAMINE/PYRIDOXINE) PRODUCT SUMMARY
14H: COLLEGE OF PHARMACY RECOMMENDATIONS
14I: UTILIZATION DETAILS OF ANTI-EMETIC MEDICATIONS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 15:</u> **ANNUAL REVIEW OF PHOSPHATE BINDERS AND 30-DAY NOTICE TO PRIOR AUTHORIZE FOSRENOL® (LANTHANUM CARBONATE), VELPHORO® (SUCROFERRIC OXYHYDROXIDE), AND AURYXIA™ (FERRIC CITRATE)**

15A: INTRODUCTION
15B: UTILIZATION OF PHOSPHATE BINDERS
15C: MARKET NEWS AND UPDATES
15D: PHOSPHATE BINDERS PRODUCT COMPARISON
15E: FOSRENOL® (LANTHANUM CARBONATE) PRODUCT SUMMARY
15F: VELPHORO® (SUCROFERRIC OXYHYDROXIDE) PRODUCT SUMMARY
15G: AURYXIA™ (FERRIC CITRATE) PRODUCT SUMMARY
15H: COLLEGE OF PHARMACY RECOMMENDATIONS
15I: UTILIZATION DETAILS OF PHOSPHATE BINDERS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 16:</u> **30-DAY NOTICE TO PRIOR AUTHORIZE DEFITELIO® (DEFIBROTIDE SODIUM)**

16A: HEPATIC VENO-OCCLUSIVE DISEASE (VOD) BACKGROUND INFORMATION
16B: DEFITELIO® (DEFIBROTIDE SODIUM) PRODUCT SUMMARY
16C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 17:</u> **ANNUAL REVIEW OF TESTOSTERONE PRODUCTS**

17A: CURRENT PRIOR AUTHORIZATION CRITERIA
17B: UTILIZATION OF TESTOSTERONE PRODUCTS
17C: PRIOR AUTHORIZATION OF TESTOSTERONE PRODUCTS
17D: MARKET NEWS AND UPDATES
17E: COLLEGE OF PHARMACY RECOMMENDATIONS
17F: UTILIZATION DETAILS OF TESTOSTERONE PRODUCTS

Materials included in agenda packet; Non-presentation; Questions only

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 18:</u> **FDA AND DEA UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 19:</u> **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**
No Meeting Scheduled for January 2017

19A: SEIZURE MEDICATIONS
19B: BOTULINUM TOXINS
19C: KANUMA® (SEBELIPASE ALFA)
19D: PARKINSON'S DISEASE MEDICATIONS
19E: XURIDEN™ (URIDINE TRIACETATE)
19F: ANTI-MIGRAINE MEDICATIONS
19G: HYPERKALEMIA MEDICATIONS
19H: ACTINIC KERATOSIS MEDICATIONS

****FUTURE BUSINESS SUBJECT TO CHANGE.***

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 20:</u> **ADJOURNMENT**

The meeting was adjourned at 5:22 p.m.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: December 15, 2016

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

From: Melissa Abbott, Pharm.D.
Clinical Pharmacist
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of December 14, 2016

Recommendation 1: Chronic Medication Adherence Program Update

NO ACTION REQUIRED.

The College of Pharmacy will continue to monitor member adherence with the goal of achieving a member Proportion of Days Covered (PDC) of 80% of greater and a five star rating of prescriber percentage of adherent members. Once several mailings have been processed under the new format with consistent prescribers, the College of Pharmacy will reevaluate prescriber percentages of adherent members by just those included in the mailings. Results of the new format will be reported to the Drug Utilization Review (DUR) Board.

Recommendation 2: Proposed Executive Session as Recommended by the Office of Legal Services and Authorized by the Open Meetings Act, 25 O.S. § 307(B)(4) – Discussion of Pending and Potential Litigation/Claims

MOTION CARRIED by unanimous approval.

Recommendation 3: Vote to Prior Authorize Acticlate® (Doxycycline Hyclate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Acticlate® (doxycycline hyclate) 75mg capsules with the following criteria:

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.

Recommendation 4: Vote to Prior Authorize Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone)

MOTION CARRIED by unanimous approval.

Based on the low net cost of Exjade® (deferasirox) and significant cost savings if members using Jadenu™ (deferasirox) or Ferriprox® (deferiprone) switched to Exjade® (deferasirox), the College of Pharmacy recommends the prior authorization of Jadenu™ (deferasirox) and Ferriprox® (deferiprone) with the following criteria:

Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason other than convenience why the member cannot use Exjade® (deferasirox) must be provided; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Recommendation 5: Vote to Prior Authorize Pancreaze® (Pancrelipase), Pertzye® (Pancrelipase), and Viokace® (Pancrelipase)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Pancreaze®, Pertzye®, and Viokace® with the following criteria:

Pancreaze®, Pertzye®, and Viokace® Approval Criteria:

1. An FDA approved diagnosis of pancreatic insufficiency; and
2. Documented trials of inadequate response to Creon® and Zenpep® or a patient-specific, clinically significant reason why the member cannot use Creon® or Zenpep®.

Based on the lower net cost of Creon® and Zenpep®, the College of Pharmacy does not recommend the prior authorization of Creon® or Zenpep® at this time.

Recommendation 6: Vote to Prior Authorize BromSite™ (Bromfenac 0.075% Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the placement of BromSite™ (bromfenac 0.075% ophthalmic solution) into Tier-2 of the Ophthalmic Nonsteroidal Anti-Inflammatory Drugs Product Based Prior Authorization Category (PBPA). Current Tier-2 criteria for this category will apply.

Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	
Tier-1	**Tier-2**
diclofenac (Voltaren®) 0.1% solution	bromfenac (Bromday™) 0.09% solution
flurbiprofen (Ocufen®) 0.03% solution*	**bromfenac (BromSite™) 0.075% solution**
ketorolac (Acular®) 0.5% solution	bromfenac (Prolensa™) 0.07% solution
	ketorolac (Acular LS®) 0.4% solution
	ketorolac (Acuvail®) 0.45% solution
	nepafenac (Nevanac™) 0.1% suspension
	nepafenac (Ilevro™) 0.3% suspension

*Not a required Tier-1 trial. Does not have to be attempted for approval of a Tier-2 medication.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

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

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

Recommendation 7: Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir)

NO ACTION REQUIRED.

Recommendation 8: 30-Day Notice to Prior Authorize Exondys 51™ (Eteplirsen)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Otic Anti-Infective Medications and 30-Day Notice to Prior Authorize Otovel® (Ciprofloxacin/Fluocinolone Acetonide)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Maintenance Asthma & Chronic Obstructive Pulmonary Disease (COPD) Medications & 30-Day Notice to Prior Authorize Cinqair® (Reslizumab) and Bevespi Aerosphere® (Glycopyrrolate/ Formoterol Fumarate)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Syndros™ (Dronabinol), Sustol® (Granisetron), and Bonjesta® (Doxylamine/Pyridoxine)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Phosphate Binders and 30-Day Notice to Prior Authorize Fosrenol® (Lanthanum Carbonate), Velphoro® (Sucroferric Oxyhydroxide), and Auryxia™ (Ferric Citrate)

NO ACTION REQUIRED.

Recommendation 13: 30-Day Notice to Prior Authorize Defitelio® (Defibrotide Sodium)

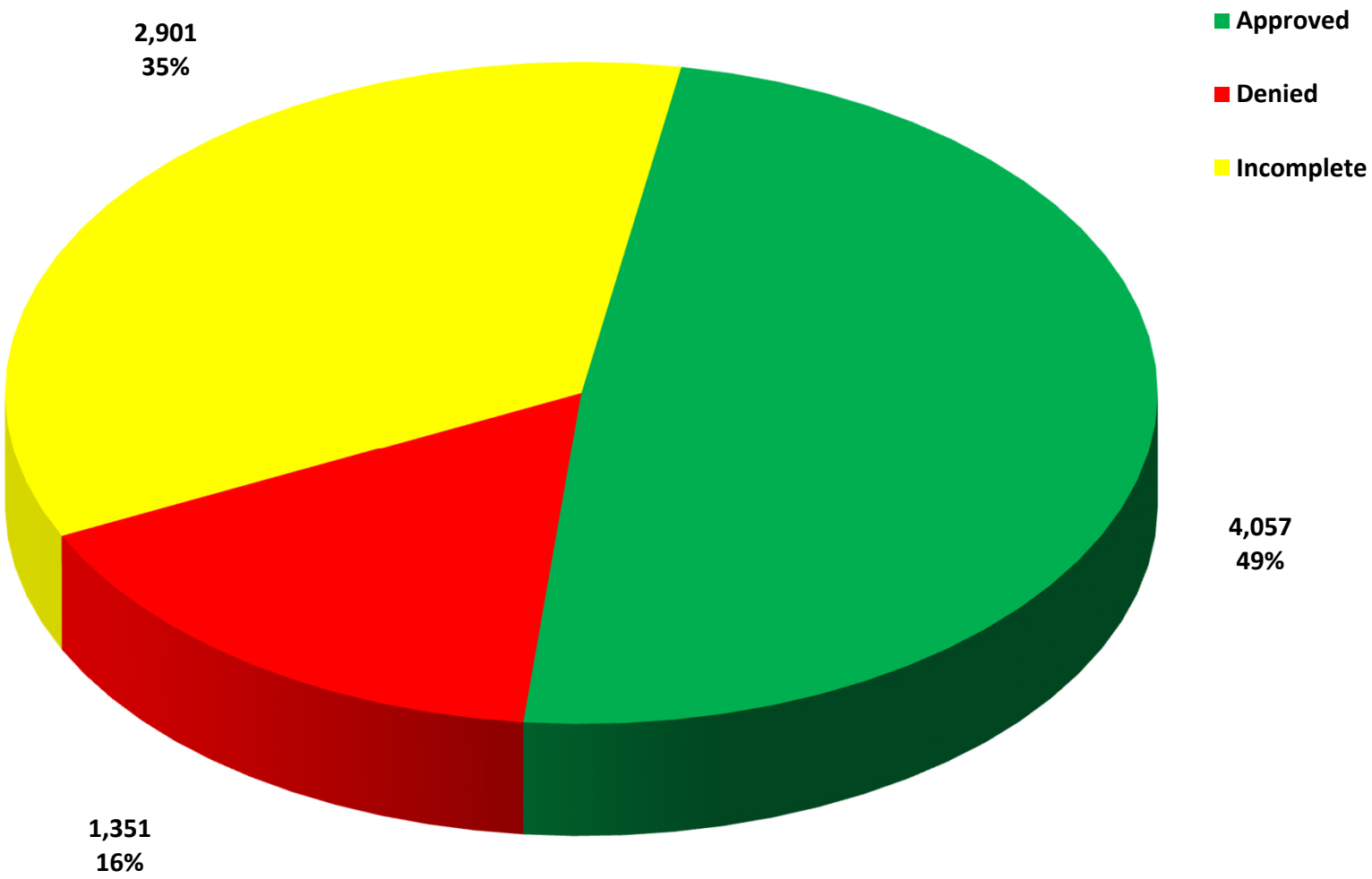
NO ACTION REQUIRED.

Recommendation 14: Annual Review of Testosterone Products

NO ACTION REQUIRED.

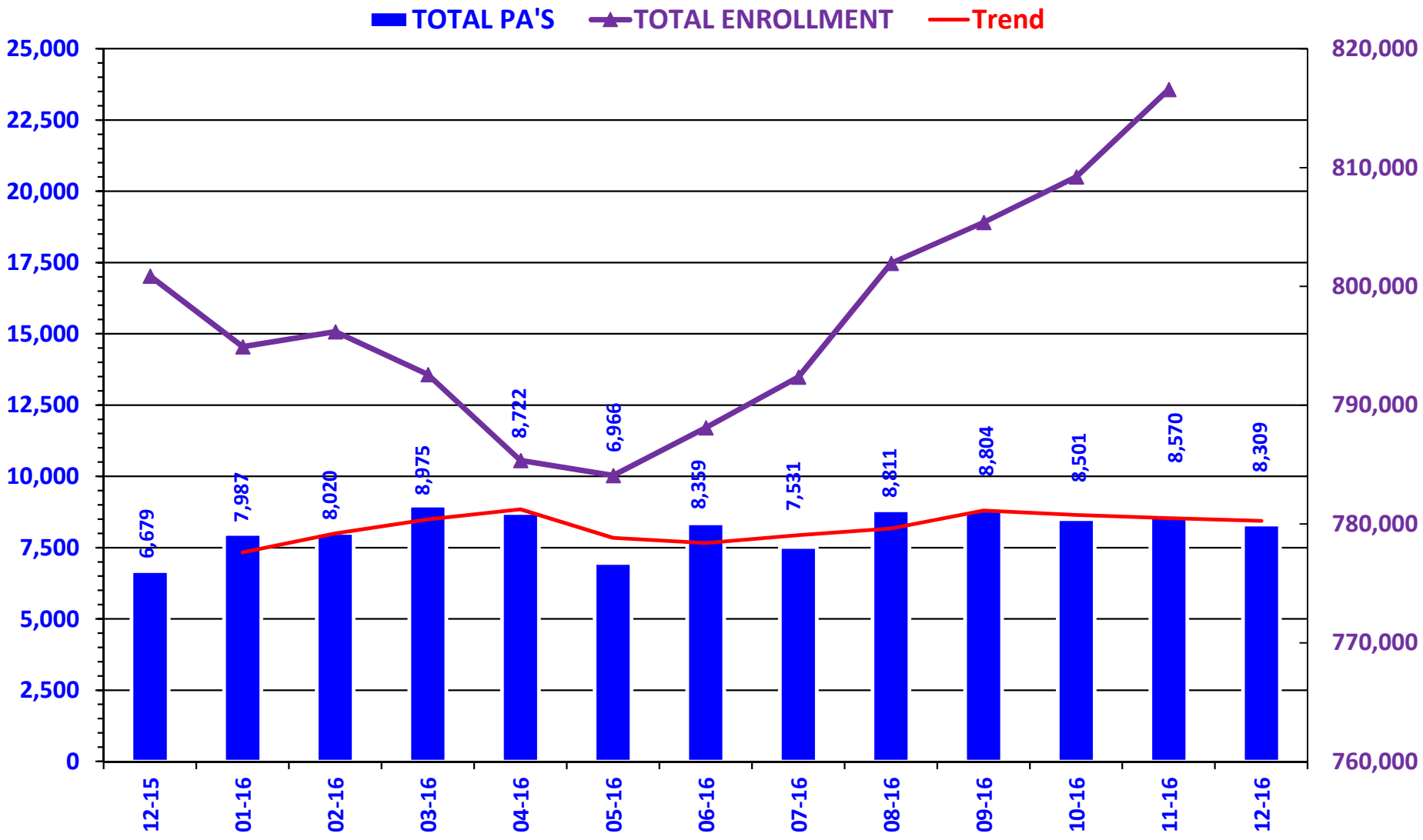
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: DECEMBER 2016



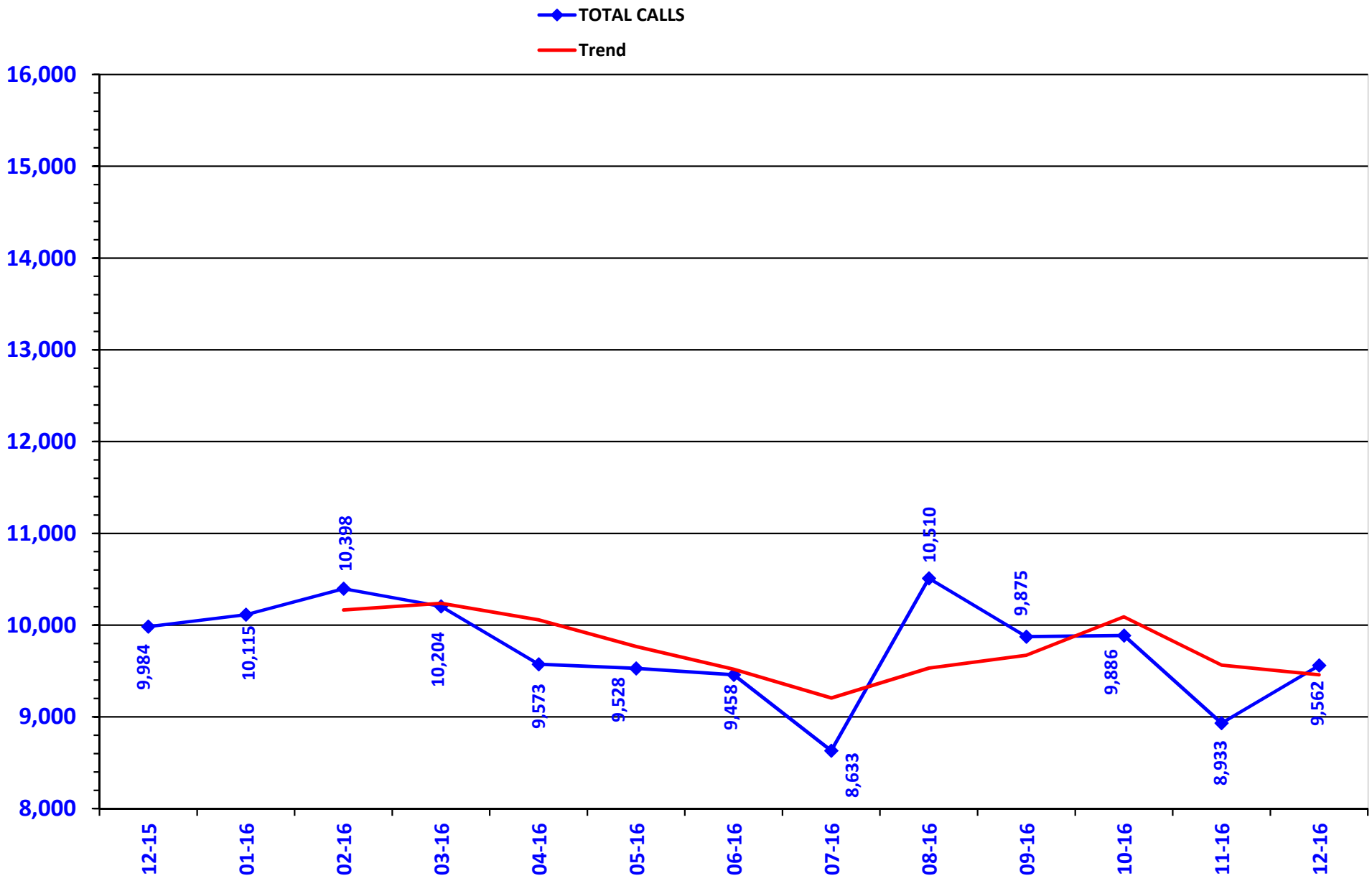
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: DECEMBER 2015 – DECEMBER 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
DECEMBER 2015 – DECEMBER 2016



Prior Authorization Activity

12/1/2016 Through 12/31/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	394	204	47	143	154
Analgesic - NonNarcotic	21	0	4	17	0
Analgesic, Narcotic	515	281	48	186	165
Angiotensin Receptor Antagonist	20	4	4	12	280
Antiasthma	81	18	12	51	328
Antibiotic	23	12	3	8	116
Anticonvulsant	95	52	14	29	350
Antidepressant	74	14	19	41	310
Antidiabetic	194	81	27	86	353
Antifungal	10	1	4	5	35
Antihistamine	183	138	15	30	357
Antimigraine	49	7	14	28	136
Antineoplastic	12	8	1	3	175
Antiulcers	119	25	46	48	182
Antiviral	90	51	19	20	8
Anxiolytic	51	23	8	20	277
Atypical Antipsychotics	428	264	31	133	196
Biologics	99	41	19	39	312
Bladder Control	52	12	17	23	333
Blood Thinners	202	128	17	57	309
Botox	48	31	12	5	345
Buprenorphine Medications	296	221	17	58	71
Cardiovascular	102	44	22	36	320
Cephalosporins	12	8	0	4	13
Chronic Obstructive Pulmonary Disease	178	23	51	104	329
Constipation/Diarrhea Medications	123	21	41	61	215
Contraceptive	18	13	3	2	353
Dermatological	100	24	44	32	178
Diabetic Supplies	502	282	15	205	208
Endocrine & Metabolic Drugs	77	51	8	18	145
Erythropoietin Stimulating Agents	15	9	1	5	97
Fibromyalgia	186	23	106	57	293
Fish Oils	13	2	4	7	358
Gastrointestinal Agents	93	26	19	48	106
Glaucoma	13	3	3	7	246
Growth Hormones	69	49	9	11	135
Hepatitis C	85	44	19	22	16
HFA Rescue Inhalers	82	20	17	45	327
Insomnia	27	4	7	16	154
Insulin	89	18	22	49	337
Miscellaneous Antibiotics	29	4	8	17	13
Multiple Sclerosis	41	18	5	18	170
Muscle Relaxant	50	10	17	23	124
Nasal Allergy	64	3	16	45	82
Neurological Agents	54	32	9	13	335
NSAIDs	204	29	69	106	257
Ocular Allergy	31	5	10	16	83

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

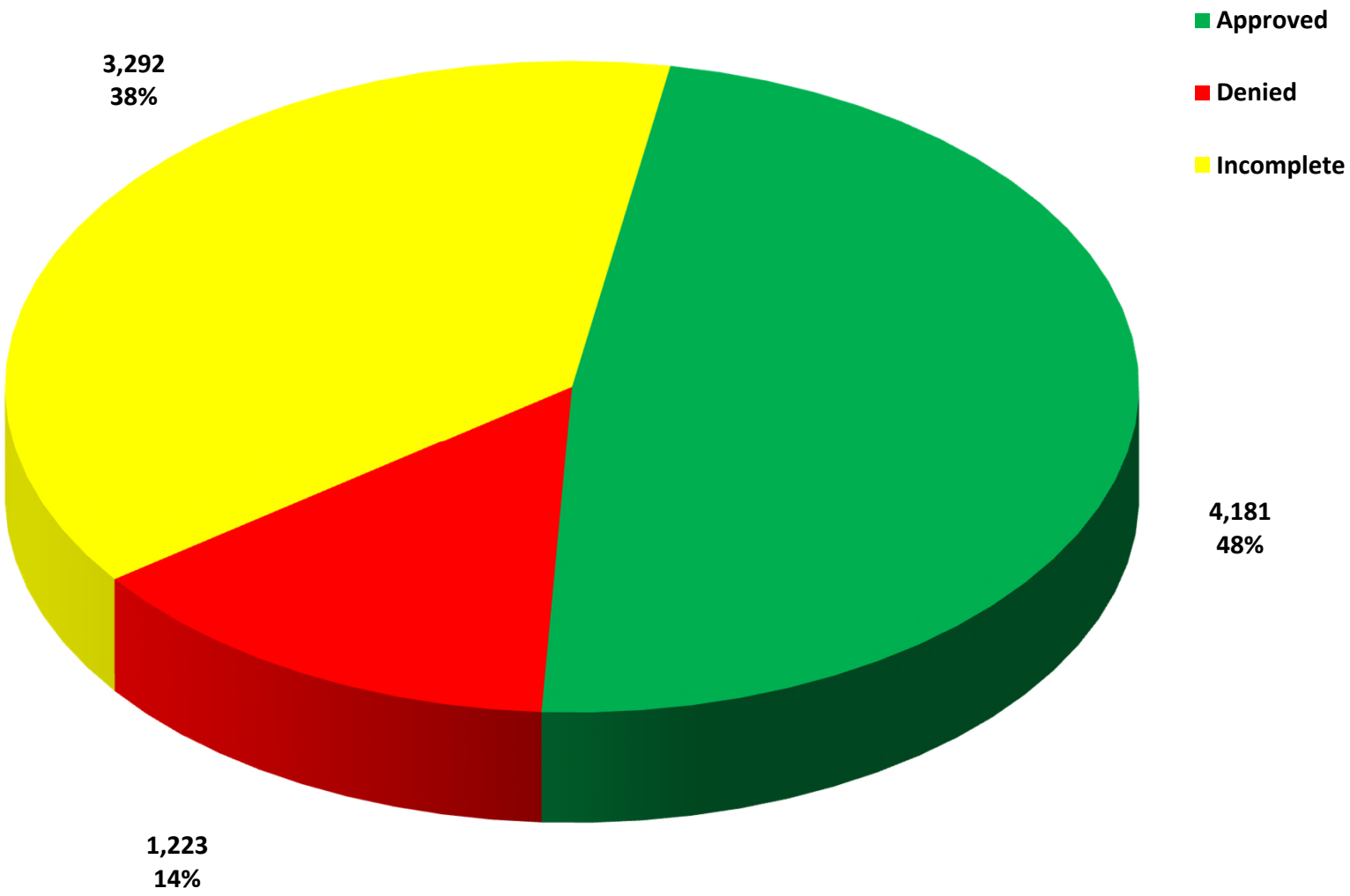
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Ophthalmic Anti-infectives	12	3	3	6	18
Osteoporosis	30	10	9	11	303
Other*	311	37	109	165	172
Otic Antibiotic	20	4	4	12	7
Pediculicide	21	6	2	13	5
Respiratory Agents	14	8	1	5	155
Statins	36	8	9	19	358
Stimulant	717	348	95	274	340
Synagis	177	91	41	45	111
Testosterone	47	18	14	15	326
Topical Antifungal	28	3	6	19	24
Topical Corticosteroids	81	1	26	54	90
Vitamin	85	29	37	19	303
Pharmacotherapy	71	67	1	3	303
Emergency PAs	0	0	0	0	
Total	**6,963**	**3,014**	**1,280**	**2,669**	
Overrides					
Brand	46	22	9	15	267
Cumulative Early Refill	4	4	0	0	180
Diabetic Supplies	2	2	0	0	222
Dosage Change	343	318	1	24	12
High Dose	5	2	2	1	181
Ingredient Duplication	35	29	0	6	10
Lost/Broken Rx	113	99	7	7	11
NDC vs Age	142	100	9	33	250
Nursing Home Issue	52	47	0	5	11
Opioid Quantity	16	13	2	1	137
Other*	22	22	0	0	13
Quantity vs. Days Supply	549	374	42	133	250
STBS/STBSM	13	8	0	5	41
Stolen	6	4	1	1	7
Temporary Unlock	2	2	0	0	28
Third Brand Request	18	16	0	2	18
Overrides Total	**1,346**	**1,043**	**71**	**232**	
Total Regular PAs + Overrides	**8,309**	**4,057**	**1,351**	**2,901**	

Denial Reasons	
Unable to verify required trials.	2,219
Does not meet established criteria.	1,369
Lack required information to process request.	637

Other PA Activity	
Duplicate Requests	486
Letters	7,462
No Process	6
Changes to existing PAs	605
Helpdesk Initiated Prior Authorizations	603
PAs Missing Information	29

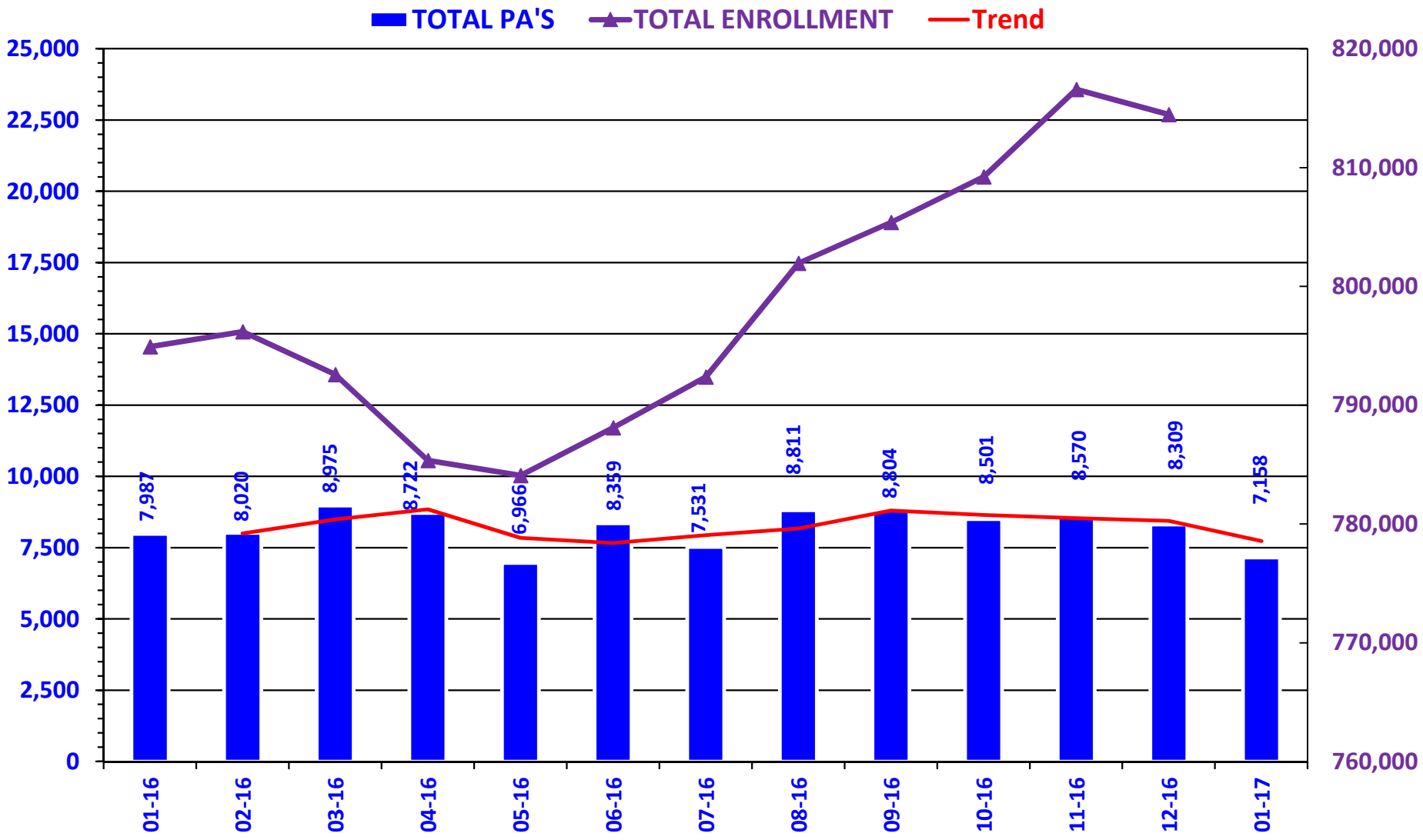
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY 2017



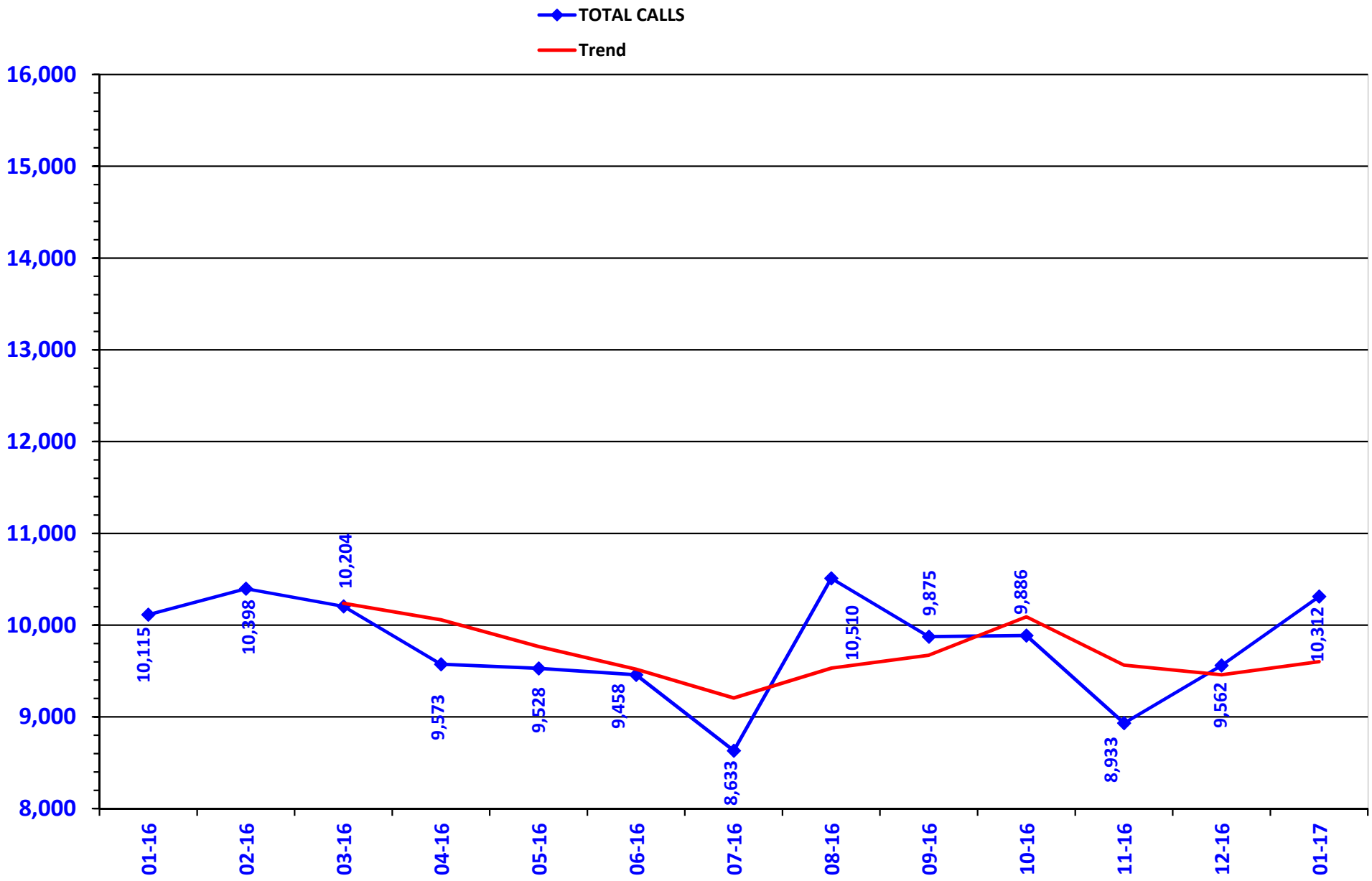
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2016 – JANUARY 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JANUARY 2016 – JANUARY 2017



Prior Authorization Activity

1/1/2017 Through 1/31/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	148	24	28	96	260
Analgesic - NonNarcotic	20	0	2	18	0
Analgesic, Narcotic	548	302	39	207	161
Angiotensin Receptor Antagonist	11	4	2	5	357
Antiasthma	59	10	11	38	359
Antibiotic	23	8	1	14	234
Anticonvulsant	132	63	13	56	341
Antidepressant	94	21	20	53	357
Antidiabetic	216	91	26	99	346
Antifungal	10	1	5	4	83
Antigout	10	7	1	2	358
Antihistamine	419	379	7	33	354
Antimigraine	26	2	6	18	183
Antineoplastic	23	12	0	11	148
Antiparasitic	10	0	0	10	0
Antiulcers	137	30	49	58	158
Antiviral	78	47	6	25	9
Anxiolytic	63	35	4	24	272
Atypical Antipsychotics	218	107	24	87	295
Biologics	90	48	13	29	294
Bladder Control	58	11	19	28	332
Blood Thinners	230	123	14	93	331
Botox	27	18	7	2	319
Buprenorphine Medications	296	209	15	72	75
Cardiovascular	112	47	16	49	268
Cephalosporins	15	9	0	6	7
Chronic Obstructive Pulmonary Disease	207	24	50	133	335
Constipation/Diarrhea Medications	191	32	71	88	254
Contraceptive	21	14	2	5	332
Dermatological	85	8	51	26	152
Diabetic Supplies	523	286	30	207	203
Endocrine & Metabolic Drugs	104	59	6	39	129
Erythropoietin Stimulating Agents	40	19	8	13	95
Fibromyalgia	202	23	93	86	334
Gastrointestinal Agents	129	27	32	70	103
Glaucoma	12	1	2	9	360
Growth Hormones	57	46	0	11	142
Hepatitis C	95	51	19	25	8
HFA Rescue Inhalers	75	15	23	37	336
Insomnia	42	3	17	22	135
Insulin	88	18	18	52	348
Miscellaneous Antibiotics	17	4	1	12	94
Multiple Sclerosis	45	16	11	18	182
Muscle Relaxant	65	11	21	33	23
Nasal Allergy	67	5	21	41	302
Neurological Agents	41	19	10	12	348
NSAIDs	181	27	46	108	253
Ocular Allergy	37	8	12	17	115

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Osteoporosis	15	3	5	7	358
Other*	237	39	58	140	233
Otic Antibiotic	26	3	3	20	7
Pediculicide	10	1	2	7	7
Respiratory Agents	17	7	0	10	238
Statins	56	16	13	27	356
Stimulant	900	433	73	394	344
Synagis	110	50	27	33	76
Testosterone	44	10	21	13	340
Topical Antifungal	25	5	5	15	17
Topical Corticosteroids	180	5	64	111	63
Vitamin	76	36	25	15	315
Pharmacotherapy	65	57	0	8	265
Emergency PAs	0	0	0	0	
Total	**7,158**	**2,989**	**1,168**	**3,001**	
Overrides					
Brand	199	172	7	20	131
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	3	3	0	0	34
Dosage Change	301	275	1	25	13
High Dose	3	3	0	0	157
Ingredient Duplication	33	26	1	6	8
Lost/Broken Rx	90	79	0	11	10
NDC vs Age	237	163	16	58	278
Nursing Home Issue	22	20	0	2	6
Opioid Quantity	17	14	3	0	166
Other*	34	32	0	2	27
Quantity vs. Days Supply	550	370	28	152	248
STBS/STBSM	19	18	1	0	86
Stolen	10	8	0	2	16
Temporary Unlock	1	1	0	0	28
Third Brand Request	39	25	1	13	14
Overrides Total	**1,538**	**1,192**	**55**	**291**	
Total Regular PAs + Overrides	**8,696**	**4,181**	**1,223**	**3,292**	

Denial Reasons	
Unable to verify required trials.	2,411
Does not meet established criteria.	1,240
Lack required information to process request.	846
Other PA Activity	
Duplicate Requests	586
Letters	7,409
No Process	3
Changes to existing PAs	776
Helpdesk Initiated Prior Authorizations	681
PAs Missing Information	49

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

SoonerPsych Program Update

Oklahoma Health Care Authority
February 2017

Prescriber Mailing Summary

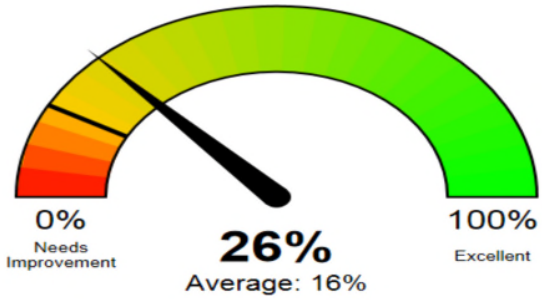
The SoonerPsych program is an educational quarterly mailing to prescribers treating members with atypical antipsychotic medications. Each mailing includes a gauge showing prescribers how their practice compares to those of other SoonerCare prescribers of atypical antipsychotic medications regarding potential differences from evidence-based prescribing practices. Each mailing also includes an informational page with evidence-based material related to the mailing topic. Mailing topics rotate between four modules: polypharmacy, adherence, metabolic monitoring, and diagnosis.

The SoonerPsych program has been using a "report card" format since April 2014 with one topic covered per mailing (all four modules covered in one year). Previously, prescribers were selected randomly to receive letters if they met the inclusion criteria for the mailing module. Beginning in April 2016, educational letters have been sent to the same group of prescribers with all modules included in each mailing. Included prescribers have received four letters this year, to better inform them of their SoonerCare patients using atypical antipsychotic medications and to make it more convenient to track patients and prescribing over time including any improvements or changes. Inclusion criteria requires the prescriber to have five or more SoonerCare patients taking atypical antipsychotic medications. A total of 225 prescribers were selected for inclusion in the 2016 mailings. The following list outlines definitions for each module included in the revised SoonerPsych mailing.

- **Polypharmacy:**
  - Members whose pharmacy claims history indicated concurrent use of two or more atypical antipsychotic medications for more than 90 days.
- **Adherence:**
  - Members whose proportion of days covered (PDC) or adherence calculated from pharmacy claims history was less than 80%.
- **Metabolic Monitoring:**
  - Members whose recent twelve-month medical claims history lacked glucose testing. Also includes members with a diagnosis of hyperlipidemia whose recent twelve-month medical claims history lacked lipid testing.
- **Diagnosis:**
  - Members whose recent twelve-month medical claims history lacked a diagnosis with a strong indication for prescribing an antipsychotic medication.

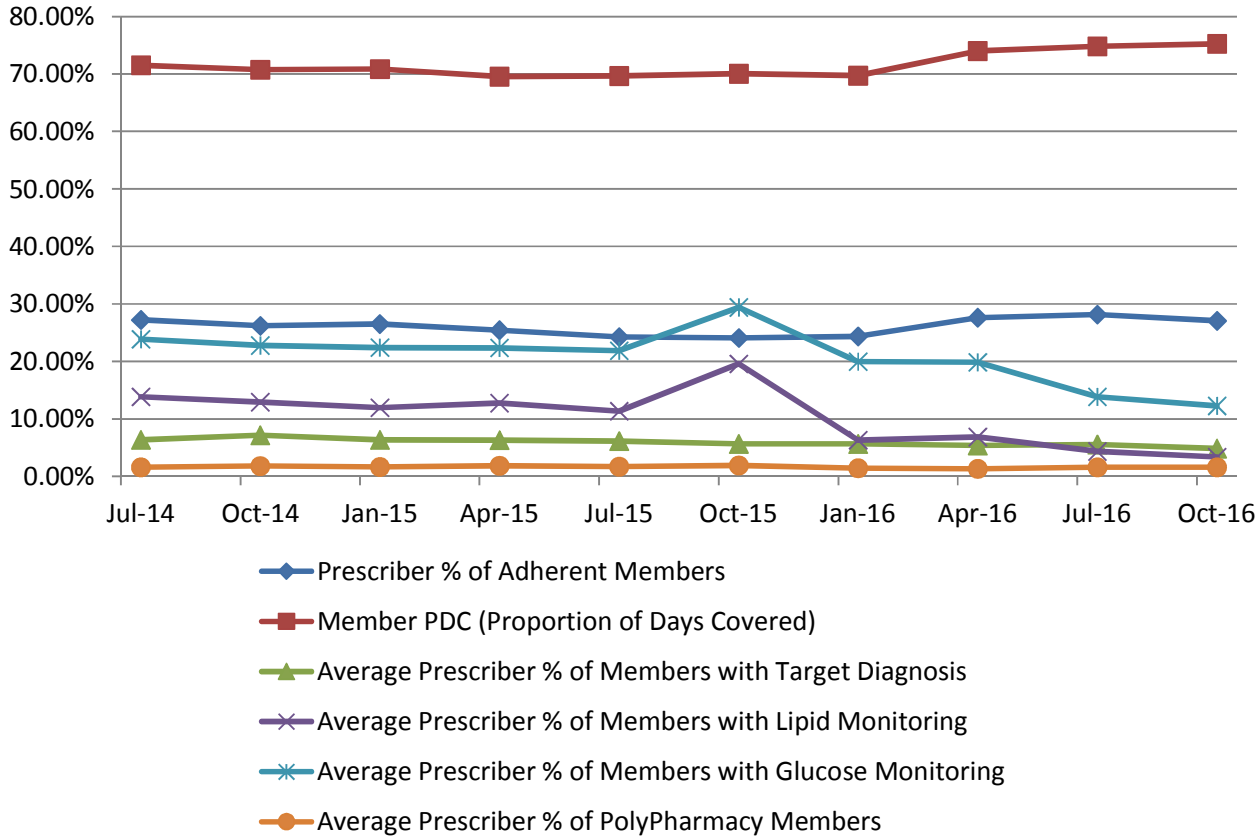
Example Gauge

Each gauge includes the individual prescriber's performance in relation to the specific module as well as the average of other SoonerCare prescribers for comparison.



SoonerPsych Trends

Each time a mailing was processed all modules or topics were tracked. The line graph below shows prescriber trends for each module and depicts the percentage for all atypical antipsychotic SoonerCare prescribers. It does not differentiate those prescribers who received a mailing and prescribers who did not receive a mailing.



All modules were included in the April 2016, July 2016, and October 2016 mailing. Starting with the SoonerPsych mailing in January 2017, data collection was expanded from a previous research-based approach to include additional diagnosis fields and monitoring (lipids and glucose) fields to provide a more clinically meaningful percentage to send to prescribers. Future results of the combined mailing and the expanded data collection will be reviewed with the Drug Utilization Review (DUR) board as they become available.

Conclusions

Most mailings appear to be effective in improving evidence-based care in the quarter immediately following the initial mailing for each topic, but then the effect of the intervention appears to decline over time. Educational mailings may be most effective in their initial round, with subsequent mailings having less effect on improvement in potential differences from generally accepted evidence-based prescribing practices. Consistently receiving evidence-based educational mailings reminds providers of evidence-based practices, and averts some potentially inappropriate prescribing. Recent changes to the mailing format (including all modules in each mailing and mailing to consistent prescribers), as well as expanding our data collection process, are intended to sustain improvements and reduce waning interventions. The College of Pharmacy will continue to work with the Oklahoma Health Care Authority to improve educational mailings with the goal of improving the quality of care for SoonerCare members utilizing atypical antipsychotic medications.

Appendix C

Vote to Prior Authorize Syndros™ (Dronabinol), Sustol® (Granisetron), and Bonjesta® (Doxylamine/Pyridoxine)

Oklahoma Health Care Authority
February 2017

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

- **Syndros™ (dronabinol) oral solution** is a cannabinoid and was approved by the U.S. Food and Drug Administration (FDA) in July 2016 for the treatment of anorexia associated with weight loss in adult patients with acquired immunodeficiency syndrome (AIDS) and for the treatment of nausea and vomiting associated with cancer chemotherapy in adult patients who have failed to respond adequately to conventional antiemetic treatments. Dronabinol is currently available generically as oral capsules (brand name Marinol®), with the same FDA approved indications as Syndros™. Marinol® was granted orphan drug designation for use in the stimulation of appetite and prevention of weight loss in patients with a confirmed diagnosis of AIDS, and was first FDA approved in 1985. The effectiveness of Syndros™ was established based on clinical studies of Marinol®.
- **Sustol® (granisetron) subcutaneous injection** is a serotonin-3 (5-HT_3) receptor antagonist and was approved by the FDA in August 2016 for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens, in combination with other anti-emetic medications in adult patients. Granisetron is also currently available generically as oral tablets and vials for IV infusion (brand name Kytril®), and under brand name Sancuso® as extended-release transdermal patches. All are indicated for similar indications as Sustol®. Kytril® vials for IV infusion were first FDA approved in 1993, followed by Kytril® oral tablets in 1995, and Sancuso® transdermal patches in 2008.
- **Bonjesta® (doxylamine/pyridoxine 20mg/20mg) oral tablets** are a fixed-dose combination product of doxylamine, an antihistamine, and pyridoxine, a vitamin B_6 analog, and was approved by the FDA in November 2016 for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. Doxylamine/pyridoxine is currently available as oral tablets containing 10mg doxylamine and 10mg pyridoxine in each tablet (brand name Diclegis®). Diclegis® is indicated for the same indications as Bonjesta®, and also has the same recommended dosing with regard to total milligram dose per day (maximum recommended dose of 40mg doxylamine and 40mg pyridoxine per day). Diclegis® was first FDA approved in 2013, followed by the generic product in August 2016; however, generic Diclegis® is not yet available. Doxylamine 25mg is also available as an over-the-counter (OTC) product (available generically and as brand name Unisom® SleepTabs®), and pyridoxine (vitamin B_6) is available as an OTC product in multiple strengths, including 25mg, 50mg, and 100mg. The effectiveness of Bonjesta® was established based on clinical studies of Diclegis®; there have been no efficacy and safety trials conducted with Bonjesta®.

Recommendations

The College of Pharmacy recommends the prior authorization of Syndros™ (dronabinol oral solution), Sustol® (granisetron subcutaneous injection), and Bonjesta® (doxylamine/pyridoxine 20mg/20mg oral tablets) with the following criteria:

Marinol® and Syndros™ (Dronabinol) and Cesamet® (Nabilone) Approval Criteria:

1. Approval can be granted for six months for the diagnosis of HIV related loss of appetite.
2. The diagnosis of chemotherapy induced nausea and vomiting requires the following:
   a. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response.
3. Approval length will be based on duration of need.
4. For Marinol® (dronabinol) and Cesamet® (nabilone), a quantity limit of 60 capsules per 30 days will apply.
5. For Syndros™ (dronabinol) oral solution, the quantity approved will be patient-specific depending on patient diagnosis, maximum recommended dosage, and manufacturer packaging.
6. For Syndros™ (dronabinol) oral solution, an age restriction of six years and younger will apply. Members older than six years of age will require a patient-specific, clinically significant reason why dronabinol oral capsules cannot be used.

Sustol® (Granisetron Subcutaneous Injection) Approval Criteria:

1. An FDA approved indication for use in the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens; and
2. Chemotherapy regimen must be listed on the prior authorization request; and
3. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response is required for authorization in members receiving MEC; and
4. No ondansetron trial is required for authorization of granisetron in members receiving AC combination chemotherapy regimens; and
5. A patient-specific, clinically significant reason why the member cannot use Kytril® (granisetron hydrochloride injection); and
6. A quantity limit of one injection every seven days will apply.

Diclegis® and Bonjesta® (Doxylamine/Pyridoxine) Approval Criteria:

1. An FDA approved diagnosis of nausea and vomiting associated with pregnancy that is not responsive to conservative management; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin B_6 (pyridoxine).
4. If the daily net cost of Bonjesta® (doxylamine/pyridoxine 20mg/20mg) is greater than the daily net cost of Diclegis® (doxylamine/pyridoxine 10mg/10mg), authorization of

Bonjesta® would also require a patient-specific, clinically significant reason why member cannot use Diclegis®.

---

[1] U.S. Food and Drug Administration (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 10/2016. Last accessed 12/16/2016.
[2] Syndros™ Prescribing Information. Drugs@FDA. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/205525s000lbl.pdf. Last revised 07/2016. Last accessed 12/16/2016.
[3] Marinol® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/marinol-2/. Last revised 12/09/2016. Last accessed 12/16/2016.
[4] Sustol® Prescribing Information. Heron Therapeutics. Available online at: http://sustol.com/public/pdfs/PI.pdf. Last revised 11/2016. Last accessed 12/16/2016.
[5] Micromedex 2.0: Granisetron Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/. Last revised 12/12/2016. Last accessed 12/16/2016.
[6] Bonjesta® Prescribing Information. Drugs@FDA. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/209661lbl.pdf. Last revised 11/2016. Last accessed 12/16/2016.
[7] Diclegis® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/diclegis-1/. Last revised 05/18/2016. Last accessed 12/16/2016.

Appendix D

Vote to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir)

Oklahoma Health Care Authority
February 2017

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

- Epclusa® (sofosbuvir [SOF]/velpatasvir [VEL]) is a fixed-dose combination of SOF, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and VEL, a HCV NS5A inhibitor, indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection with or without compensated cirrhosis and in decompensated cirrhosis in combination with ribavirin. The recommended dosage of SOF/VEL is one tablet by mouth once daily with or without food. The recommended treatment regimens and duration can be found in the following table:

Patient Population	Treatment Regimen	Duration
Patients w/o cirrhosis and patients w/ compensated cirrhosis	**SOF/VEL**	12 weeks
Patients w/ decompensated cirrhosis	**SOF/VEL** + RBV	12 weeks

w/o = without; w/ = with; SOF = sofosbuvir; VEL = velpatasvir; RBV = ribavirin

- Viekira XR™ [ombitasvir (OMB)/paritaprevir (PAR)/ritonavir (RIT)/dasabuvir (DAS)] is a fixed-dose combination of DAS, a HCV non-nucleoside NS5B palm polymerase inhibitor, OMB, a HCV NS5A inhibitor, PAR, a HCV NS3/4A protease inhibitor, and RIT, a CYP3A inhibitor. OMB/PAR/RIT/DAS is indicated for patients with genotype-1b infection without cirrhosis or with compensated cirrhosis and genotype-1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin. Viekira XR™ is a once-daily version of Viekira Pak™; Viekira XR™ is dosed as three tablets once daily with a meal. Previously approved Viekira Pak™ is dosed as two tablets containing OMB, PAR, and RIT in the morning, along with one DAS tablet in the morning and one in the evening, each time with a meal. The recommended treatment regimens and duration can be found in the following table:

Patient Population	Treatment	Duration
Genotype-1a, w/o cirrhosis	**OMB/PAR/RIT/DAS** + RBV	12 weeks
Genotype-1a, w/ compensated cirrhosis	**OMB/PAR/RIT/DAS** + RBV	24 weeks
Genotype-1b, with or w/o compensated cirrhosis	**OMB/PAR/RIT/DAS**	12 weeks

w/o = without; w/ = with; PAR = paritaprevir; RIT = ritonavir; OMB = ombitasvir; DAS = dasabuvir; RBV = ribavirin

Recommendations

The College of Pharmacy recommends the following:

1. The prior authorization of Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Epclusa® (sofosbuvir/velpatasvir) with criteria similar to the other prior authorized hepatitis C medications.

2. The removal of the minimum METAVIR fibrosis score of F2. The removal of the fibrosis score requirement will be phased in as follows: Members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018.
3. Updating the criteria regarding alcohol and illicit IV drug use for all direct-acting antivirals (DAAs) to the following: Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy.

The following table highlights the preferred regimens for each genotype in treatment-naïve and PEG-IFN and RBV-experienced members (listed in alphabetical order). Additional regimens other than those listed may be considered based on patient-specific clinical situations.

Genotype	Patient Factors	Preferred Regimen(s)
Genotype-1		
1	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 8 or 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 12 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 24 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 12 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks

Genotype	Patient Factors	Preferred Regimen(s)
1	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks 1a: Harvoni® + RBV for 12 weeks 1b: Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ or Viekira XR™ + RBV for 24 weeks 1b: Viekira Pak™ or Viekira XR™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
Genotype-2		
2	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
Genotype-3		
3	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated or RAV Y93H) Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks (with RBV with RAV Y93H) Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, cirrhotic	Epclusa® + RBV for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
Genotype-4		
4	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks

Genotype	Patient Factors	Preferred Regimen(s)
4	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
4	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks Harvoni® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
Genotype-5 or 6		
5 or 6	Treatment-naïve or experienced, non-cirrhotic or cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks

Not all regimens included are FDA approved.
All regimens are either FDA approved, recommended in AASLD/IDSA treatment guidance, or have study data indicating efficacy.
If not specified, regimen applies to all genotypic subtypes.
RBV = Ribavirin; PEG IFN = peginterferon alfa; RAV= resistance-associated polymorphisms
Preferred regimens based on clinical efficacy data, guideline recommendations, supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Viekira Pak™ and Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), and Zepatier™ (elbasvir/grazoprevir) are the preferred direct-acting antivirals for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (daclatasvir) in combination for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira™, Epclusa®, Harvoni®, Sovaldi® with peginterferon and ribavirin, or Zepatier™ (elbasvir/grazoprevir) are not appropriate for the member. Detailed criteria for medications with no changes to the coverage criteria are not included in the criteria on the following pages. The criteria for each medication may include FDA approved regimens or AASLD guideline recommended regimens that are not included in the SoonerCare preferred regimens table. Preferred regimens for each genotype can be found in the preferred regimens table. Additional regimens other than those listed in the preferred regimens table may be considered based on patient-specific clinical situations.

Viekira Pak™ and Viekira XR™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)
Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and

4. Viekira Pak™ or Viekira XR™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, genotypic subtype, and cirrhosis will apply:
   a. **Genotype 1a, without cirrhosis:**
      i. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 12 weeks
   b. **Genotype 1a, with compensated cirrhosis:**
      i. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 24 weeks
      ii. Viekira Pak™ or Viekira XR™ with weight-based ribavirin for 12 weeks may be considered for some patients based on prior treatment history.
   c. **Genotype 1b, without cirrhosis or with compensated cirrhosis:**
      i. Viekira Pak™ or Viekira XR™ for 12 weeks
   d. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for those on ribavirin); and
16. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and
17. Member must not be taking the following medications: alfuzosin, ranolazine, dronedarone, carbamazepine, phenytoin, phenobarbital, colchicine, gemfibrozil, rifampin, lurasidone, pimozide, ergotamine, dihydroergotamine, methylergonovine, ethinyl estradiol, cisapride, St. John's wort, lovastatin, simvastatin, efavirenz, sildenafil, triazolam, oral midazolam, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine, and salmeterol; and

18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Epclusa® (Sofosbuvir/Velpatasvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1, genotype-2, genotype-3, genotype-4, genotype-5, or genotype-6; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request (members with a fibrosis score of F1 will be eligible for approval July 1, 2017 and members with a fibrosis score of F0 will be eligible for approval January 1, 2018); and
4. Epclusa® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on cirrhosis status will apply:
   a. **Genotype-1, -2, -3, -4, -5, -6:**
      i. **Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A):**
         1. Epclusa® for 12 weeks
      ii. **Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C):**
         1. Epclusa® + weight-based ribavirin for 12 weeks
   b. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and

11. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses greater than 40mg famotidine equivalent, amiodarone, omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses exceeding 10mg; and
16. If member is using antacids they must agree to separate antacid and Epclusa® administration by four hours; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

[1] U.S. Food and Drug Administration (FDA). FDA approved Epclusa® for treatment of chronic Hepatitis C virus infection. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm508915.htm. Issued 06/28/2016. Last accessed 1/31/17.

[2] Epclusa® Product Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf. Last revised 06/2016. Last accessed 1/31/17.

[3] Lowes, R. FDA Approves Once-Daily Viekira XR for Hepatitis C. *Medscape*. Available online at: http://www.medscape.com/viewarticle/866680. Issued 07/2016. Last accessed 11/09/2016.

[4] Viekira XR™ Product Information. AbbVie Inc. Available online at: http://www.rxabbvie.com/pdf/viekiraxr_pi.pdf. Last revised 07/2016. Last accessed 11/09/2016.

[5] American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA). Recommendations for testing, managing, and treating hepatitis C. Available online at: http://www.hcvguidelines.org. Last revised 09/27/2016. Last accessed 1/31/17.

Appendix E

Vote to Prior Authorize Exondys 51™ (Eteplirsen)

Oklahoma Health Care Authority
February 2017

Introduction[1,2,3,4]

Duchenne muscular dystrophy (DMD) is due to the inheritance of an X-linked recessive mutation characterized by a defective gene for dystrophin (a protein in the muscles). Dystrophin is essential to the structural stability of the muscle fibers. Without dystrophin, muscles are susceptible to mechanical injury and undergo repeated cycles of necrosis and regeneration. This can result in cardiac fibrosis leading to cardiac output failure and pulmonary congestion as well as cardiac conduction abnormalities which can cause fatal arrhythmias. DMD is the most common muscular dystrophy affecting 1 in 3,500 boys born worldwide. Most patients are wheelchair bound by age 12. DMD remains an incurable illness with a mortality rate of 100%. Death often occurs by age 25.

Glucocorticoids are the mainstay of treatment for DMD. The current guidelines suggest prednisone should be offered for improving strength and pulmonary function, and may be offered for improving timed motor function, reducing the need for scoliosis surgery, and delaying cardiomyopathy onset by 18 years of age. Other treatments are based on individual needs.

In September 2016, the U.S. Food and Drug Administration (FDA) granted accelerated approval of Exondys 51™ (eteplirsen) for the treatment of patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. This mutation is present in approximately 13% of patients with DMD. Eteplirsen is an antisense oligonucleotide and is the first FDA approved medication for DMD. Eteplirsen is designed to bind to exon 51 of dystrophin pre-messenger ribonucleic acid (mRNA), resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 51 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein. This truncated dystrophin is thought to decrease the severity of DMD. Approval of eteplirsen was based on an increase in dystrophin in skeletal muscle observed in some patients treated with eteplirsen. A clinical benefit of eteplirsen has not been established. The approval of eteplirsen was not supported by the FDA review committee due to the lack of evidence for efficacy. However, the director of the FDA's Center for Drug Evaluation and Research overruled the committee's decision. With the approval, the manufacturer is required to conduct a randomized trial to verify the clinical benefit of eteplirsen. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

Below is the cost information for eteplirsen based on the approximate weight range from age of onset to young adulthood based on the recommended dosing of 30mg/kg given once weekly.

Medication	Cost Per mL	Cost Per 30 Days of Therapy*
Exondys 51™ (eteplirsen)	**$800.00**	**$32,000.00 - $160,000.00**

*Cost does not reflect rebated price or net cost. Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Exondys 51™ (eteplirsen) with the following criteria:

Exondys 51™ (Eteplirsen) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping; and
2. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

---

[1] Nair DG. Dystrophinopathies. *Medscape*. Available online at: http://emedicine.medscape.com/article/1173204-overview. Last revised 10/05/2016. Last accessed 12/29/2016.

[2] Darras BT. Treatment of Duchenne and Becker Muscular Dystrophy. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/treatment-of-duchenne-and-becker-muscular-dystrophy?source=search_result&search=duchenne&selectedTitle=2%7E69#H4016787759. Last revised 10/28/2016. Last accessed 12/29/2016.

[3] Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. *Neurology* 2016; 86(5): 465-472.

[4] U.S. Food and Drug Administration (FDA). Exondys 51™ Prescribing Information. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/206488lbl.pdf. Last revised 09/2016. Last accessed 12/29/2016.

Appendix F

Vote to Prior Authorize Otovel® (Ciprofloxacin/Fluocinolone Acetonide)

Oklahoma Health Care Authority
February 2017

Introduction[1]

Otovel® is a combination of ciprofloxacin, a fluoroquinolone antibacterial, and fluocinolone acetonide, a corticosteroid, indicated in pediatric patients (6 months of age and older) for the treatment of acute otitis media with tympanostomy tubes (AOMT) due to *Staphylococcus aureus, Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Pseudomonas aeruginosa*. Ciprofloxacin, a fluoroquinolone antibiotic, interferes with enzyme deoxyribonucleic acid (DNA) gyrase, which is needed for the synthesis of bacterial DNA. Fluocinolone acetonide, a corticosteroid, inhibits the local biosynthesis of prostaglandins, which explains part of its anti-inflammatory efficacy. At the cellular level, corticosteroids induce peptides called lipocortins. Lipocortins antagonize phospholipase A2, an enzyme which causes the breakdown of leukocyte lysosomal membranes to release arachidonic acid. This action decreases the subsequent formation and release of endogenous inflammatory mediators including prostaglandins, kinins, histamine, liposomal enzymes, and the complement system. Otovel® is available as an otic solution containing ciprofloxacin 0.3% and fluocinolone acetonide 0.025%. It is supplied in single-dose, preservative-free vials containing 0.25mL of solution. Fourteen single-dose vials are packaged in a protective foil pouch contained in a carton. The recommended dosing is one single-dose vial (0.25mL) instilled into the affected ear canal twice daily for seven days. The national drug acquisition cost (NADAC) has become available since the last report. The current NADAC is $13.46 per vial, resulting in a cost per treatment of $188.44 per affected ear.

Recommendations

The College of Pharmacy recommends the placement of Otovel® (ciprofloxacin/fluocinolone 0.3%/0.025%) into Tier-2 of the Otic Anti-Infective Medications Product Based Prior Authorization (PBPA) category. Current Tier-2 criteria for this category will apply.

Otic Anti-Infective Medications		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	ciprofloxacin (Cetraxal®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	**ciprofloxacin/fluocinolone (Otovel®)**	
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Coly-Mycin® S)	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	
	ofloxacin (Floxin® Otic)	

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. HC = hydrocortisone

Otic Anti-Infective Medications 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.

Otic Anti-Infective Medications Special Prior Authorization (PA) Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent (within six 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.

---

[1] Otovel® Prescribing Information. Arbor Pharmaceuticals, LLC. Available online at: https://www.otovel.com/hcp. Last revised 04/2016. Last accessed 12/29/2016.

Appendix G

Vote to Prior Authorize Cinqair® (Reslizumab) and Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate)

Oklahoma Health Care Authority
February 2017

Introduction[1,2]

- Cinqair® (reslizumab) is an interleukin (IL)-5 antagonist monoclonal antibody indicated for the add-on maintenance treatment of patients 18 years of age and older with severe asthma with an eosinophilic phenotype.
- Bevespi Aerosphere® (glycopyrrolate/formoterol fumarate) is a combination of glycopyrrolate, an anticholinergic, and formoterol fumarate, a long-acting beta$_2$-adrenergic agonist (LABA) indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).

Recommendations

The College of Pharmacy recommends the prior authorization of Cinqair® (reslizumab) and Bevespi Aerosphere® (glycopyrrolate/formoterol fumarate) with the following criteria:

Cinqair® (Reslizumab) Approval Criteria:

1. An FDA approved indication of add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype; and
2. Member must be 18 years of age or older; and
3. Member must have a blood eosinophil count of at least 400/mcL (within three to four weeks of dosing); and
4. Member must have had at least two asthma exacerbations requiring systemic corticosteroids within the last 12 months or require daily systemic corticosteroids despite compliant use of high-dose inhaled corticosteroid (ICS) plus at least one additional controller medication; and
5. Member must have failed a high-dose ICS used compliantly for at least the past 12 months (for ICS/LABA combination medications, the highest approved dose meets this criteria); and
6. Member must have failed at least one other asthma controller medication used in addition to the high-dose ICS compliantly for at least the past three months; and
7. Cinqair® must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
8. Cinqair® must be prescribed by an allergist, pulmonologist, or pulmonary specialist or the member must have been evaluated by an allergist, pulmonologist, or pulmonary specialist within the last twelve months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, or pulmonary specialist); and
9. Initial approvals will be for the duration of six months after which time compliance will be evaluated for continued approval.

10. Member's weight should be provided on prior authorization requests. Weights should have been taken within the last four weeks to provide accurate weight-based dosing.

Bevespi Aerosphere® (Glycopyrrolate/Formoterol Fumarate) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD); and
3. A patient-specific, clinically significant reason why the member cannot use Tier-1 long-acting beta$_2$ agonist (LABA) and long-acting muscarinic antagonist (LAMA) individual components.

---

[1] Cinqair® Prescribing Information. Teva Respiratory, LLC. Available online at: http://www.cinqair.com/pdf/PrescribingInformation.pdf. Last revised 05/2016. Last accessed 11/2016.
[2] Bevespi Aerosphere™ Prescribing Information. AstraZeneca Pharmaceuticals. Available online at: http://www.azpicentral.com/bevespi/bevespi_pi.pdf. Last revised 04/2016. Last accessed 11/2016.

Appendix H

Vote to Prior Authorize Fosrenol® (Lanthanum Carbonate), Velphoro® (Sucroferric Oxyhydroxide), and Auryxia™ (Ferric Citrate)

Oklahoma Health Care Authority
February 2017

Introduction[1,2,3,4]

Patients with chronic kidney disease (CKD) are unable to effectively excrete phosphate. High serum levels of phosphorus may lead to renal bone disease, vascular calcification, hyperparathyroidism, and mortality. The National Kidney Foundation released guidelines regarding the management of hyperphosphatemia in patients with renal impairment. For CKD patients who are not on dialysis, moderate restriction of phosphate intake is recommended, provided this can be done without compromising nutritional status. In non-dialysis CKD patients who have a high serum phosphorus level despite dietary phosphate restriction, administration of phosphate binders to maintain serum phosphorus levels in the normal range is suggested. For CKD patients on dialysis, the three most common methods to treat hyperphosphatemia include restricting dietary phosphate intake, administering phosphate binders, and increasing dialysis.

Phosphate Binder Product Comparison[1]

Comparison of Phosphate Binders

Phosphate Binder	Available Products	RPBC	Initial Dose
calcium carbonate	Various products available as tablets; suspension in various strengths (e.g., Tums®)	1.0	500mg TID with meals
calcium acetate	PhosLo® 667mg capsule; Phoslyra® 667mg/5mL solution; others	1.0	1,334mg TID with meals
sevelamer carbonate	Renvela® 800mg tablet; Renvela® 800mg, 2,400mg powder packet for oral suspension	0.75	800mg to 1,600mg TID with meals
sevelamer hydrochloride	Renagel® 400mg, 800mg tablet	0.75	800mg to 1,600mg TID with meals
lanthanum carbonate	Fosrenol® 500mg, 750mg, 1,000mg chewable tablet; Fosrenol® 750mg, 1,000mg oral powder	2.0	500mg TID with meals
sucroferric oxyhydroxide	Velphoro® 500mg chewable tablet	Not known	500mg TID with meals

Phosphate Binder	Available Products	RPBC	Initial Dose
ferric citrate	Auryxia™ 1g tablet	Not known	2g TID with meals

Table modified from: Comparison of Phosphate Binders. *Pharmacist's Letter/Prescriber's Letter.*
RPBC = Relative Phosphate-Binding Coefficients (calcium carbonate as index); TID = Three times daily

Recommendations

The College of Pharmacy recommends the prior authorization of Velphoro® (sucroferric oxyhydroxide) and Auryxia™ (ferric citrate) with the following criteria:

Velphoro® (Sucroferric Oxyhydroxide) and Auryxia™ (Ferric Citrate) Approval Criteria:

1. A diagnosis of hyperphosphatemia in patients with chronic kidney disease (CKD) on dialysis; and
2. Documented trials of inadequate response to at least two of the phosphate binders available without a prior authorization or a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization.
3. For Auryxia™, a quantity limit of 12 tablets per day will apply based on maximum recommended dose.

Additionally, the College of Pharmacy recommends the prior authorization of Fosrenol® (lanthanum carbonate) 1,000mg chewable tablets, 750mg packets, and 1,000mg packets with the following criteria:

Fosrenol® (Lanthanum Carbonate) 1,000mg Chewable Tablets, 750mg Oral Powder, and 1,000mg Oral Powder Approval Criteria:

1. A diagnosis of hyperphosphatemia in patients with end stage renal disease (ESRD); and
2. Documented trials of inadequate response to at least two of the phosphate binders available without a prior authorization or a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization; and
3. For the approval of Fosrenol® oral powder, a patient-specific, clinically significant reason why a special formulation is needed over a phosphate binder available without a prior authorization, such as Fosrenol® 500mg or 750mg chewable tablets which can be crushed, must be provided; and
4. For the approval of Fosrenol® 1,000mg chewable tablets, a patient-specific, clinically significant reason why the member cannot use a phosphate binder available without a prior authorization, such as Fosrenol® 500mg or 750mg chewable tablets, must be provided.

Based on the lower net cost of generic calcium acetate containing products, Phoslyra®, Renvela®, Renagel®, and Fosrenol® 500mg and 750mg chewable tablets, the College of Pharmacy does not recommend the prior authorization of these products at this time.

[1] PL Detail-Document, Comparison of Phosphate Binders. *Pharmacist's Letter/Prescriber's Letter*. August 2015.
[2] Hutchison, Alastair. Oral Phosphate Binders. *Kidney International.* 2009: 75(9): 906-914.
[3] Berkoben M, Quarles L. Treatment of Hyperphosphatemia in Chronic Kidney Disease. *UpToDate*. Available online at: http://www.uptodate.com/contents/treatment-of-hyperphosphatemia-in-chronic-kidney-disease?source=search_result&search=phosphate+binders&selectedTitle=1%7E150. Last revised 05/04/2016. Last accessed 11/09/2016.
[4] Foote E. Few advantages proven for a particular phosphate binder in patients with kidney disease. APHA DrugInfoLine®. Available online at: http://www.aphadruginfoline.com/nephrology/few-advantages-proven-particular-phosphate-binder-patients-kidney-disease. Issued 11/01/2016. Last accessed 11/09/2016.

Appendix I

Vote to Prior Authorize Defitelio® (Defibrotide Sodium)

Oklahoma Health Care Authority
February 2017

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

Hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), is a potentially life-threatening complication that occurs most commonly following hematopoietic stem-cell transplant (HSCT). The management of VOD depends at least partially on the severity of the disease. Severe VOD predicts a poor outcome and warrants more aggressive therapy. Supportive care is a key component in the management of all patients with VOD. Supportive measures that should be considered include maintaining euvolemia (daily weights and measures of fluid intake and output are critical), minimizing exposure to hepatotoxic agents (e.g., alcohol, nonsteroidal anti-inflammatory drugs, excessive use of acetaminophen, certain herbal remedies), pain control, and paracentesis. However, patients with severe VOD have high mortality rates with supportive care alone.

In March 2016, the U.S. Food and Drug Administration (FDA) approved Defitelio® (defibrotide sodium) to treat adult and pediatric patients who develop VOD with additional kidney or lung abnormalities after HSCT. Defitelio® is the first FDA-approved therapy for the treatment of this rare and life-threatening liver condition. The recommended dose for adult and pediatric patients is 6.25mg/kg every 6 hours given as a 2-hour intravenous infusion. Defibrotide sodium is administered for a minimum of 21 days. If after 21 days the signs and symptoms of hepatic VOD have not resolved, defibrotide sodium is continued until resolution of VOD or up to a maximum of 60 days.

Recommendations

The College of Pharmacy recommends the prior authorization of Defitelio® (defibrotide sodium) with the following criteria:

Defitelio® (Defibrotide Sodium) Approval Criteria:

1. An FDA approved diagnosis of hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation.
2. Initial approvals will be for one month of therapy. An additional month of therapy (maximum of 60 days) may be granted if the physician documents the continued need for therapy.

[1] Negrin R, Bonis P. Diagnosis of hepatic sinusoidal obstruction syndrome (veno-occlusive disease) following hematopoietic cell transplantation. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/diagnosis-of-hepatic-sinusoidal-obstruction-syndrome-veno-occlusive-disease-following-hematopoietic-cell-transplantation?source=see_link. Last revised 09/14/2016. Last accessed 01/17/2017.

[2] Negrin, Robert. Treatment and prevention of hepatic sinusoidal obstruction syndrome following hematopoietic cell transplantation. *Up-To-Date*. Available online at: http://www.uptodate.com/contents/treatment-and-prevention-of-hepatic-sinusoidal-obstruction-syndrome-following-hematopoietic-cell-transplantation?source=search_result&search=vod&selectedTitle=2%7E104. Last revised 04/01/2016. Last accessed 01/17/2017.

[3] Jazz Pharmaceuticals Announces FDA Approval of Defitelio® (defibrotide sodium) for the Treatment of Hepatic Veno-Occlusive Disease (VOD) with Renal or Pulmonary Dysfunction Following Hematopoietic Stem-Cell Transplantation (HSCT). Jazz Pharmaceuticals. Available online at: http://www.prnewswire.com/news-releases/jazz-pharmaceuticals-announces-fda-approval-of-defitelio-defibrotide-sodium-for-the-treatment-of-hepatic-veno-occlusive-disease-vod-with-renal-or-pulmonary-dysfunction-following-hematopoietic-stem-cell-transplantation-hsct-300243563.html. Issued 03/30/2016. Last accessed 11/04/2016.

[4] U.S. Food and Drug Administration (FDA). FDA approves first treatment for rare disease in patients who receive stem cell transplant from blood or bone marrow. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm493225.htm. Issued 03/30/2016. Last accessed 10/12/2016.

[5] Defitelio® Prescribing Information. Jazz Pharmaceuticals. Available online at: https://defitelio.com/DefitelioPI.pdf. Last revised 03/2016. Last accessed 10/12/2016.

Appendix J

Fiscal Year 2016 Annual Review of Seizure Medications and 30-Day Notice to Prior Authorize Briviact® (Brivaracetam), Fycompa™ (Perampanel Oral Suspension), and Carnexiv™ (Carbamazepine Injection)

Oklahoma Health Care Authority
February 2017

Current Prior Authorization Criteria

1. Anticonvulsants are included in the mandatory generic plan.
    a. All brand-name anticonvulsants (with a generic equivalent) will require prior authorization.
        i. Brand-name medications (with a generic equivalent) will be approved for all members who are currently stable on these medications and have a seizure diagnosis.
2. Prior authorization will be required for certain non-standard dosage forms of medications when the drug is available in standard dosage forms.
    a. Members 12 years of age and older must have a documented medical reason demonstrating the need for non-standard dosage forms.
    b. Criteria for approval of extended-release formulations:
        i. Previously stabilized on the short-acting formulation; and
        ii. Dosing is not more than once daily; and
        iii. A reason why the short-acting formulation is not adequate must be provided; and
        iv. Dose packs will not be approved if standard dosage forms are available.
3. Quantity limit restrictions will be placed on lower strength tablets and capsules. The highest strengths will continue to have no quantity restrictions unless a maximum dose is specified for a particular medication.

Onfi® (Clobazam) Approval Criteria:

1. An FDA approved diagnosis of severe seizures or generalized tonic, atonic, or myoclonic seizures; and
2. Previous failure of at least two non-benzodiazepine anticonvulsants; and
3. Previous failure of clonazepam; and
4. Initial approvals will be for the duration of three months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

Aptiom® (Eslicarbazepine) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Member must not currently be taking oxcarbazepine (concurrent use is contraindicated); and

3. A patient-specific, clinically significant reason why member cannot use oxcarbazepine.
4. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (200mg and 400mg) and 60 tablets per 30 days on the higher strength tablets (600mg and 800mg).

Felbatol® (Felbamate) Approval Criteria:

1. Initial prescription must be written by a neurologist; and
2. Member must have failed therapy with at least three other medications commonly used for seizures.

Vimpat® (Lacosamide) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three* other medications commonly used for seizures. (*Vimpat® has currently provided a supplemental rebate to require a trial with one other medication; however, Vimpat® will follow the original criteria and require trials with three other medications if the manufacturer chooses not to participate in supplemental rebates.)
4. Members currently stable on Vimpat® (lacosamide) and who have a seizure diagnosis will be grandfathered.

Spritam® (Levetiracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures, myoclonic seizures, or primary generalized tonic-clonic (PGTC) seizures; and
2. A patient-specific, clinically significant reason why the member cannot use generic formulations of levetiracetam.
3. A quantity limit of 60 tablets per 30 days will apply.

Oxtellar XR™ (Oxcarbazepine Extended-Release) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation.
2. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (150mg and 300mg).

Fycompa™ (Perampanel) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of partial-onset seizures with or without secondarily generalized seizures or primary generalized tonic-clonic (PGTC) seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three* other medications commonly used for seizures. (*Fycompa™ has currently provided a supplemental rebate to require a trial with one other medication; however, Fycompa™ will follow the original criteria and require trials with three other medications if the manufacturer chooses not to participate in supplemental rebates.)

4. Members currently stable on Fycompa™ (perampanel) and who have a seizure diagnosis will be grandfathered.

Banzel® (Rufinamide) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut Syndrome; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Banzel® (rufinamide) and who have a seizure diagnosis will be grandfathered.

Qudexy™ XR (Topiramate Extended-Release) Approval Criteria:

1. An FDA approved diagnosis of partial onset or primary generalized tonic-clonic seizures or as adjunctive therapy in seizures associated with Lennox-Gastaut syndrome; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate).
3. A quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (150mg and 200mg).

Trokendi XR® (Topiramate Extended-Release) Approval Criteria:

1. An FDA approved diagnosis of partial onset or primary generalized tonic-clonic seizures or as adjunctive therapy in seizures associated with Lennox-Gastaut syndrome; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate).
3. A quantity limit of 30 capsules per 30 days will apply on the lower strength capsules (25mg, 50mg, and 100mg) and 60 capsules per 30 days on the higher strength capsules (200mg).

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of refractory complex seizures in adults and pediatric patients 10 years of age or older, or infantile spasms in children 1 month to 2 years of age; and
2. Members with refractory complex seizures must have previous trials of at least three other antiepileptic medications; or
3. Members with infantile spasms must have had a previous trial with adrenocorticotropic hormone (ACTH) or have a diagnosis of infantile spasms with tuberous sclerosis; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the SHARE program and maintain enrollment throughout therapy.

Utilization of Seizure Medications: Fiscal Year 2016

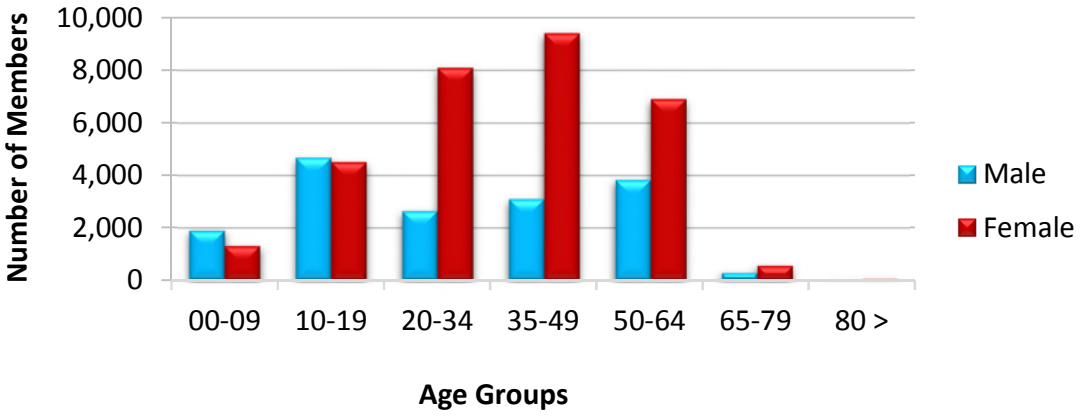
The following utilization data includes seizure medications used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate.

Comparison of Fiscal Years: Seizure Medications

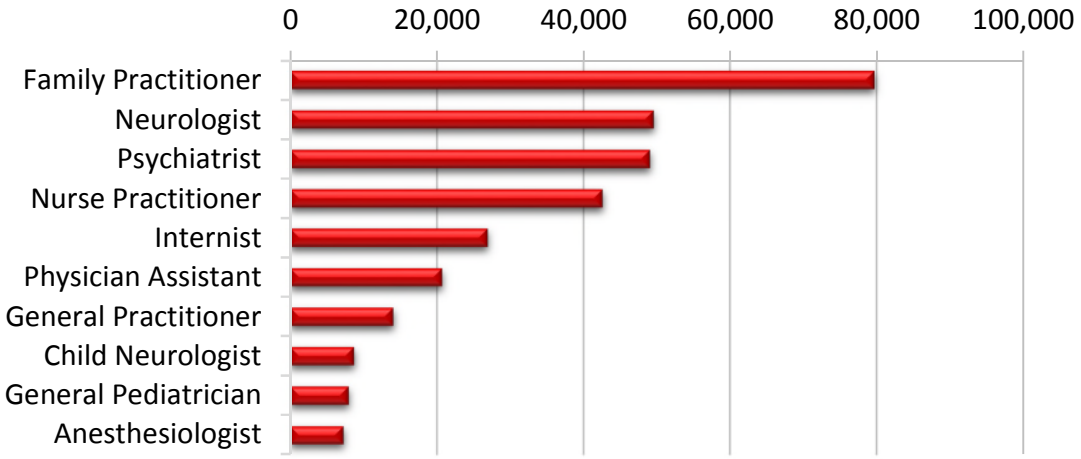
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	46,604	325,120	$21,863,640.27	$67.25	$2.24	30,472,726	9,776,104
2016	47,241	333,039	$23,324,248.37	$70.03	$2.32	31,530,461	10,050,389
% Change	**1.40%**	**2.40%**	**6.70%**	**4.10%**	**3.60%**	**3.50%**	**2.80%**
Change	**637**	**7,919**	**$1,460,608.10**	**$2.78**	**$0.08**	**1,057,735**	**274,285**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Seizure Medications

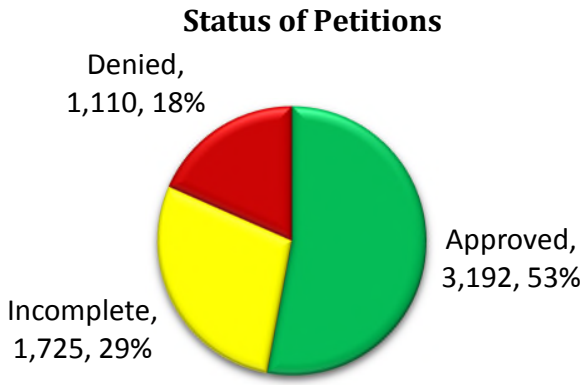


Top Prescriber Specialties of Seizure Medications by Number of Claims



Prior Authorization of Seizure Medications

There were 6,027 prior authorization requests submitted for seizure medications during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12]

Anticipated Patent Expiration(s):

- Spritam® (levetiracetam): February 2018
- Lyrica® (pregabalin): December 2018
- Vimpat® (lacosamide): March 2022
- Banzel® (rufinamide): May 2023
- Fycompa™ (perampanel): May 2026
- Oxtellar XR™ (oxcarbazepine extended-release): April 2027
- Trokendi XR® (topiramate extended-release): April 2028
- Aptiom® (eslicarbazepine): April 2030
- Qudexy™ XR (topiramate extended-release): March 2033

New FDA Approval(s) and Indication(s):

- **February 2016:** The U.S. Food and Drug Administration (FDA) approved Briviact® (brivaracetam) as adjunctive therapy for the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy.
- **April 2016:** The FDA approved Fycompa™ (perampanel) oral suspension as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures, and primary generalized tonic-clonic (PGTC) seizures in patients 12 years of age and older with epilepsy. Fycompa™ oral tablets were FDA approved in 2012 for the same indications.
- **June 2016:** The FDA approved a modified Risk Evaluation and Mitigation Strategy (REMS) for Sabril® (vigabatrin); however, streamlining of the REMS program is not due to any change in the risk of Sabril®-induced permanent vision loss. The SABRIL REMS program, formerly known as SHARE, has been changed after the FDA determined that some of the program's requirements are no longer necessary to ensure that the benefits of Sabril® outweigh the risks. The modified REMS program will alleviate some of the burden

associated with prescribing Sabril®, as physicians will have fewer forms to submit (previously, five forms were required; now, only two forms are required). The new SABRIL REMS program went in effect on July 21, 2016.

- **August 2016:** The FDA approved a supplemental new drug application (sNDA) for Trokendi XR® (topiramate extended-release) to expand its indication for the monotherapy treatment of partial onset or PGTC seizures to patients 6 years of age and older. Trokendi XR® was previously FDA approved for use in patients 10 years of age and older.
- **October 2016:** The FDA approved Carnexiv™ (carbamazepine) injection for intravenous (IV) use as replacement therapy for oral carbamazepine formulations, when oral administration is temporarily not feasible, in adults patients with the following seizure types:
    - Partial seizures with complex symptomatology
    - Generalized tonic-clonic seizures
    - Mixed seizure patterns which include the above, or other partial or generalized seizures

  Carbamazepine is also available generically as various oral formulations, including suspension, chewable tablets, tablets, extended-release (ER) tablets, and ER capsules.

Other News:

- **April 2016:** Results of a blinded Phase 3 clinical study showed Aptiom® (eslicarbazepine) to be non-inferior to ER carbamazepine given as monotherapy. Eslicarbazepine was dosed once daily, while ER carbamazepine was dosed twice daily, with dose increases for both medications based on patient response. The study included 815 adult patients with new-onset seizures, and the primary endpoint of the study was the proportion of patients with seizure freedom at 26 weeks. The study showed that 71.1% of patients receiving eslicarbazepine and 75.6% receiving carbamazepine were seizure-free for six or more months. Also, eslicarbazepine monotherapy demonstrated a safety profile that was similar or more favorable than that of ER carbamazepine in the study population.
- **April 2016:** Qudexy™ XR (topiramate ER) received tentative approval from the FDA for a sNDA submitted to expand its indications to include the prophylaxis of migraine headaches in adult patients. Qudexy™ XR was FDA approved in 2014 and is indicated as initial monotherapy or as adjunctive therapy in patients 2 years of age and older with partial onset or PGTC seizures and as adjunctive therapy in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome (LGS).
- **August 2016:** Trokendi XR® (topiramate ER) received tentative approval from the FDA for a sNDA submitted to expand its indications to include the prophylaxis of migraine headaches in adult patients. Trokendi XR® was FDA approved in 2013 and is indicated as initial monotherapy or as adjunctive therapy in patients 6 years of age and older with partial onset or PGTC seizures and as adjunctive therapy in patients 6 years of age and older with seizures associated with LGS.

Pipeline:

- **July 2016:** The FDA approved Elepsia XR™ (levetiracetam extended-release 1,000mg and 1,500mg tablets) in March 2015 as an adjunctive treatment of partial-onset seizures in patients 12 years of age and older with epilepsy. However, in September 2015, the FDA withdrew their approval of Elepsia XR™ due to regulatory issues at the manufacturing plant. The pharmaceutical company and manufacturer of Elepsia XR™ are currently working with the FDA to resolve the manufacturing issues, and in July 2016 the research company licensed Elepsia XR™ to its parent company as a way to speed up U.S. market entry.
- **September 2016:** Positive results of the second randomized, double-blind, placebo-controlled Phase 3 clinical trial were announced for the investigational medication Epidiolex® (cannabidiol or CBD) for the treatment of seizures associated with LGS. In this trial, when added to the patient's current treatment, Epidiolex® achieved the primary endpoint for both dose levels with high statistical significance. This trial follows the announcement in June 2016 of positive results in the first pivotal Phase 3 trial of Epidiolex® for the treatment of seizures associated with LGS, and the March 2016 announcement of positive results in the treatment of seizures associated with Dravet syndrome. The pharmaceutical company expects to submit a new drug application (NDA) to the FDA in the first half of 2017.
- **December 2016:** Positive results were announced from a Phase 3 study that evaluated the use of Lyrica® (pregabalin) as adjunctive therapy for pediatric epilepsy patients 4 to 16 years of age with partial-onset seizures. Results showed that adjunctive treatment with Lyrica® 10mg/kg/day resulted in a statistically significant reduction in seizure frequency versus placebo, which was the primary efficacy endpoint. The Lyrica® Pediatric Epilepsy Program is composed of a total of six studies in patients with epilepsy evaluating Lyrica® as adjunctive therapy, three of which have been completed and three are actively enrolling. Lyrica® was FDA approved in 2004 and is indicated for adjunctive therapy for adult patients with partial-onset seizures, as well as for the management of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, and fibromyalgia.

Briviact® (Brivaracetam) Product Summary[13]

Indications: Briviact® (brivaracetam) is indicated as adjunctive therapy in the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy.

Dosing:

- Brivaracetam is available as a 50mg/5mL injection for IV use, 10mg/mL oral solution, and 10mg, 25mg, 50mg, 75mg, and 100mg oral tablets.
- When initiating treatment, gradual dose escalation is not required. Brivaracetam can be initiated with either IV or oral administration. The recommended starting dosage is 50mg twice daily. Based on individual patient tolerability and therapeutic response, the dosage may be adjusted down to 25mg twice daily or up to 100mg twice daily.
- Brivaracetam injection may be used when oral administration is temporarily not feasible and should be administered at the same dosage and the same frequency as

brivaracetam tablets and oral solution. Brivaracetam injection is for IV use only and should be administered over 2 to 15 minutes.

- Brivaracetam tablets should be taken as whole tablets and should not be chewed or crushed. Brivaracetam tablets and oral solution may be taken with or without food.
- Brivaracetam oral solution may be administered using a nasogastric tube or gastrostomy tube.

Mechanism of Action: The precise mechanism by which brivaracetam exerts its anticonvulsant activity is not known. Brivaracetam displays a high and selective affinity for synaptic vesicle protein 2A (SV2A) in the brain, which may contribute to the anticonvulsant effect.

Contraindications: Brivaracetam is contraindicated in patients with hypersensitivity to brivaracetam or any of the inactive ingredients in Briviact®.

Safety:

- Suicidal Behavior and Ideation: Antiepileptic drugs (AEDs), including brivaracetam, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients taking AEDs for any indication should be monitored for emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in behavior.
- Neurological Adverse Reactions: Brivaracetam causes somnolence, fatigue, dizziness, and disturbance in coordination. Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on brivaracetam to gauge whether it adversely affects their ability to drive or operate machinery.
- Psychiatric Adverse Reactions: Brivaracetam causes psychiatric adverse reactions. In the Phase 3 controlled adjunctive epilepsy trials, psychiatric adverse reactions were reported in approximately 13% of patients who received brivaracetam compared to 8% of patients who received placebo. Psychiatric events included both non-psychotic symptoms (irritability, anxiety, nervousness, aggression, belligerence, anger, agitation, restlessness, depression, depressed mood, tearfulness, apathy, altered mood, mood swings, affect lability, psychomotor hyperactivity, abnormal behavior, and adjustment disorder) and psychotic symptoms (psychotic disorder along with hallucination, paranoia, acute psychosis, and psychotic behavior).
- Hypersensitivity: Brivaracetam can cause hypersensitivity reactions, including bronchospasm and angioedema. If a patient develops hypersensitivity after treatment with brivaracetam, the drug should be discontinued.
- Withdrawal of AEDs: As with most AEDs, brivaracetam should be gradually withdrawn because of the risk of increased seizure frequency and status epilepticus. However, if withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered.
- Drug Abuse and Dependence: Brivaracetam is listed as a Schedule V controlled substance. In a human abuse potential study, single doses of brivaracetam at therapeutic and supratherapeutic doses were compared to alprazolam (1.5mg and 3mg), which is a Schedule IV controlled substance. Brivaracetam at the recommended single

dose (50mg) caused fewer sedative and euphoric effects than alprazolam; however, brivaracetam at supratherapeutic single doses (200mg and 1,000mg) was similar to alprazolam on other measures of abuse. There was no evidence of physical dependence potential or withdrawal syndrome with brivaracetam in a pooled review of placebo-controlled adjunctive therapy studies.

- Renal Impairment: Dose adjustments are not required for patients with impaired renal function. There are no data in patients with end-stage renal disease undergoing dialysis; therefore, use of brivaracetam is not recommended in this patient population.
- Hepatic Impairment: Because of increases in brivaracetam exposure, dosage adjustment is recommended for all stages of hepatic impairment. The recommended starting dosage for all stages of hepatic impairment is 25mg twice daily and the recommended maximum dosage is 75mg twice daily.
- Pediatric Use: The safety and efficacy of brivaracetam in pediatric patients less than 16 years of age have not been established.

Drug Interactions:

- Rifampin: Coadministration with rifampin decreases brivaracetam plasma concentrations likely because of CYP2C19 induction. Prescribers should increase the brivaracetam dose by up to 100% (i.e., double the dosage) in patients while receiving concomitant treatment with rifampin.
- Carbamazepine: Coadministration with carbamazepine may increase exposure to carbamazepine-epoxide, the active metabolite of carbamazepine. Though available data did not reveal any safety concerns, if tolerability issues arise when coadministered, carbamazepine dose reduction should be considered.
- Phenytoin: Because brivaracetam can increase plasma concentrations of phenytoin, phenytoin levels should be monitored in patients when concomitant brivaracetam is added to or discontinued from ongoing phenytoin therapy.
- Levetiracetam: Brivaracetam provided no added therapeutic benefit to levetiracetam when the two drugs were coadministered.

Adverse Reactions: The most common adverse reactions to brivaracetam reported in clinical trials, that occurred at least 2% more frequently than placebo, include somnolence and sedation, dizziness, fatigue, nausea/vomiting symptoms, irritability, cerebellar coordination and balance disturbances (ataxia, balance disorder, abnormal coordination, and nystagmus), and constipation.

Efficacy:

- The effectiveness of brivaracetam as adjunctive therapy in partial-onset seizures with or without secondary generalization was established in three fixed-dose, randomized, double-blind, placebo-controlled, multicenter studies, which included 1,550 patients.
- Patients enrolled had partial-onset seizures that were not adequately controlled with one to two concomitant AEDs. The median baseline seizure frequency across the three studies was nine seizures per 28 days.

- All trials had an 8-week baseline period, during which patients were required to have at least eight partial-onset seizures. The baseline period was followed by a 12-week treatment period.
- Brivaracetam was administered in equally divided twice daily doses. Study 1 compared doses of brivaracetam 50mg/day and 100mg/day with placebo. Study 2 compared a dose of brivaracetam 50mg/day with placebo. Study 3 compared doses of brivaracetam 100mg/day and 200mg/day with placebo.
- The primary efficacy outcome in Study 1 and Study 2 was the percent reduction in 7-day partial-onset seizure frequency over placebo, while the primary efficacy outcome in Study 3 was the percent reduction in 28-day partial-onset seizure frequency over placebo. In Study 2 and Study 3, treatment with brivaracetam showed statistical significance over placebo. The percent reduction in partial-onset seizure frequency for brivaracetam over placebo for all three studies is shown in the following table:

	Percent Reduction Over Placebo (%)
Study 1*	
Placebo (n=100)	
50mg/day (n=99)	9.5
100mg/day (n=100)	17.0
Study 2*	
Placebo (n=96)	
50mg/day (n=101)	16.9¥
Study 3^	
Placebo (n=259)	
100mg/day (n=252)	25.2¥
200mg/day (n=249)	25.7¥

* based upon 7-day seizure frequency
^ based upon 28-day seizure frequency
¥ statistically significant ($p<0.05$)

Cost: The wholesale acquisition cost (WAC) of Briviact® tablets is $16.67 per tablet, regardless of strength, which results in a monthly cost of $1,000.20 based on twice daily dosing. Briviact® 10mg/mL oral solution has a WAC of $3.33 per mL, resulting in a monthly cost of $999.00 based on the recommended dosage of 50mg twice daily. Briviact® 50mg/5mL injection has a WAC of $8.57 per mL, resulting in a daily cost of $85.70 based on the recommended dosage of 50mg twice daily and short-term use (the injection is for use when oral administration is temporarily not feasible, and the clinical study experience with Briviact® injection is limited to four consecutive days of treatment).

Fycompa™ (Perampanel Oral Suspension) Product Summary[14]

Indications: Fycompa™ (perampanel) oral suspension is indicated for adjunctive therapy in patients with epilepsy 12 years of age and older in the treatment of:

- Partial-onset seizures with or without secondarily generalized seizures
- Primary generalized tonic-clonic (PGTC) seizures

Dosing:

- Perampanel oral suspension is available as a 0.5mg/mL liquid suspension.
- The recommended dosing of perampanel for partial-onset seizures in patients not receiving concomitant AEDs is 2mg once daily at bedtime, increasing the dose by 2mg increments no more frequently than weekly intervals, to a recommended maintenance dose of 8mg to 12mg once daily.
    - A dose of 12mg once daily resulted in somewhat greater reductions in seizure rates than the dose of 8mg once daily, but with a substantial increase in adverse reactions. Individual dosing should be adjusted based on clinical response and tolerability.
- The recommended dosing of perampanel for PGTC seizures in patients not receiving concomitant enzyme-inducing AEDs is 2mg once daily at bedtime, increasing the dose by 2mg increments no more frequently than weekly intervals, to a recommended maintenance dose of 8mg once daily.
    - Patients who are tolerating perampanel well at 8mg once daily and require further control of seizures may benefit from a dose increase up to 12mg once daily if tolerated. Individual dosing should be adjusted based on clinical response and tolerability.
- Perampanel oral suspension should be shaken well before every administration, and the provided adapter and graduated oral dosing syringe should always be used to administer perampanel oral suspension.
- Perampanel oral suspension should be discarded 90 days after first opening the bottle. Perampanel oral suspension is supplied in an amber polyethylene terephthalate (PET) bottle containing 340mL.

Comparison to Currently Available Products: Perampanel is currently available as 2mg, 4mg, 6mg, 8mg, 10mg, and 12mg oral tablets (Fycompa™). Fycompa™ oral tablets were FDA approved in 2012 for the same indications as Fycompa™ oral suspension (*see above indications*).

Cost: The WAC of Fycompa™ oral suspension is $2.82 per mL, which results in a monthly cost of $1,353.60 based on the recommended maintenance dose of 8mg once daily. The National Average Drug Acquisition Cost (NADAC) of Fycompa™ 8mg tablets is $23.84 per tablets, resulting in a monthly cost of $715.20.

Carnexiv™ (Carbamazepine Injection) Product Summary[15,16]

Indications: Carnexiv™ (carbamazepine injection) is indicated as replacement therapy for oral carbamazepine formulations, when oral administration is temporarily not feasible, in adults with the following seizure types:

- Partial seizures with complex symptomatology
- Generalized tonic-clonic seizures
- Mixed seizure patterns which include the above, or other partial or generalized seizures

Dosing:

- Carnexiv™ (carbamazepine) is available as a 200mg/20mL (10mg/mL) injection for IV use in a single-dose vial.
- Carnexiv™ is a replacement therapy for oral carbamazepine. Carbamazepine treatment should generally be initiated with an oral carbamazepine formulation.
- The total daily dose of Carnexiv™ is 70% of the total daily oral carbamazepine dose from which patients are being switched. The total daily dose of Carnexiv™ should be equally divided in four 30-minute infusions, separated by 6 hours.
- Patients should be switched back to oral carbamazepine administration at their previous total daily oral dose and frequency of administration as soon as clinically appropriate. The use of Carnexiv™ for periods of more than 7 days has not been studied.

Comparison to Currently Available Products: Carbamazepine is currently available generically as various oral formulations, including suspension, chewable tablets, tablets, extended-release (ER) tablets, and ER capsules and is indicated for similar indications as Carnexiv™ (*see above indications*), as well as for bipolar I disorder and trigeminal neuralgia. Carbamazepine oral tablets were first FDA approved in 1968.

Cost: Cost information for Carnexiv™ is not currently available at this time.

Recommendations

The College of Pharmacy recommends updating the current criteria for Sabril® (vigabatrin) to include the new, modified REMS program, and recommends the prior authorization of Briviact® (brivaracetam), Fycompa™ (perampanel oral suspension), and Carnexiv™ (carbamazepine injection) with the following criteria:

Sabril® (Vigabatrin) Approval Criteria:

1. An FDA approved diagnosis of refractory complex seizures in adults and pediatric patients 10 years or older, or infantile spasms in children ages 1 month to 2 years of age; and
2. Members with refractory complex seizures must have previous trials of at least three other antiepileptic medications; or
3. Members with infantile spasms must have had a previous trial with adrenocorticotropic hormone (ACTH) or have a diagnosis of infantile spasms with tuberous sclerosis; and
4. Prescription must be written by a neurologist; and
5. Member, prescriber, and pharmacy must all register in the ~~SHARE~~ SABRIL REMS program and maintain enrollment throughout therapy.

Briviact® (Brivaracetam) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least two other medications commonly used for seizures.
4. Members currently stable on Briviact® and who have a seizure diagnosis will be grandfathered.

5. Approval length for Briviact® injection will be for a maximum of seven days of therapy. Further approval may be granted if prescriber documents an ongoing need for Briviact® intravenous (IV) therapy over oral Briviact® formulations.

Fycompa™ (Perampanel) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of partial-onset seizures with or without secondarily generalized seizures or primary generalized tonic-clonic (PGTC) seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three* other medications commonly used for seizures. (*Fycompa™ has currently provided a supplemental rebate to require a trial with one other medication; however, Fycompa™ will follow the original criteria and require trials with three other medications if the manufacturer chooses not to participate in supplemental rebates.)
4. For Fycompa™ (perampanel) oral suspension, a patient-specific, clinically significant reason why Fycompa™ (perampanel) oral tablets cannot be used.
5. Members currently stable on Fycompa™ (perampanel) and who have a seizure diagnosis will be grandfathered.

Carnexiv™ (Carbamazepine Injection) Approval Criteria:

1. An FDA approved indication; and
2. Initial prescription must be written by a neurologist; and
3. Member must currently be stable on oral carbamazepine; and
4. Member must have a current condition in which oral administration is temporarily not feasible and needing Carnexiv™ for replacement therapy; and
5. Approval length will be for a maximum of seven days of therapy. Further approval may be granted if prescriber documents an ongoing need for Carnexiv™ intravenous (IV) therapy over oral carbamazepine formulations.

Utilization Details of Seizure Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
GABAPENTIN PRODUCTS						
GABAPENTIN CAP 300MG	35,107	10,920	$294,225.43	$0.26	$8.38	1.26%
GABAPENTIN TAB 600MG	21,842	4,929	$497,717.12	$0.74	$22.79	2.13%
GABAPENTIN TAB 800MG	12,088	2,305	$302,834.37	$0.83	$25.05	1.30%
GABAPENTIN CAP 100MG	8,431	3,322	$50,027.05	$0.20	$5.93	0.21%
GABAPENTIN CAP 400MG	5,149	1,461	$47,632.19	$0.31	$9.25	0.20%
GABAPENTIN SOL 250MG/5ML	713	132	$42,824.44	$1.98	$60.06	0.18%
NEURONTIN CAP 300MG	12	1	$3,888.55	$10.80	$324.05	0.02%
NEURONTIN TAB 800MG	12	1	$8,526.85	$23.69	$710.57	0.04%
SUBTOTAL	**83,354**	**23,071**	**$1,247,676.00**	**$0.48**	**$14.97**	**5.35%**
BENZODIAZEPINE PRODUCTS						
CLONAZEPAM TAB 1MG	20,852	4,565	$98,578.61	$0.16	$4.73	0.42%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CLONAZEPAM TAB 0.5MG	14,297	3,980	$59,088.91	$0.15	$4.13	0.25%
CLONAZEPAM TAB 2MG	5,982	1,189	$32,348.74	$0.18	$5.41	0.14%
DIAZEPAM GEL 10MG	1,344	740	$537,732.49	$67.00	$400.10	2.31%
ONFI TAB 20MG	846	94	$1,147,313.30	$45.40	$1,356.16	4.92%
ONFI TAB 10MG	834	118	$629,465.86	$25.49	$754.76	2.70%
CLONAZEP ODT TAB 0.25MG	720	231	$38,283.68	$2.20	$53.17	0.16%
ONFI SUS 2.5MG/ML	568	75	$721,519.18	$43.38	$1,270.28	3.09%
CLONAZEP ODT TAB 0.5MG	425	131	$17,355.73	$1.71	$40.84	0.07%
CLONAZEP ODT TAB 0.125MG	322	124	$16,389.90	$2.27	$50.90	0.07%
DIAZEPAM GEL 20MG	292	159	$137,742.08	$68.53	$471.72	0.59%
CLONAZEP ODT TAB 1MG	215	61	$10,045.86	$1.87	$46.72	0.04%
DIASTAT ACDL GEL 5-10MG	170	104	$90,913.98	$52.70	$534.79	0.39%
DIAZEPAM GEL 2.5MG	162	103	$73,335.28	$43.91	$452.69	0.31%
DIASTAT ACDL GEL 12.5-20MG	97	45	$50,705.05	$59.86	$522.73	0.22%
CLONAZEP ODT TAB 2MG	68	21	$2,924.82	$2.33	$43.01	0.01%
DIASTAT PED GEL 2.5MG	44	38	$19,927.89	$70.42	$452.91	0.09%
KLONOPIN TAB 2MG	12	1	$2,675.58	$7.43	$222.97	0.01%
KLONOPIN TAB 1MG	9	1	$2,208.39	$8.18	$245.38	0.01%
SUBTOTAL	**47,259**	**11,780**	**$3,688,555.33**	**$2.82**	**$78.05**	**15.81%**
DIVALPROEX, VALPROATE, & VALPROIC ACID PRODUCTS						
DIVALPROEX TAB 500MG DR	8,167	1,565	$145,789.13	$0.59	$17.85	0.63%
DIVALPROEX TAB 500MG ER	7,089	1,403	$652,126.34	$3.02	$91.99	2.80%
DIVALPROEX TAB 250MG DR	5,896	1,338	$68,205.12	$0.39	$11.57	0.29%
DIVALPROEX TAB 250MG ER	3,363	775	$256,944.41	$2.54	$76.40	1.10%
DIVALPROEX CAP 125MG	2,150	331	$234,101.29	$3.68	$108.88	1.00%
VALPROIC ACD SYP 250MG/5ML	2,031	291	$53,274.93	$0.89	$26.23	0.23%
DIVALPROEX TAB 125MG DR	1,628	393	$13,487.26	$0.28	$8.28	0.06%
VALPROIC ACD CAP 250MG	1,236	255	$30,230.66	$0.84	$24.46	0.13%
DEPAKOTE SPR CAP 125MG	249	36	$73,705.12	$9.84	$296.00	0.32%
VALPROIC ACD SOL 250MG/5ML	231	66	$4,073.35	$0.64	$17.63	0.02%
DEPAKOTE ER TAB 500MG	97	14	$41,273.85	$14.25	$425.50	0.18%
DEPAKOTE TAB 500MG DR	74	11	$42,616.45	$18.73	$575.90	0.18%
DEPAKOTE TAB 250MG DR	57	10	$10,665.08	$6.54	$187.11	0.05%
DEPAKOTE ER TAB 250MG	48	6	$18,856.04	$13.22	$392.83	0.08%
VALPROATE INJ 500MG/5ML	25	2	$1,823.43	$24.31	$72.94	0.01%
VALPROATE INJ 100MG/ML	20	2	$6,572.89	$17.76	$328.64	0.03%
DEPAKENE SYP 250MG/5ML	15	3	$376.49	$0.84	$25.10	0.00%
DEPAKOTE TAB 125MG DR	13	2	$1,313.06	$3.37	$101.00	0.01%
SUBTOTAL	**32,389**	**6,503**	**$1,655,434.90**	**$1.70**	**$51.11**	**7.10%**
LAMOTRIGINE PRODUCTS						
LAMOTRIGINE TAB 100MG	10,161	2,295	$73,889.87	$0.24	$7.27	0.32%
LAMOTRIGINE TAB 25MG	7,910	2,761	$75,310.39	$0.31	$9.52	0.32%
LAMOTRIGINE TAB 200MG	7,571	1,372	$60,661.01	$0.25	$8.01	0.26%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LAMOTRIGINE TAB 150MG	4,251	908	$35,658.86	$0.27	$8.39	0.15%
LAMOTRIGINE CHW 25MG	316	57	$13,787.85	$1.43	$43.63	0.06%
LAMICTAL TAB 200MG	171	16	$140,395.17	$27.22	$821.02	0.60%
LAMOTRIGINE CHW 5MG	143	45	$5,228.88	$1.24	$36.57	0.02%
LAMICTAL TAB 150MG	104	10	$89,046.99	$29.11	$856.22	0.38%
LAMOTRIGINE TAB 300MG ER	96	15	$49,671.40	$16.26	$517.41	0.21%
LAMOTRIGINE TAB 200MG ER	95	16	$49,249.76	$17.30	$518.42	0.21%
LAMICTAL TAB 100MG	69	8	$51,412.72	$23.48	$745.11	0.22%
LAMOTRIGINE TAB 50MG ODT	48	12	$15,168.06	$10.56	$316.00	0.07%
LAMOTRIGINE TAB 100MG	45	6	$19,521.25	$14.29	$433.81	0.08%
LAMOTRIGINE TAB 250MG ER	44	5	$44,092.05	$33.40	$1,002.09	0.19%
LAMICTAL ODT TAB 100MG	43	7	$19,899.72	$16.38	$462.78	0.09%
LAMICTAL XR TAB 200MG	30	4	$30,231.13	$33.59	$1,007.70	0.13%
LAMOTRIGINE TAB 50MG ER	28	11	$6,292.67	$7.49	$224.74	0.03%
LAMOTRIGINE TAB 100MG ER	25	7	$9,460.52	$13.14	$378.42	0.04%
LAMICTAL TAB 25MG	18	3	$13,259.65	$24.74	$736.65	0.06%
LAMOTRIGINE TAB 25MG ODT	18	5	$5,943.50	$11.01	$330.19	0.03%
LAMICTAL XR TAB 300MG	17	2	$28,010.42	$54.92	$1,647.67	0.12%
LAMICTAL ODT TAB 25MG	12	1	$6,056.56	$16.82	$504.71	0.03%
LAMICTAL ODT TAB 50MG	11	1	$6,842.00	$20.73	$622.00	0.03%
LAMICTAL ODT TAB 200MG	10	1	$7,904.24	$26.35	$790.42	0.03%
LAMOTRIGINE TAB 200MG	4	2	$2,214.84	$18.46	$553.71	0.01%
LAMICTAL KIT START 49	3	2	$1,572.94	$17.87	$524.31	0.01%
LAMOTRIGINE KIT ODT	1	1	$349.42	$11.65	$349.42	0.00%
LAMOTRIGINE TAB 25MG ER	1	1	$232.92	$5.55	$232.92	0.00%
LAMICTAL XR TAB 50MG	1	1	$1,053.27	$35.11	$1,053.27	0.00%
LAMICTAL XR TAB 100MG	1	1	$1,127.93	$37.60	$1,127.93	0.00%
LAMICTAL XR TAB 25MG	1	1	$528.54	$17.62	$528.54	0.00%
SUBTOTAL	**31,248**	**7,577**	**$864,074.53**	**$0.90**	**$27.65**	**3.70%**
TOPIRAMATE PRODUCTS						
TOPIRAMATE TAB 50MG	9,246	2,862	$66,826.70	$0.24	$7.23	0.29%
TOPIRAMATE TAB 100MG	8,584	1,868	$67,728.47	$0.26	$7.89	0.29%
TOPIRAMATE TAB 25MG	8,019	3,147	$52,126.14	$0.21	$6.50	0.22%
TOPIRAMATE TAB 200MG	3,846	639	$46,205.16	$0.39	$12.01	0.20%
TOPIRAMATE CAP 15MG	539	135	$20,217.97	$1.28	$37.51	0.09%
TOPIRAMATE CAP 25MG	497	97	$31,935.79	$2.21	$64.26	0.14%
TOPAMAX TAB 100MG	46	5	$39,370.93	$26.25	$855.89	0.17%
TROKENDI XR CAP 100MG	41	6	$22,873.15	$18.60	$557.88	0.10%
TOPAMAX TAB 200MG	25	3	$23,469.28	$31.29	$938.77	0.10%
TROKENDI XR CAP 50MG	24	5	$6,727.09	$9.34	$280.30	0.03%
TROKENDI XR CAP 25MG	17	2	$3,654.67	$7.17	$214.98	0.02%
TOPAMAX TAB 25MG	17	2	$2,723.56	$5.34	$160.21	0.01%
TROKENDI XR CAP 200MG	16	3	$21,845.67	$30.34	$1,365.35	0.09%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TOPAMAX SPR CAP 25MG	10	1	$24,644.31	$77.01	$2,464.43	0.11%
TOPAMAX SPR CAP 15MG	2	1	$51.64	$0.86	$25.82	0.00%
TOPIRAMATE CAP ER 150MG	1	1	$389.93	$13.00	$389.93	0.00%
QUDEXY XR CAP 200MG/24HR	1	1	$1,289.92	$43.00	$1,289.92	0.01%
SUBTOTAL	**30,931**	**8,778**	**$432,080.38**	**$0.46**	**$13.97**	**1.85%**
LEVETIRACETAM PRODUCTS						
LEVETIRACETA SOL 100MG/ML	10,165	1,557	$215,434.24	$0.69	$21.19	0.92%
LEVETIRACETA TAB 500MG	8,863	1,968	$111,390.38	$0.42	$12.57	0.48%
LEVETIRACETA TAB 1000MG	4,825	813	$137,437.09	$0.94	$28.48	0.59%
LEVETIRACETA TAB 750MG	3,829	697	$74,560.09	$0.64	$19.47	0.32%
LEVETIRACETA TAB 250MG	1,431	357	$13,231.08	$0.31	$9.25	0.06%
LEVETIRACETA TAB 500MG ER	620	127	$21,117.89	$1.15	$34.06	0.09%
LEVETIRACETA TAB 750MG ER	589	98	$32,031.86	$1.81	$54.38	0.14%
KEPPRA XR TAB 500MG	107	11	$85,069.55	$26.50	$795.04	0.36%
KEPPRA SOL 100MG/ML	90	12	$47,960.32	$17.64	$532.89	0.21%
KEPPRA XR TAB 750MG	78	8	$79,716.15	$31.48	$1,022.00	0.34%
KEPPRA TAB 1000MG	76	9	$79,222.40	$35.53	$1,042.40	0.34%
KEPPRA TAB 750MG	58	8	$51,673.68	$23.92	$890.93	0.22%
KEPPRA TAB 500MG	44	6	$22,050.84	$16.71	$501.16	0.09%
LEVETIRACETM INJ 500MG/5ML	34	2	$4,811.00	$16.09	$141.50	0.02%
KEPPRA TAB 250MG	19	2	$12,496.80	$21.04	$657.73	0.05%
SUBTOTAL	**30,828**	**5,675**	**$988,203.37**	**$1.06**	**$32.06**	**4.24%**
OXCARBAZEPINE PRODUCTS						
OXCARBAZEPIN TAB 300MG	11,070	2,332	$180,401.89	$0.54	$16.30	0.77%
OXCARBAZEPIN TAB 600MG	7,994	1,353	$237,355.16	$0.99	$29.69	1.02%
OXCARBAZEPIN TAB 150MG	7,510	2,032	$90,217.00	$0.40	$12.01	0.39%
OXCARBAZEPIN SUS 300MG/5ML	2,561	420	$502,473.03	$6.37	$196.20	2.15%
TRILEPTAL SUS 300MG/5ML	331	44	$184,364.19	$18.64	$556.99	0.79%
OXTELLAR XR TAB 600MG	73	11	$57,482.21	$23.85	$787.43	0.25%
TRILEPTAL TAB 600MG	72	7	$92,224.60	$42.11	$1,280.90	0.40%
OXTELLAR XR TAB 300MG	43	7	$9,961.34	$7.72	$231.66	0.04%
TRILEPTAL TAB 300MG	14	2	$5,594.56	$13.32	$399.61	0.02%
OXTELLAR XR TAB 150MG	13	4	$1,902.77	$4.88	$146.37	0.01%
SUBTOTAL	**29,681**	**6,212**	**$1,361,976.75**	**$1.53**	**$45.89**	**5.84%**
PREGABALIN PRODUCTS						
LYRICA CAP 150MG	3,668	662	$1,487,298.55	$13.71	$405.48	6.38%
LYRICA CAP 75MG	2,520	631	$974,767.09	$13.08	$386.81	4.18%
LYRICA CAP 100MG	2,164	462	$925,979.08	$14.42	$427.90	3.97%
LYRICA CAP 300MG	1,178	174	$436,000.17	$12.33	$370.12	1.87%
LYRICA CAP 50MG	1,136	321	$464,341.77	$13.57	$408.75	1.99%
LYRICA CAP 200MG	958	166	$350,674.52	$12.28	$366.05	1.50%
LYRICA CAP 225MG	412	67	$166,397.94	$13.40	$403.88	0.71%
LYRICA CAP 25MG	109	37	$37,186.93	$11.34	$341.16	0.16%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LYRICA SOL 20MG/ML	1	1	$74.95	$2.50	$74.95	0.00%
SUBTOTAL	**12,146**	**2,521**	**$4,842,721.00**	**$13.41**	**$398.71**	**20.76%**
CARBAMAZEPINE PRODUCTS						
CARBAMAZEPIN TAB 200MG	4,798	966	$293,213.39	$2.03	$61.11	1.26%
CARBAMAZEPIN CHW 100MG	997	171	$53,321.97	$1.77	$53.48	0.23%
EPITOL TAB 200MG	613	170	$31,892.06	$1.72	$52.03	0.14%
CARBAMAZEPIN TAB 400MG ER	606	93	$93,067.63	$5.00	$153.58	0.40%
CARBAMAZEPIN TAB 200MG ER	536	106	$59,885.92	$3.65	$111.73	0.26%
CARBAMAZEPIN CAP 300MG ER	506	68	$51,976.32	$3.37	$102.72	0.22%
CARBAMAZEPIN CAP 200MG ER	313	55	$29,444.78	$3.09	$94.07	0.13%
CARBAMAZEPIN SUS 100MG/5ML	307	41	$40,151.00	$4.52	$130.79	0.17%
TEGRETOL-XR TAB 100MG	178	48	$14,901.04	$2.72	$83.71	0.06%
CARBAMAZEPIN CAP 100MG ER	150	37	$14,566.31	$3.16	$97.11	0.06%
TEGRETOL TAB 200MG	99	11	$27,886.80	$9.43	$281.68	0.12%
TEGRETOL-XR TAB 400MG	96	10	$29,563.37	$9.82	$307.95	0.13%
TEGRETOL SUS 100MG/5ML	88	9	$25,506.67	$9.28	$289.85	0.11%
CARBATROL CAP 200MG	60	5	$11,880.41	$6.60	$198.01	0.05%
TEGRETOL-XR TAB 200MG	47	7	$13,442.73	$8.05	$286.02	0.06%
CARBAMAZEPIN TAB 100MG ER	32	20	$2,328.42	$2.35	$72.76	0.01%
CARBATROL CAP 300MG	30	6	$4,295.79	$4.77	$143.19	0.02%
CARBATROL CAP 100MG	1	1	$59.76	$1.99	$59.76	0.00%
SUBTOTAL	**9,457**	**1,824**	**$797,384.37**	**$2.78**	**$84.32**	**3.42%**
PHENYTOIN & FOSPHENYTOIN PRODUCTS						
PHENYTOIN EX CAP 100MG	6,029	995	$194,927.52	$1.08	$32.33	0.84%
DILANTIN CAP 100MG	700	113	$73,620.79	$3.47	$105.17	0.32%
PHENYTOIN CHW 50MG	276	44	$9,172.34	$1.06	$33.23	0.04%
PHENYTOIN SUS 125MG/5ML	257	42	$9,459.23	$1.28	$36.81	0.04%
DILANTIN CHW 50MG	104	15	$10,813.27	$3.29	$103.97	0.05%
PHENYTEK CAP 300MG	102	19	$11,223.78	$3.41	$110.04	0.05%
PHENYTEK CAP 200MG	84	14	$8,225.25	$3.14	$97.92	0.04%
DILANTIN CAP 30MG	80	8	$2,996.99	$1.24	$37.46	0.01%
PHENYTOIN EX CAP 300MG	25	12	$2,007.58	$2.48	$80.30	0.01%
DILANTIN-125 SUS 125MG/5ML	20	2	$2,651.63	$4.42	$132.58	0.01%
PHENYTOIN EX CAP 200MG	19	9	$1,717.68	$2.73	$90.40	0.01%
CEREBYX INJ 100/2ML	6	1	$847.12	$70.59	$141.19	0.00%
PHENYTOIN INJ 50MG/ML	1	1	$33.96	$6.79	$33.96	0.00%
SUBTOTAL	**7,703**	**1,275**	**$327,697.14**	**$1.42**	**$42.54**	**1.40%**
LACOSAMIDE PRODUCTS						
VIMPAT TAB 200MG	1,811	236	$1,270,169.13	$23.58	$701.36	5.45%
VIMPAT TAB 100MG	1,349	237	$870,192.00	$21.77	$645.06	3.73%
VIMPAT TAB 150MG	732	134	$473,407.60	$21.66	$646.73	2.03%
VIMPAT SOL 10MG/ML	656	86	$431,422.18	$23.01	$657.66	1.85%
VIMPAT TAB 50MG	565	125	$213,471.10	$12.83	$377.82	0.92%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
VIMPAT INJ 200MG/20ML	33	2	$14,136.23	$62.83	$428.37	0.06%
SUBTOTAL	**5,146**	**820**	**$3,272,798.24**	**$21.63**	**$635.99**	**14.03%**
ZONISAMIDE PRODUCTS						
ZONISAMIDE CAP 100MG	2,983	436	$56,926.22	$0.64	$19.08	0.24%
ZONISAMIDE CAP 50MG	811	165	$11,854.34	$0.48	$14.62	0.05%
ZONISAMIDE CAP 25MG	454	115	$5,764.69	$0.43	$12.70	0.02%
ZONEGRAN CAP 100MG	23	2	$29,288.42	$42.45	$1,273.41	0.13%
SUBTOTAL	**4,271**	**718**	**$103,833.67**	**$0.81**	**$24.31**	**0.45%**
PHENOBARBITAL PRODUCTS						
PHENOBARB TAB 64.8MG	882	103	$30,445.92	$1.13	$34.52	0.13%
PHENOBARB TAB 32.4MG	671	103	$25,920.24	$1.27	$38.63	0.11%
PHENOBARB ELX 20MG/5ML	664	126	$46,436.67	$2.47	$69.93	0.20%
PHENOBARB SOL 20MG/5ML	570	127	$30,196.42	$1.89	$52.98	0.13%
PHENOBARB TAB 97.2MG	334	42	$12,850.57	$1.23	$38.47	0.06%
PHENOBARB TAB 30MG	135	27	$2,549.81	$0.64	$18.89	0.01%
PHENOBARB TAB 16.2MG	132	22	$2,591.58	$0.67	$19.63	0.01%
PHENOBARB TAB 15MG	68	11	$1,553.22	$0.75	$22.84	0.01%
PHENOBARB TAB 60MG	58	14	$956.06	$0.55	$16.48	0.00%
PHENOBARB TAB 100MG	40	6	$722.96	$0.61	$18.07	0.00%
SUBTOTAL	**3,554**	**581**	**$154,223.45**	**$1.46**	**$43.39**	**0.66%**
ETHOSUXIMIDE PRODUCTS						
ETHOSUXIMIDE CAP 250MG	665	125	$70,764.02	$3.53	$106.41	0.30%
ETHOSUXIMIDE SOL 250/5ML	528	100	$47,445.08	$2.98	$89.86	0.20%
ZARONTIN CAP 250MG	31	4	$7,909.18	$8.55	$255.13	0.03%
SUBTOTAL	**1,224**	**229**	**$126,118.28**	**$3.42**	**$103.04**	**0.54%**
PRIMIDONE PRODUCTS						
PRIMIDONE TAB 50MG	519	116	$4,740.17	$0.28	$9.13	0.02%
PRIMIDONE TAB 250MG	334	48	$4,772.37	$0.46	$14.29	0.02%
MYSOLINE TAB 250MG	21	2	$73,107.13	$117.35	$3,481.29	0.31%
MYSOLINE TAB 50MG	7	1	$74.38	$0.35	$10.63	0.00%
SUBTOTAL	**881**	**167**	**$82,694.05**	**$2.95**	**$93.86**	**0.35%**
ACETAZOLAMIDE PRODUCTS						
ACETAZOLAMID TAB 250MG	498	139	$68,904.19	$4.73	$138.36	0.30%
ACETAZOLAMID CAP 500MG	232	88	$36,356.83	$5.30	$156.71	0.16%
ACETAZOLAMID TAB 125MG	60	21	$7,799.55	$4.57	$129.99	0.03%
SUBTOTAL	**790**	**248**	**$113,060.57**	**$4.89**	**$143.11**	**0.48%**
RUFINAMIDE PRODUCTS						
BANZEL TAB 400MG	386	54	$773,577.97	$66.66	$2,004.09	3.32%
BANZEL SUS 40MG/ML	275	33	$407,193.64	$50.19	$1,480.70	1.75%
BANZEL TAB 200MG	118	20	$70,370.53	$19.95	$596.36	0.30%
SUBTOTAL	**779**	**107**	**$1,251,142.14**	**$53.82**	**$1,606.09**	**5.36%**
FELBAMATE PRODUCTS						
FELBAMATE TAB 600MG	239	28	$77,801.14	$10.39	$325.53	0.33%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
FELBAMATE SUS 600/5ML	118	13	$99,043.85	$30.68	$839.35	0.42%
FELBAMATE TAB 400MG	68	9	$12,430.65	$5.77	$182.80	0.05%
FELBATOL TAB 400MG	47	6	$31,559.08	$22.38	$671.47	0.14%
FELBATOL TAB 600MG	35	6	$43,980.51	$41.89	$1,256.59	0.19%
FELBATOL SUS 600/5ML	10	1	$10,214.05	$34.05	$1,021.41	0.04%
SUBTOTAL	**517**	**63**	**$275,029.28**	**$17.60**	**$531.97**	**1.18%**
PERAMPANEL PRODUCTS						
FYCOMPA TAB 6MG	176	50	$86,594.84	$16.47	$492.02	0.37%
FYCOMPA TAB 4MG	123	36	$70,033.02	$19.31	$569.37	0.30%
FYCOMPA TAB 8MG	120	24	$65,376.36	$18.28	$544.80	0.28%
FYCOMPA TAB 2MG	41	17	$13,773.40	$11.95	$335.94	0.06%
FYCOMPA TAB 10MG	34	9	$18,762.29	$18.82	$551.83	0.08%
FYCOMPA TAB 12MG	11	2	$7,701.39	$23.34	$700.13	0.03%
SUBTOTAL	**505**	**138**	**$262,241.30**	**$17.55**	**$519.29**	**1.12%**
TIAGABINE PRODUCTS						
TIAGABINE TAB 4MG	89	12	$44,718.39	$16.91	$502.45	0.19%
GABITRIL TAB 12MG	25	3	$10,348.99	$13.80	$413.96	0.04%
GABITRIL TAB 16MG	12	3	$2,138.71	$5.94	$178.23	0.01%
TIAGABINE TAB 2MG	9	2	$2,765.42	$10.24	$307.27	0.01%
GABITRIL TAB 2MG	3	1	$1,234.65	$13.72	$411.55	0.01%
SUBTOTAL	**138**	**21**	**$61,206.16**	**$14.88**	**$443.52**	**0.26%**
VIGABATRIN PRODUCTS						
SABRIL POW 500MG	91	11	$1,207,647.46	$442.36	$13,270.85	5.18%
SABRIL TAB 500MG	12	2	$108,849.00	$302.36	$9,070.75	0.47%
SUBTOTAL	**103**	**13**	**$1,316,496.46**	**$426.0**	**$12,781.5**	**5.64%**
ESLICARBAZEPINE PRODUCTS						
APTIOM TAB 800MG	40	8	$34,299.23	$28.37	$857.48	0.15%
APTIOM TAB 600MG	25	5	$43,807.89	$57.57	$1,752.32	0.19%
APTIOM TAB 400MG	7	3	$4,732.73	$25.31	$676.10	0.02%
APTIOM TAB 200MG	2	1	$1,102.81	$18.38	$551.41	0.00%
SUBTOTAL	**74**	**17**	**$83,942.66**	**$37.86**	**$1,134.36**	**0.36%**
METHSUXIMIDE PRODUCTS						
CELONTIN CAP 300MG	59	6	$14,584.30	$8.39	$247.19	0.06%
SUBTOTAL	**59**	**6**	**$14,584.30**	**$8.39**	**$247.19**	**0.06%**
BRIVARACETAM PRODUCTS						
BRIVIACT TAB 50MG	2	2	$1,074.04	$17.90	$537.02	0.00%
SUBTOTAL	**2**	**2**	**$1,074.04**	**$17.90**	**$537.02**	**0.00%**
TOTAL	**333,039**	**47,241***	**$23,324,248.37**	**$2.32**	**$70.03**	**100.00**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

The utilization details above include seizure medications used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate.

[1] U.S. Food and Drug Administration (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 11/2016. Last accessed 01/06/2017.
[2] Briviact® Prescribing Information. UCB, Inc. Available online at: https://www.briviact.com/briviact-PI.pdf?v=1479316368. Last revised 03/2016. Last accessed 01/19/2017.
[3] PR Newswire: Eisai Announces FDA Approval of Fycompa™ (perampanel) Oral Suspension for Adjunctive Therapy in the Treatment of Partial-Onset Seizures and Primary Generalized Tonic-Clonic Seizures. Available online at: http://www.prnewswire.com/news-releases/eisai-announces-fda-approval-of-fycompa-perampanel-oral-suspension-for-adjunctive-therapy-in-the-treatment-of-partial-onset-seizures-and-primary-generalized-tonic-clonic-seizures-300260456.html. Issued 05/02/2016. Last accessed 01/19/2017.
[4] Lundbeck Press Release: U.S. FDA Approves Changes to the Sabril® (vigabatrin) REMS Program. Available online at: https://www.lundbeck.com/upload/us/files/pdf/2016_Releases/LundbeckUS.com_Sabril%20REMS%20Press%20Release_6.23.16.pdf. Issued 06/23/2016. Last accessed 01/27/2017.
[5] FDA sNDA Approval: Trokendi XR® Oral Tablets. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/201635Orig1s014ltr.pdf. Issued 08/18/2016. Last accessed 01/19/2017.
[6] Carnexiv™ Prescribing Information. Lundbeck. Available online at: http://www.lundbeck.com/upload/us/files/pdf/Products/Carnexiv_PI_US_EN.pdf. Last revised 10/2016. Last accessed 01/19/2017.
[7] Anderson P. Once-Daily Epilepsy Drug Equivalent to Twice-Daily Drug. *Medscape.* Available online at: http://www.medscape.com/viewarticle/862272. Issued 04/21/2016. Last accessed 01/19/2017.
[8] FDA Tentative sNDA Approval: Qudexy™ XR Oral Tablets. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/205122Orig1s003TAltr.pdf. Issued 04/15/2016. Last accessed 01/19/2017.
[9] FDA Tentative sNDA Approval: Trokendi XR® Oral Tablets. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/201635Orig1s014ltr.pdf. Issued 08/18/2016. Last accessed 01/19/2017.
[10] Lane EJ. Sun Pharma Research Unit Licenses Epilepsy Drug Elepsia XR to Parent. *FiercePharma*. Available online at: http://www.fiercepharma.com/pharma-asia/sun-pharma-research-unit-licenses-epilepsy-drug-elepsia-xr-to-parent. Issued 07/20/2016. Last accessed 01/19/2017.
[11] GW Pharmaceuticals Press Release: GW Pharmaceuticals Announces Second Positive Phase 3 Pivotal Trial for Epidiolex® (cannabidiol) in the Treatment of Lennox-Gastaut Syndrome. Available online at: http://dev-gwpharma.pantheonsite.io/about-us/news/gw-pharmaceuticals-announces-second-positive-phase-3-pivotal-trial-epidiolex. Issued 09/26/2016. Last accessed 01/19/2017.
[12] Pfizer Press Release: Lyrica® (pregabalin) Phase 3 Trial in Pediatric Epilepsy Meets Primary Endpoint. Available online at: http://press.pfizer.com/press-release/lyrica-pregabalin-phase-3-trial-pediatric-epilepsy-meets-primary-endpoint. Issued 12/01/2016. Last accessed 01/19/2017.
[13] Briviact® Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/briviact-1/. Last revised 04/25/2016. Last accessed 01/19/2017.
[14] Fycompa™ Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/fycompa/. Last revised 04/30/2016. Last accessed 01/19/2017.
[15] Carnexiv™ Package Insert. MedLibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/carnexiv/. Last revised 10/20/2016. Last accessed 01/19/2017.
[16] Micromedex 2.0: Carbamazepine Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/. Last revised 01/03/2017. Last accessed 01/19/2017.

Appendix K

Fiscal Year 2016 Annual Review of Parkinson's Disease Medications and 30-Day Notice to Prior Authorize Nuplazid™ (Pimavanserin)

Oklahoma Health Care Authority
February 2017

Current Prior Authorization Criteria

Requip XL® (Ropinirole) & Mirapex ER® (Pramipexole) Approval Criteria:

1. An FDA approved diagnosis of Parkinson's disease; and
2. A patient-specific, clinically significant reason why the immediate-release products cannot be used.

Neupro® (Rotigotine Transdermal System) Approval Criteria:

1. For the diagnosis of Parkinson's disease the following criteria apply:
   a. An FDA approved indication for the treatment of signs and symptoms of Parkinson's disease; and
   b. Member must be 18 years of age or older; and
   c. Failed treatment, intolerance, or a patient-specific, clinically significant reason why the member cannot use oral dopamine agonists.
2. For the diagnosis of Restless Leg Syndrome the following criteria apply:
   a. An FDA approved indication of Restless Leg Syndrome; and
   b. Member must be 18 years of age or older; and
   c. Documented treatment attempts at recommended dose with at least two of the following that did not yield adequate relief:
      i. carbidopa/levodopa; or
      ii. pramipexole; or
      iii. ropinirole.

Duopa™ (Carbidopa/Levodopa Enteral Suspension) Approval Criteria:

1. An FDA approved diagnosis of advanced Parkinson's disease; and
2. For long-term administration, member or caregivers must be willing and able to administer Duopa™ through a percutaneous endoscopic gastrostomy; and
3. Patients must be experiencing three hours or more of "off" time on their current Parkinson's disease drug treatment and they must have demonstrated a clear responsiveness to treatment with levodopa; and
4. Approvals will be for a quantity of one cassette per day.

Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) Approval Criteria

1. An FDA approved diagnosis of Parkinson's disease, post-encephalitic parkinsonism, or parkinsonism that may follow carbon monoxide intoxication or manganese intoxication; and

2. A patient-specific, clinically significant reason why the member cannot use other generic carbidopa/levodopa combinations including Sinemet® CR (carbidopa/levodopa extended-release tablets).

Utilization of Parkinson's Disease Medications: Fiscal Year 2016

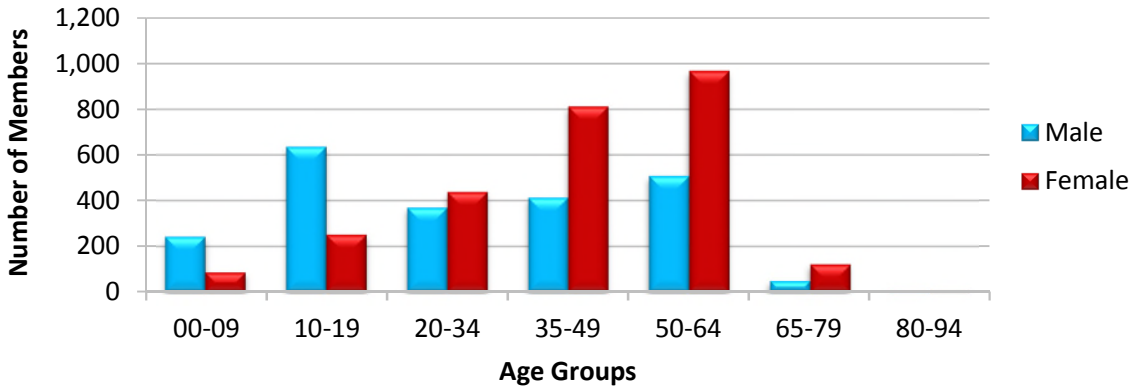
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	4,945	25,279	$736,210.39	$29.12	$0.91	1,571,567	806,894
2016	4,909	25,631	$774,237.11	$30.21	$0.95	1,695,763	818,502
% Change	**-0.70%**	**1.40%**	**5.20%**	**3.70%**	**4.40%**	**7.90%**	**1.40%**
Change	**-36**	**352**	**$38,026.72**	**$1.09**	**$0.04**	**124,196**	**11,608**

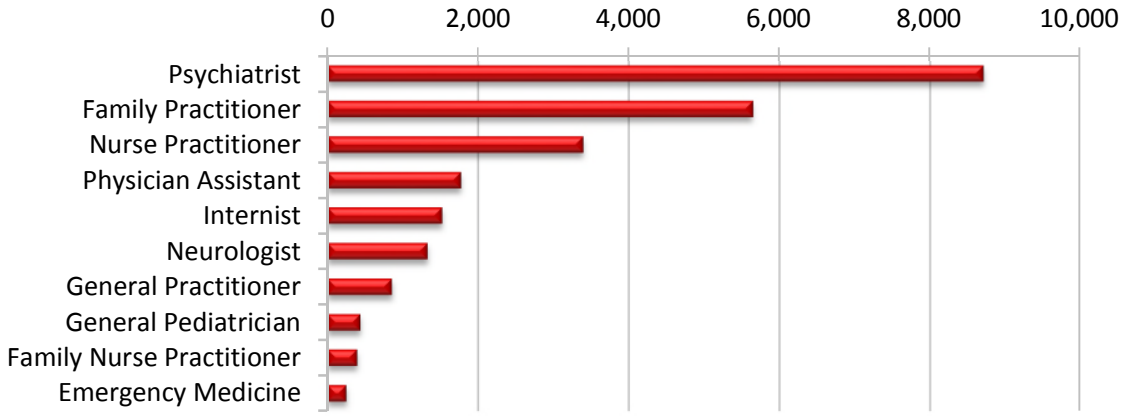
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- There were no paid medical claims for Duopa™ (carbidopa/levodopa enteral suspension) during fiscal year 2016.

Demographics of Members Utilizing Parkinson's Disease Medications

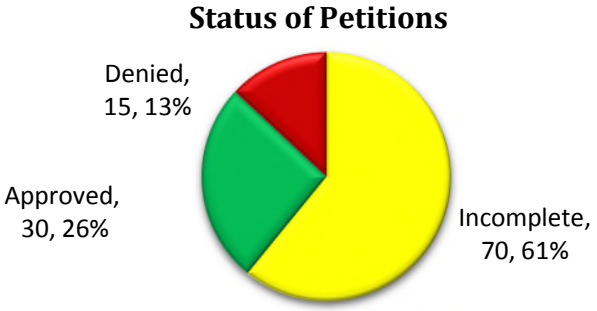


Top Prescriber Specialties of Parkinson's Disease Medications by Number of Claims



Prior Authorization of Parkinson's Disease Medications

There were 115 prior authorization requests submitted for Parkinson's disease medications during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12]

Anticipated Patent Expiration(s):

- Duopa™ (carbidopa/levodopa enteral suspension): January 2022
- Azilect® (rasagiline): August 2027
- Neupro® (rotigotine): September 2027
- Nuplazid™ (pimavanserin): June 2028
- Rytary™ (carbidopa/levodopa ER capsule): December 2028

News:

- **June 2016:** Following a 12-week single-center randomized controlled trial, researchers reported at the Movement Disorders Society meeting that atomoxetine did not improve cognition in Parkinson's patients with mild cognitive impairment. The primary endpoint was an effect on a composite of attention, working memory, information processing speed, and set-shifting. There was no statistical difference in scores on neuropsychological testing but there was a statistical difference for inattention and impulsivity for atomoxetine group versus placebo. Atomoxetine is a norepinephrine reuptake inhibitor the U.S. Food and Drug Administration (FDA) approved to treat attention deficit hyperactivity disorder (ADHD).
- **August 2016:** The FDA granted Fast Track Designation for APL-130277, a sublingual thin-film containing apomorphine, for the treatment of "off" episodes in patients with Parkinson's disease (PD). Apomorphine is the only molecule approved for acute, intermittent treatment of "off" episodes for advanced PD patients, but is currently only approved as a subcutaneous injection in the United States. A New Drug Application (NDA) is expected to be submitted in the first half of 2017. Sunovion Pharmaceuticals acquired Cynapsus Therapeutics, which included Cynapsus' apomorphine product, APL-130277, in October 2016.
- **September 2016:** A NDA was re-submitted to the FDA for Xadago® (safinamide) after the FDA's Complete Response Letter (CRL) in March 2016 and the determination date set at March 21, 2017. The CRL requested clinical evaluation of potential abuse and

dependence/withdrawal effects; however, after a meeting in July 2016, the FDA agreed to no longer require additional evaluation studies. Xadago® (safinamide) was approved by the European Medicines Agency in February 2015 for the treatment of adult patients with idiopathic PD as add-on therapy to a stable dose of levodopa alone or in combination with other Parkinson drugs in patients with mid- to late-stage motor-fluctuating disease.

- **October 2016:** A NDA was submitted to the FDA for amantadine extended-release known as ADS-5102 for treatment of levodopa-induced dyskinesia (LID) in patients with PD. The FDA has designated LID in patients with PD as an orphan disease. There are currently no approved drugs in the United States for the treatment of LID in patients with PD. ADS-5102's Phase 3 trials comparing ADS-5102 340mg oral dose given at bedtime versus placebo met the primary and key secondary endpoints. The open-label safety study known as EASE LID 2 is currently ongoing and patients enrolled are being followed for up to two years.

New FDA Approval(s):

- **April 2016:** Nuplazid™ (pimavanserin) is the first drug approved to treat hallucinations and delusions associated with Parkinson's disease psychosis.

Nuplazid™ (Pimavanserin) Product Summary[13,14]

Indications: Nuplazid™ (pimavanserin) is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

Dosing:

- Nuplazid™ is available as a 17mg oral tablet.
- The recommended dosing of pimavanserin is 34mg, taken orally as two 17mg tablets once daily, without titration.
- Pimavanserin can be taken with or without food.

Mechanism of Action:

- The mechanism of action of pimavanserin in the treatment of hallucinations and delusions associated with Parkinson's disease psychosis is unknown. However, the effect of pimavanserin could be mediated through a combination of inverse agonist and antagonist activity at serotonin 5-HT2A receptors and to a lesser extent at serotonin 5-HT2C receptors.

Contraindications:

- None.

Warnings and Precautions:

- Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Antipsychotic drugs increase the all-cause risk of death in elderly patients with dementia-related psychosis. Analyses of 17 dementia-related psychosis placebo-controlled trials revealed a risk of death in the drug-treated patients of between 1.6- to 1.7- times that in placebo-treated patients. Pimavanserin is not approved for the treatment of patients with

dementia-related psychosis unrelated to hallucinations and delusions associated with PD psychosis.

- QT Interval Prolongation: Pimavanserin prolongs the QT interval. The use of pimavanserin should be avoided in patients with known QT interval prolongations or in combination with other drugs known to prolong the QT interval. Pimavanserin should also be avoided in patients with risk factors for prolonged QT interval.

Drug Interactions:

- Coadministration with Strong CYP3A4 Inhibitors: The recommended dose of pimavanserin when coadministered with strong CYP3A4 inhibitors (e.g., ketoconazole) is 17mg orally once daily.
- Coadministration with Strong CYP3A4 Inducers: Patients should be monitored for reduced efficacy if pimavanserin is used concomitantly with strong CYP3A4 inducers; an increase in pimavanserin dosage may be needed.

Adverse Reactions: The most common adverse reactions (≥5% and twice the rate of placebo) reported during pimavanserin clinical trials were peripheral edema and confusional state.

Efficacy: The safety and efficacy of pimavanserin were based on a 6-week clinical study of 199 patients with PD psychosis randomized to pimavanserin or placebo.

- Pimavanserin was shown to be superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions, as demonstrated by the change in the PD-adapted Scale for the Assessment of Positive Symptoms (SAPS-PD) after six weeks of treatment (placebo-subtracted difference from baseline in SAPS-PD: -3.06, [95% CI: -4.91, -1.20]).
- Pimavanserin did not show an effect vs. placebo on motor function, as measured by the motor function change from baseline to week six in the Unified Parkinson's Disease Rating Scale Parts II and III (-1.4 vs. -1.7, respectively).

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Nuplazid™ (pimavanserin) 17mg tablet	$32.50	$1,950.00	$23,400.00

Costs do not reflect rebated prices or net costs.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Nuplazid™ (pimavanserin) with the following criteria:

Nuplazid™ (Pimavanserin) Approval Criteria:

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease psychosis; and
2. Member must have concomitant diagnosis of Parkinson's disease; and
3. Nuplazid™ will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis; and

4. Initial approvals will be for the duration of three months. For continuation, the prescriber must include information regarding improved response/effectiveness of this medication.
5. A quantity limit of two tablets daily will apply.

Utilization Details of Parkinson's Disease Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
AMANTADINE PRODUCTS						
AMANTADINE CAP 100MG	4,037	736	$309,088.67	$2.56	$76.56	39.92%
AMANTADINE TAB 100MG	1,175	431	$145,246.09	$4.12	$123.61	18.76%
AMANTADINE SYP 50MG/5ML	337	98	$4,444.36	$0.46	$13.19	0.57%
SUBTOTAL	**5,549**	**1,265**	**$458,779.12**	**$2.77**	**$82.68**	**59.25%**
BENZTROPINE PRODUCTS						
BENZTROPINE TAB 1MG	5,234	1,077	$50,279.43	$0.31	$9.61	6.49%
BENZTROPINE TAB 2MG	2,570	508	$27,713.37	$0.34	$10.78	3.58%
BENZTROPINE TAB 0.5MG	1,559	315	$15,772.64	$0.34	$10.12	2.04%
SUBTOTAL	**9,363**	**1,900**	**$93,765.44**	**$0.32**	**$10.01**	**12.11%**
ROPINIROLE PRODUCTS						
ROPINIROLE TAB 1MG	1,578	440	$12,733.29	$0.22	$8.07	1.64%
ROPINIROLE TAB 0.5MG	1,019	325	$9,539.42	$0.26	$9.36	1.23%
ROPINIROLE TAB 2MG	787	211	$6,566.12	$0.22	$8.34	0.85%
ROPINIROLE TAB 0.25MG	491	187	$4,150.50	$0.25	$8.45	0.54%
ROPINIROLE TAB 3MG	211	54	$1,902.95	$0.26	$9.02	0.25%
ROPINIROLE TAB 4MG	201	64	$1,844.80	$0.21	$9.18	0.24%
ROPINIROLE TAB 5MG	73	17	$1,053.95	$0.39	$14.44	0.14%
SUBTOTAL	**4,360**	**1,298**	**$37,791.03**	**$0.24**	**$8.67**	**4.89%**
TRIHEXPHENIDYL PRODUCTS						
TRIHEXYPHEN TAB 5MG	1,477	269	$15,628.02	$0.34	$10.58	2.02%
TRIHEXYPHEN TAB 2MG	1,249	306	$7,430.99	$0.19	$5.95	0.96%
TRIHEXYPHEN ELX 0.4MG/ML	80	16	$2,064.61	$0.93	$25.81	0.27%
SUBTOTAL	**2,806**	**591**	**$25,123.62**	**$0.29**	**$8.95**	**3.25%**
CARBIDOPA/LEVODOPA PRODUCTS						
CARB/LEVO TAB 25-100MG	882	183	$13,281.30	$0.48	$15.06	1.72%
CARB/LEVO TAB 25-250MG	256	41	$6,634.87	$0.88	$25.92	0.86%
CARB/LEVO TAB 10-100MG	231	53	$3,102.13	$0.38	$13.43	0.40%
CARB/LEVO ER TAB 50-200MG	169	31	$5,583.52	$0.98	$33.04	0.72%
CARB/LEVO ER TAB 25-100MG	99	23	$2,524.54	$0.82	$25.50	0.33%
CARB/LEVO100 TAB /ENTACAP	13	2	$2,346.27	$6.59	$180.48	0.30%
CARB/LEVO150 TAB /ENTACAP	13	1	$2,876.11	$7.37	$221.24	0.37%
CARB/LEVO TAB 10-100MG	12	1	$345.74	$0.96	$28.81	0.04%
CARB/LEVO TAB 25-100MG	9	2	$532.18	$2.01	$59.13	0.07%
RYTARY CAP 195MG	5	1	$3,001.50	$20.01	$600.30	0.39%
CARB/LEVO TAB 25-250MG	3	1	$259.39	$2.73	$86.46	0.03%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CARB/LEVO200 TAB /ENTACAP	2	2	$400.87	$3.58	$200.44	0.05%
SUBTOTAL	**1,694**	**341**	**$40,888.42**	**$0.76**	**$24.14**	**5.28%**
PRAMIPEXOLE PRODUCTS						
PRAMIPEXOLE TAB 0.5MG	406	102	$2,502.17	$0.17	$6.16	0.32%
PRAMIPEXOLE TAB 0.125MG	390	119	$2,495.05	$0.19	$6.40	0.32%
PRAMIPEXOLE TAB 0.25MG	371	127	$2,032.84	$0.15	$5.48	0.26%
PRAMIPEXOLE TAB 1MG	237	59	$2,158.50	$0.25	$9.11	0.28%
PRAMIPEXOLE TAB 1.5MG	64	17	$483.41	$0.17	$7.55	0.06%
PRAMIPEXOLE TAB 0.75MG	5	5	$59.22	$0.28	$11.84	0.01%
MIRAPEX TAB 0.5MG	2	1	$13.36	$0.22	$6.68	0.00%
SUBTOTAL	**1,475**	**430**	**$9,744.55**	**$0.18**	**$6.61**	**1.25%**
BROMOCRIPTINE PRODUCTS						
BROMOCRIPTIN TAB 2.5MG	269	65	$46,244.49	$5.70	$171.91	5.97%
BROMOCRIPTIN CAP 5MG	23	5	$8,961.39	$12.62	$389.63	1.16%
SUBTOTAL	**292**	**70**	**$55,205.88**	**$6.23**	**$189.06**	**7.13%**
ENTACAPONE PRODUCTS						
ENTACAPONE TAB 200MG	36	6	$16,252.91	$15.42	$451.47	2.10%
SUBTOTAL	**36**	**6**	**$16,252.91**	**$15.42**	**$451.47**	**2.10%**
RASAGILINE PRODUCTS						
AZILECT TAB 1MG	37	8	$24,420.24	$19.05	$660.01	3.15%
AZILECT TAB 0.5MG	7	1	$6,266.58	$29.84	$895.23	0.81%
SUBTOTAL	**44**	**9**	**$30,686.82**	**$20.57**	**$697.43**	**3.96%**
ROTIGOTINE PRODUCTS						
NEUPRO DIS 4MG/24HR	7	1	$4,102.09	$19.53	$586.01	0.53%
NEUPRO DIS 1MG/24HR	1	1	$562.05	$18.73	$562.05	0.07%
NEUPRO DIS 2MG/24HR	1	1	$597.02	$19.90	$597.02	0.08%
NEUPRO DIS 8MG/24HR	1	1	$601.02	$20.03	$601.02	0.08%
SUBTOTAL	**10**	**4**	**$5,862.18**	**$19.54**	**$586.22**	**0.76%**
SELEGILINE PRODUCTS						
SELEGILINE TAB 5MG	2	1	$137.14	$3.19	$68.57	0.02%
SUBTOTAL	**2**	**1**	**$137.14**	**$3.19**	**$68.57**	**0.02%**
TOTAL	**25,631**	**4,909***	**$774,237.11**	**$0.95**	**$30.21**	**100%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 11/2016. Last accessed 01/2017.

[2] Adamas™ Pharma ADS-5102 in LID. Available online at: http://www.adamaspharma.com/ads-5102-in-lid/. Issued 2016. Last accessed 01/2017.

[3] Clinical Neurology News. "Extended-release amantadine may improve levodopa dyskinesia control." Available online at: http://www.mdedge.com/clinicalneurologynews/article/108233/movement-disorders/extended-release-amantadine-may-improve. Issued 04/2016. Last accessed 01/2017.

[4] Fiore, Kristina. "ADHD Drug Fails to Boost Cognition in Parkinson's." *MedPage Today*. Available online at: http://www.medpagetoday.com/meetingcoverage/mds/58746. Issued 06/2016. Last accessed 01/2017.

[5] Newron Pharmaceuticals Press Release. "US FDA considers Newron's re-submitted NDA for Xadago® to be a complete, class 2 response to Complete Response Letter PDUFA date March 21, 2017". Available online at: http://www.newron.com/ENG/Default.aspx?SEZ=5&PAG=19&MOD=NWRPRS&YR=204. Issued 10/2016. Last accessed 01/2017.

[6] Newron Pharmaceuticals Press Release. "Newron re-submits US NDA for Xadago® (safinamide)." Available online at: http://www.newron.com/ENG/Default.aspx?SEZ=5&PAG=19&MOD=NWRPRS&YR=204. Issued 09/2016. Last accessed 01/2017.

[7] Newron Pharmaceuticals Press Release. "Newron to re-submit US NDA for Xadago® (safinamide) FDA agrees to no additional evaluation of abuse liability or dependence/withdrawal effects in humans is required." Available online at: http://www.newron.com/ENG/Default.aspx?SEZ=5&PAG=19&MOD=NWRPRS&YR=204. Issued 07/2016. Last accessed 01/2017.

[8] Newron Pharmaceuticals Press Release. "Newron receives Complete Response Letter from US FDA for Xadago® (safinamide)." Available online at: http://www.newron.com/ENG/Default.aspx?SEZ=5&PAG=19&MOD=NWRPRS&YR=204. Issued 03/2016. Last accessed 01/2017.

[9] European Medicines Agency Science Medicines Health. EPAR summary for public: Xadago® (safinamide). Available online at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/002396/WC500184968.pdf . Last updated 02/2015. Last accessed 01/2017.

[10] NASDAQ Globe Newswire. "Cynapsus Receives FDA Fast Track Designation for APL-130277 for the Treatment of OFF Episodes in Patients with Parkinson's Disease". Available online at: https://globenewswire.com/news-release/2016/08/29/867552/0/en/Cynapsus-Receives-FDA-Fast-Track-Designation-for-APL-130277-for-the-Treatment-of-OFF-Episodes-in-Patients-with-Parkinson-s-Disease.html . Issued 08/2016. Last accessed 01/2017.

[11] Sunovion News & Media. "Sunovion Pharmaceuticals Completes Acquisition of Cynapsus Therapeutics." Available online at: http://www.sunovion.com/news/pressReleases/20161021.pdf . Issued 10/2016. Last accessed 01/2017.

[12] FDA News Release. "FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease". Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm498442.htm. Issued 04/2016. Last accessed 01/2017.

[13] Nuplazid™ Prescribing Information. Acadia Pharmaceuticals Inc. Available online at: https://www.nuplazidhcp.com/pdf/NUPLAZID_Prescribing_Information.pdf. Last revised 04/2016. Last accessed 01/2017.

[14] Nuplazid™ New Drug Approval. OptumRx. Available online at: https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Nuplazid_2016-0502.pdf. Issued 2016. Last accessed 01/2017.

Appendix L

Calendar Year 2016 Annual Review of Hyperkalemia Medications and 30-Day Notice to Prior Authorize Veltassa® (Patiromer)

Oklahoma Health Care Authority
February 2017

Chronic Hyperkalemia[1,2,3,4]

Hyperkalemia is a common clinical problem defined as a serum potassium level greater than 5.5mEq/L. Chronic or mild to moderate hyperkalemia (potassium greater than 5mEq/L) can be safely managed in an outpatient setting. However, acute hyperkalemia requires urgent correction and severe hyperkalemia (potassium greater than 6mEq/L with EKG changes or greater than 6.5mEq/L with or without EKG changes) should be managed in an inpatient setting. Common etiologies of hyperkalemia include chronic kidney disease (CKD), heart failure, and potassium-altering medications [e.g., angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), potassium supplements, potassium sparing diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs)]. Many patients with hyperkalemia are asymptomatic, but if symptoms occur, they are often non-specific and can range from paresthesias, muscle weakness, and fatigue to EKG changes and fatal ventricular arrhythmias.

Management of chronic hyperkalemia is a patient specific process usually involving multiple simultaneous strategies including dietary modifications and pharmacological intervention. First line strategies include limiting dietary potassium and adding a potassium-eliminating diuretic (thiazide or loop diuretic). Dietary potassium intake is recommended to be limited to 40-60mEq/day although adherence rates are often low due to a lack of awareness of potassium content in foods and gastrointestinal adverse events including constipation. Thiazide diuretics are preferred in patients with normal kidney function while loop diuretics are preferred in patients with a creatinine clearance of less than 30mL/min, but caution should be used in volume depleted patients. If further serum potassium lowering is needed, potassium binders may be considered. Sodium polystyrene sulfonate is a potassium binder that has been available for more than 50 years for the treatment of hyperkalemia. Sodium polystyrene sulfonate is available as a powder, pre-mixed suspension, and enema. Sodium polystyrene sulfonate is an ion exchange resin that removes potassium by exchanging sodium ions for potassium ions in the intestine; therefore, sodium polystyrene sulfonate should be used with caution in patients with heart failure, severe hypertension, and edema due to the high sodium content. Sodium polystyrene sulfonate should be separated from all other medications by at least six hours due to potential for drug interactions.

In October 2015, a new potassium binder, Veltassa® (patiromer), was approved by the U.S. Food and Drug Administration (FDA) for the treatment of hyperkalemia. Veltassa® is available as a non-absorbable oral powder in single-use packets to be mixed with water and works by exchanging calcium ions for potassium in the intestinal lumen. Veltassa® was effective in clinical trials at lowering potassium levels in hyperkalemic patients with CKD who were on at

least one drug that inhibited the renin-angiotensin-aldosterone system (RAAS). Veltassa® should be separated from all other medications by at least three hours to prevent potential drug interactions. Veltassa® has a delayed-onset of action and should not be used as an emergency treatment for life-threatening hyperkalemia.

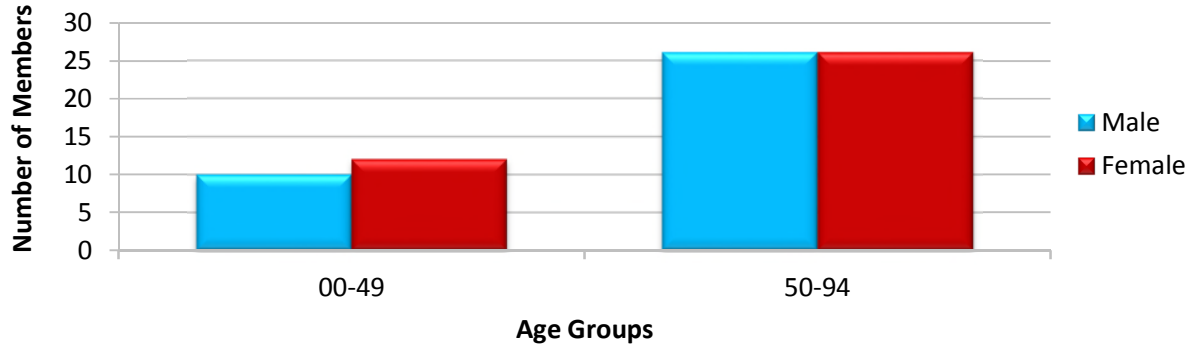
Utilization of Potassium Binders: Calendar Year 2016

Comparison of Calendar Years

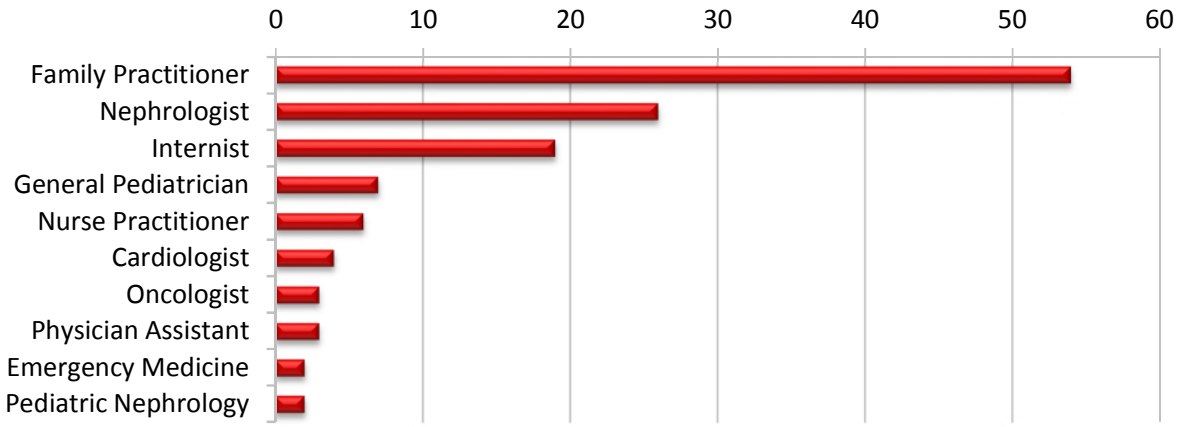
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	70	117	$5,264.38	$44.99	$3.17	43,517	1,661
2016	74	135	$8,390.58	$62.15	$5.18	43,768	1,621
% Change	**5.70%**	**15.40%**	**59.40%**	**38.10%**	**63.40%**	**0.60%**	**-2.40%**
Change	**4**	**18**	**$3,126.20**	**$17.16**	**$2.01**	**251**	**-40**

*Total number of unduplicated members.
Potassium binders do not currently require prior authorization.

Demographics of Members Utilizing Potassium Binders



Top Prescriber Specialties of Potassium Binders by Number of Claims



Market News and Updates[5,6,7,8]

News:

- **October 2015:** The FDA is requiring the manufacturer of Kayexalate® (sodium polystyrene sulfonate), Concordia Pharmaceuticals, to conduct drug interaction studies to investigate the potential of sodium polystyrene sulfonate to bind to other oral medications. Currently the approved label for sodium polystyrene sulfonate describes its potential to decrease absorption of lithium and thyroxine; however, extensive drug-drug interaction studies have not been performed. Sodium polystyrene sulfonate should be separated from all other oral medications by at least six hours at this time.
- **October 2016:** The FDA accepted a complete re-submission of a New Drug Application (NDA) for sodium zirconium cyclosilicate oral suspension (ZS-9) for the treatment of hyperkalemia. The first NDA submission received a complete response letter (CRL) from the FDA citing issues from a pre-approval manufacturing inspection. ZS-9 is also currently under review in the European Union and Australia and decisions are expected in the first half of 2017.

New FDA Approval(s):

- **October 2015:** Veltassa® (patiromer) was FDA approved for the treatment of hyperkalemia.

Veltassa® (Patiromer) Product Summary[9,10]

Indications: Veltassa® (patiromer) is a potassium binder indicated for the treatment of hyperkalemia.
Limitation of Use: Veltassa® (patiromer) should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

Dosing:

- Veltassa® (patiromer) is available as a powder for oral suspension. It is packaged in single-use packets containing 8.4grams, 16.8grams, or 25.2grams patiromer.
- The recommended starting dose is 8.4grams orally once daily administered with food.
- The dose should be adjusted by 8.4grams daily as needed at one week intervals to obtain desired serum potassium target range.
- Other orally administered drugs should be taken at least three hours before or three hours after patiromer.

Mechanism of Action: Patiromer is a non-absorbed, cation exchange polymer that contains a calcium-sorbitol counterion. It increases fecal excretion of potassium through binding of potassium in the lumen of the gastrointestinal tract. Binding of potassium decreases the concentration of free potassium in the gastrointestinal lumen.

Contraindications: Known hypersensitivity to Veltassa® (patiromer) or any of its components.

Warnings and Precautions:

- Worsening of Gastrointestinal Motility: Patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders,

should avoid use of patiromer, because patiromer may be ineffective and worsen gastrointestinal conditions.

- Hypomagnesemia: Patiromer binds magnesium in the colon and can lead to hypomagnesemia. Patient's serum magnesium levels should be monitored and magnesium supplementation should be considered in patients who develop low serum magnesium levels while on patiromer.

Adverse Reactions: The most common adverse reactions (≥2%) experienced during clinical trials with patiromer include the following:

- Constipation
- Hypomagnesemia
- Diarrhea
- Nausea
- Abdominal Discomfort
- Flatulence

Use in Special Populations:

- Pregnancy: Patiromer is not absorbed systemically following oral administration. Maternal use is not expected to result in fetal risk.
- Lactation: Patiromer is not absorbed systemically following oral administration. Breastfeeding is not expected to result in risk to the infant.
- Pediatric Use: The safety and effectiveness of patiromer have not been established in pediatric patients.
- Geriatric Use: Of the 666 patients treated with patiromer in clinical studies, 59.8% were 65 years of age and over, and 19.8% were 75 years of age and over. No overall differences in effectiveness between these patients and younger patients were observed. More gastrointestinal adverse reactions were reported in patients 65 years of age and older than younger patients.
- Renal Impairment: Of the 666 patients treated with patiromer in clinical studies, 93% had chronic kidney disease (CKD). Patients with renal impairment do not require special dosing adjustment of patiromer.

Efficacy: The efficacy of patiromer was demonstrated in a two-part, single-blind randomized withdrawal study in hyperkalemic patients with CKD on stable doses of at least one RAAS inhibitor (ACE inhibitor, ARB, or aldosterone antagonist).

- In Part A, 243 patients were treated with patiromer for four weeks. Patiromer effectively decreased serum potassium from baseline. For the secondary endpoint, 76% (95% CI: 70%, 81%) of patients had a serum potassium in the target range of 3.8mEq/L to <5.1mEq/L at Week 4.
- In Part B, 107 patients with a Part A baseline serum potassium of 5.5mEq/L to <6.5mEq/L and whose serum potassium was in the target range at Part A Week 4 and still receiving a RAAS inhibitor medication were randomized to continue patiromer or to receive placebo to evaluate the effect of withdrawing patiromer on serum potassium. Serum potassium rose by 0.72mEq/L (95% CI: 0.46, 0.99) in patients who were switched to placebo versus no change in patients who remained on patiromer.

Cost Comparison:

Medication	Cost Per Unit*	Cost Per Day+	Cost Per Month
Veltassa® (patiromer) packet (all strengths)	$22.17/packet	$22.17	$665.10
sodium polystyrene sulfonate powder	$0.11/gram	$1.65-$6.60	$49.50-$198.00

Costs do not reflect rebated prices or net costs.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Veltassa® (patiromer) cost is based on one packet per day. Sodium polystyrene sulfonate cost is based on the FDA approved oral dose of 15grams one to four times per day.

Recommendations

The College of Pharmacy recommends the prior authorization of Veltassa® (patiromer) with the following criteria:

Veltassa® (Patiromer) Approval Criteria:

1. An FDA approved diagnosis of hyperkalemia; and
2. A trial of a potassium-eliminating diuretic or documentation why a diuretic is not appropriate for the member; and
3. Documentation of a low potassium diet; and
4. A patient-specific, clinically significant reason why member cannot use sodium polystyrene sulfonate powder which is available without a prior authorization; and
5. A quantity limit of 30 packets per month will apply.

Utilization Details of Potassium Binders: Calendar Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SODIUM POLYSTYRENE SULFONATE PRODUCTS						
SOD POLY SUL POW	49	18	$1,806.43	$2.45	$36.87	21.53%
KIONEX SUS 15GM/60	46	33	$2,135.82	$3.98	$46.43	25.45%
SPS SUS 15GM/60	33	24	$1,011.41	$5.32	$30.65	12.05%
SOD POLY SUL SUS 15GM/60	2	2	$75.56	$8.40	$37.78	0.90%
SUBTOTAL	**130**	**77**	**$5,029.22**	**$3.42**	**$38.69**	**59.93%**
PATIROMER PRODUCTS						
VELTASSA POW 16.8GM	4	2	$2,659.52	$22.16	$664.88	31.70%
VELTASSA POW 8.4GM	1	1	$701.84	$23.39	$701.84	8.36%
SUBTOTAL	**5**	**3**	**$3,361.36**	**$22.41**	**$672.27**	**40.06%**
TOTAL	**135**	**74***	**$8,390.58**	**$5.18**	**$62.15**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Potassium binders do not currently require prior authorization.

[1] Bryant, B. Veltassa® (Patiromer) and Management of Hyperkalemia. *Pharmacist's Letter/Prescriber's Letter*. Available online at: http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=&s=PL&pt=6&fpt=31&dd=320213&pb=PL &searchid=57217174. Issued 02/2016. Last accessed 01/2017.
[2] Hester, S. Sodium Polystyrene Sulfonate for Hyperkalemia. *Pharmacist's Letter/Prescriber's Letter*. Available online at: http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=nonmp&s=PL&pt=6&fpt=31&dd=261106&pb=PL&searchid=57217174. Issued 11/2010. Last accessed 01/2017.
[3] Relypsa Newsroom. "FDA Approves Supplemental New Drug Application for Veltassa Removing Boxed Warning Regarding Drug-Drug Interactions." Available online at: http://www.relypsa.com/newsroom/press-releases/112716/. Issued 11/2016. Last accessed 01/2017.
[4] FDA News Release. "FDA approves new drug to treat hyperkalemia." Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468546.htm. Issued 10/2015. Last accessed 01/2017.
[5] AstraZeneca Media. "FDA accepts for review New Drug Application for sodium zirconium cyclosilicate (ZS-9) for the treatment of hyperkalemia." Available online at: https://www.astrazeneca.com/media-centre/press-releases/2016/fda-accepts-for-review-new-drug-application-for-sodium-zirconium-18102016.html. Issued 10/2016. Last accessed 01/2017.
[6] FDA News Release. "FDA approves new drug to treat hyperkalemia." Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468546.htm. Issued 10/2015. Last accessed 01/2017.
[7] FDA Safety. "Kayexalate (sodium polystyrene sulfonate): Drug Safety Communication- FDA Requires Drug Interaction Studies." Available at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm468720.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery. Issued: 10/2015. Last accessed: 01/2017.
[8] AstraZeneca Media. "AstraZeneca receives Complete Response Letter form US FDA for sodium zirconium cyclosilicate (ZS-9) for oral suspension for treatment of hyperkalemia." Available at: https://www.astrazeneca.com/media-centre/press-releases/2016/astrazeneca-receives-complete-response-letter-from-us-fda-for-sodium-zirconium-cyclosilicate-zs-9-for-oral-suspension-for-treatment-of-hyperkalaemia-27052016.html. Issued: 05/2016. Last accessed: 01/2017.
[9] Veltassa® Prescribing Information. Relypsa, Inc. Available online at: https://www.veltassa.com/pi.pdf. Last revised 11/2016. Last accessed 01/2017.
[10] Veltassa® New Drug Approval. OptumRx. Available online at: https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Veltassa_2015-1023.pdf. Issued 2015. Last accessed 01/2017.

Appendix M

30-Day Notice to Prior Authorize Kanuma® (Sebelipase Alfa)

Oklahoma Health Care Authority
February 2017

Lysosomal Acid Lipase Deficiency (LAL-D) Background Information[1,2,3,4]

Lysosomal acid lipase deficiency (LAL-D) is a rare autosomal recessive lysosomal storage disease caused by deleterious mutations in the *LIPA* gene. The age at onset and rate of progression vary greatly and this may relate to the nature of the underlying mutations. Infantile-onset LAL-D was historically referred to as Wolman disease and later-onset LAL-D was known as cholesteryl ester storage disease (CESD). Infants with LAL-D typically have the most rapidly progressive disease and develop symptoms in the first weeks of life and rarely survive beyond 6 months of age. Children and adults typically present with some combination of hepatomegaly, elevated transaminases, dyslipidemia, and microvesicular steatosis of the liver on biopsy. In a large proportion of patients, liver damage with progression to fibrosis, cirrhosis, and liver failure occurs. Cardiovascular disease may present as early as childhood and elevated low-density lipoprotein cholesterol (LDL-c) levels and decreased high-density lipoprotein cholesterol (HDL-c) levels are common features. LAL-D is under-recognized in clinical practice as these clinical manifestations are shared with other cardiovascular, hepatic, and metabolic diseases. There is limited published information about the incidence of LAL-D. It is estimated that Wolman disease affects one to two infants per million births, and CESD affects 25 individuals per million births. In December 2015, the U.S. Food and Drug Administration (FDA) approved Kanuma® (sebelipase alfa) for the treatment of patients with a diagnosis of LAL-D. It is currently the only FDA-approved treatment for patients with LAL-D. Prior to the approval of Kanuma®, the management of LAL-D focused on supportive therapies, such as lipid-lowering therapies, to reduce the burden of disease complications. Without treatment, infants with LAL-D can face rapid disease progression that is typically fatal in a matter of months.

Kanuma® (Sebelipase Alfa) Product Summary[5]

Indications: Kanuma® (sebelipase alfa) is a hydrolytic lysosomal cholesteryl ester and triacylglycerol-specific enzyme indicated for the treatment of patients with a diagnosis of lysosomal acid lipase deficiency.

Dosing:

- Kanuma® is available as 20mg/10mL solution in single-use vials.
- The recommended starting dose for patients with rapidly progressive LAL-D presenting within the first six months of life is 1mg/kg as an intravenous (IV) infusion once weekly. The dose may be increased to 3mg/kg once weekly for patients who do not achieve an optimal clinical response.
- For pediatric and adults patients with LAL-D, the recommended dosage is 1mg/kg as an IV infusion once every other week.

- It is recommended to administer the infusion over at least two hours. A prolonged infusion time should be considered for the 3mg/kg dose or if a hypersensitivity reaction occurs. In patients receiving the 1mg/kg dose and who tolerate the infusion, a one-hour infusion can be considered for subsequent infusions.

Mechanism of Action: LAL-D is an autosomal recessive lysosomal storage disorder characterized by a genetic defect resulting in a marked decrease or loss in activity of the LAL enzyme. The primary site of action of the LAL enzyme is the lysosome, where the enzyme normally causes the breakdown of lipid particles including LDL-c. Deficient LAL enzyme activity results in progressive complications due to the lysosomal accumulation of cholesteryl esters and triglycerides in multiple organs, including the liver, spleen, intestine, and the walls of blood vessels. The resulting lipid accumulation in the liver may lead to increased liver fat content and progression of liver disease, including fibrosis and cirrhosis. Lipid accumulation in the intestinal wall leads to malabsorption and growth failure. In parallel, dyslipidemia due to impaired degradation of lysosomal lipids is common with elevated LDL-c and triglycerides and low HDL-c. Sebelipase alfa binds to cell surface receptors via glycans expressed on the protein and is subsequently internalized into lysosomes. Sebelipase alfa catalyzes the lysosomal hydrolysis of cholesteryl esters and triglycerides to free cholesterol, glycerol, and free fatty acids.

Contraindications:

- None.

Warnings and Precautions:

- <u>Hypersensitivity Reactions Including Anaphylaxis:</u> Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with sebelipase alfa. Due to the potential for anaphylaxis, appropriate medical support should be readily available when sebelipase alfa is administered. If anaphylaxis occurs, the infusion should be immediately discontinued and appropriate medical treatment initiated. Patients should be observed closely during and after the infusion. The management of hypersensitivity reactions should be based on the severity of the reaction and may include temporarily interrupting the infusion, lowering the infusion rate, and/or treatment with antihistamines, antipyretics, and/or corticosteroids. The risks and benefits of re-administering sebelipase alfa following a severe allergic reaction should be considered and patients should be monitored, with appropriate resuscitation measures available, if the decision is made to re-administer the product.
- <u>Hypersensitivity to Eggs or Egg Products:</u> Kanuma® is produced in the egg whites of genetically engineered chickens. Patients with a known history of egg allergies were excluded from the clinical trials. The risks and benefits of treatment with Kanuma® in patients with known systemic hypersensitivity reactions to eggs or egg products should be considered.

Adverse Reactions: The most common adverse reactions occurring in ≥30% of patients with rapidly progressive disease presenting within the first six months of life receiving sebelipase alfa are:

- Diarrhea
- Vomiting

- Fever
- Rhinitis
- Anemia
- Cough
- Nasopharyngitis
- Urticaria

The most common adverse reactions in pediatric and adult patients (≥8%) receiving sebelipase alfa are:

- Headache
- Fever
- Oropharyngeal Pain
- Nasopharyngitis
- Asthenia
- Constipation
- Nausea

Use in Special Populations:

- Pregnancy: There are no available data on sebelipase alfa in pregnant women to inform any drug-associated risk. Animal reproductive studies conducted with sebelipase alfa showed no evidence of embryolethality, fetotoxicity, teratogenicity, or abnormal early embryonic development at dosages up to 164 and 526 times the human dosage of 1mg/kg every other week (based on AUC) in rats and rabbits, respectively.
- Lactation: There are no data on the presence of sebelipase alfa in human milk, the effects on the breastfed infant, or the effects on milk production. It is not known whether sebelipase alfa is present in animal milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sebelipase alfa and any potential adverse effects on the breastfed infant from sebelipase alfa or from the underlying maternal condition.
- Pediatric Use: The safety and effectiveness of sebelipase alfa have been established in pediatric patients age 1 month and older. Clinical trials were conducted in 56 pediatric patients (range 1 month to < 18 years of age).
- Geriatric Use: Clinical trials did not include any patients age 65 years and older. It is not known whether they respond differently than younger patients.

Efficacy:

- Patients with Rapidly Progressive LAL Deficiency Presenting within the First 6 Months of Life: A multicenter, open-label, single-arm clinical study of sebelipase alfa was conducted in nine infants with LAL-D who had growth failure or other evidence of rapidly progressive disease prior to 6 months of age. The age range at entry was 1 to 6 months. Patients received sebelipase alfa at a dose of 0.35mg/kg once weekly for the first two weeks and then 1mg/kg once weekly. Due to suboptimal clinical response, doses in all six surviving patients were escalated to 3mg/kg once weekly between 4 and 88 weeks after starting treatment at 1mg/kg. In one patient, the dose was escalated to 5mg/kg once weekly at Week 88 due to decreased growth velocity in a setting of positive neutralizing anti-drug antibodies to sebelipase alfa. The recommended dosage for these patients is 1mg/kg to 3mg/kg once weekly. The efficacy of sebelipase alfa was assessed by comparing the survival of nine sebelipase alfa-treated patients at 12 months of age with an untreated historical cohort of 21 patients with a similar age at disease presentation and clinical characteristics. Of the nine sebelipase alfa-treated patients, six patients survived beyond 12 months of age, compared to zero of 21 patients in the

historical cohort, all of whom died by 8 months of age. The median age of the six surviving sebelipase alfa-treated patients was 18.1 months (range 12 to 42.2 months). Following initiation of treatment with sebelipase alfa 1mg/kg once weekly, weight-for-age z-scores improved in three of the five surviving patients with growth failure, and all six surviving patients demonstrated improvements in weight-for-age z-scores following dose escalation to 3mg/kg once weekly.

- Pediatric and Adult Patients with LAL Deficiency: The safety and efficacy of sebelipase alfa were assessed in 66 pediatric and adult patients with LAL-D in a multicenter, double-blind, placebo-controlled trial. The patients ranged in age from 4 to 58 years of age (71% were less than 18 years old). Patients were randomized to receive sebelipase alfa at a dosage of 1mg/kg (n=36) or placebo (n=30) once every other week for 20 weeks in the double-blind period. At study entry, 62 of the 66 patients had LDL-c of 130mg/dL. The majority of patients (58%) had LDL-c above 190mg/dL at study entry and 24% of patients with LDL-c above 190mg/dL remained on lipid lowering medications. At completion of the 20-week double-blind period, a statistically significant improvement in percent change from baseline in LDL-c was observed in the sebelipase alfa-treated group as compared to the placebo group (mean difference and 95% CI: -22%, [-33%, -15%]; p<0.0001). LDL-c of less than 130mg/dL was achieved in 13 of 32 (41%; 95% CI: [24%, 58%]) sebelipase alfa-treated patients and in only 2 of 30 (7%; 95% CI: [0%, 16%]) placebo-treated patients with baseline LDL-c of 130mg/dL or greater. A statistically significant improvement in percent change from baseline at 20 weeks was also observed in the sebelipase alfa-treated group compared to the placebo group for other parameters related to LAL-D, including decreases in non-HDL-c (mean difference and 95% CI: -21%, [-30%, -15%]; p<0.0001) and triglycerides (mean difference and 95% CI: -14%, [-28%, -1%]; p=0.0375), and increases in HDL-c (mean difference and 95% CI: 20%, [12%, 26%]; p<0.0001). The effect of sebelipase alfa on cardiovascular morbidity and mortality has not been established. Patients treated with sebelipase alfa had larger reductions from baseline in ALT values and liver fat content (measured by MRI), compared to placebo. The significance of these findings as they relate to liver disease progression in LAL-D has not been established.

Cost: The wholesale acquisition cost (WAC) of Kanuma® is $10,000 per 20mg/10mL vial. The average cost of treatment will vary depending on patient specific circumstances.

Recommendations

The College of Pharmacy recommends the prior authorization of Kanuma® (sebelipase alfa) with the following criteria:

Kanuma® (Sebelipase Alfa) Approval Criteria:

1. An FDA approved diagnosis of Lysosomal Acid Lipase (LAL) deficiency; and
2. Kanuma® (sebelipase alfa) must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and

3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

---

[1] Reiner Z, Guardamagna O, Nair D, et al. Lysosomal acid lipase deficiency—An under recognized cause of dyslipidaemia and liver dysfunction. *Atherosclerosis*. 2014 Jul:235(1):21-30. Doi: 10.10106/j.athersclerosis.2014.04.003.
[2] Hoffman EP, Barr ML, Giovanni MA, Murray MF. Lysosomal acid lipase deficiency. *GeneReviews®*. Available online at: http://www.ncbi.nlm.nih.gov/books/NBK305870/?report=printable. Last revised 09/01/2016. Last accessed 01/17/2017.
[3] LAL-D: A Life-Threatening Genetic Disease with Ongoing, Progressive, Multiorgan Damage Leading To Premature Death. Alexion Pharmaceuticals, Inc. Available online at: http://www.laldsource.com/. Last accessed 01/23/2017.
[4] FDA Approves First Drug to Treat a Rare Enzyme Disorder in Pediatric and Adult Patients. FDA News Release. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476013.htm. Issued 12/08/2015. Last accessed 01/17/2017.
[5] Kanuma® Prescribing Information. Alexion Pharmaceuticals, Inc. Available online at: http://www.kanuma.com/docs/full-prescribing-information.pdf. Last revised 12/2015. Last accessed 11/30/2016.

Appendix N

Fiscal Year 2016 Annual Review of Solaraze® (Diclofenac Sodium 3% Gel) and 30-Day Notice to Prior Authorize Picato® (Ingenol Mebutate 0.015% and 0.05% Gel)

Oklahoma Health Care Authority
February 2017

Current Prior Authorization Criteria

Solaraze® (Diclofenac 3% Gel) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK); and
2. Patient-specific information must be documented on the prior authorization form, including all of the following:
    a. Number of AK lesions being treated; and
    b. Sizes of each lesion being treated; and
    c. Anticipated duration of treatment; and
3. Approval quantity and length will be based on patient-specific information provided, in accordance with Solaraze® prescribing information and FDA approved dosing regimen.

Utilization of Solaraze® (Diclofenac 3% Gel): Fiscal Year 2016

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	15	15	$14,329.60	$955.31	$21.91	1,500	654
2016	2	4	$2,869.71	$717.43	$47.83	400	60
% Change	**-86.70%**	**-73.30%**	**-80.00%**	**-24.90%**	**118.30%**	**-73.30%**	**-90.80%**
Change	**-13**	**-11**	**-$11,459.89**	**-$237.88**	**$25.92**	**-1,100**	**-594**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

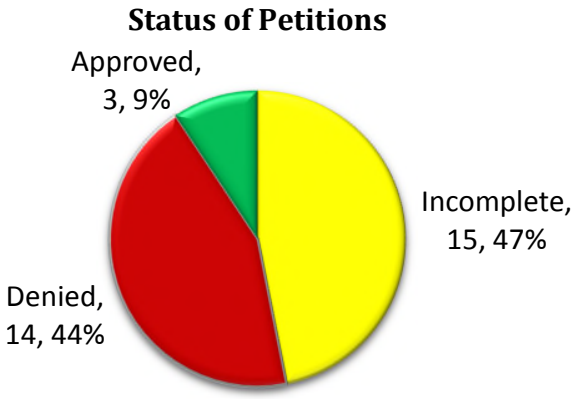
- Picato® (ingenol mebutate gel) was approved by the U.S. Food and Drug Administration (FDA) in 2012 and had no utilization in fiscal year 2016.

Demographics of Members Utilizing Solaraze® (Diclofenac 3% Gel)

- Due to the small number of members utilizing Solaraze® (diclofenac 3% gel) during fiscal year 2016, detailed demographic information could not be provided.

Prior Authorization of Solaraze® (Diclofenac 3% Gel)

There were 32 prior authorization requests submitted for Solaraze® (diclofenac 3% gel) during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates[1]

Anticipated Patent Expirations:

- Picato® (ingenol mebutate 0.015% and 0.05% gel): July 2027

Picato® (Ingenol Mebutate Gel) Product Summary[2]

Indications: Picato® (ingenol mebutate gel) is indicated for the topical treatment of actinic keratosis (AK).

Dosing:

- Picato® gel is available in two dosage strengths: 0.015% and 0.05%.
- Picato® gel is supplied in unit dose laminate tubes and the tubes should be discarded after single use.
- The recommended dosing for the treatment of AK on the face or scalp is to apply the 0.015% gel to the affected area once daily for three consecutive days.
- The recommended dosing for the treatment of AK on the trunk or extremities is to apply the 0.05% gel to the affected area once daily for two consecutive days.
- Ingenol mebutate gel may be applied to the affected area, up to one contiguous skin area approximately 25cm^2 (e.g., 5cm x 5cm) using one unit dose tube.
- The medication is for topical use only and is not for oral, ophthalmic, or intravaginal use.

Mechanism of Action: The mechanism of action by which ingenol mebutate induces cell death in treating AK lesions is unknown.

Contraindications:

- Known hypersensitivity to ingenol mebutate or any component of the formulation.

Warning and Precautions:

- Ophthalmic Adverse Reactions: Treatment should be avoided in the periocular area. Eye disorders, including severe pain, chemical conjunctivitis, corneal burn, eyelid edema, eyelid ptosis, or periorbital edema can occur after exposure. Patients should be instructed to wash hands well after applying ingenol mebutate gel to avoid transfer of the drug into the eyes and to the periocular area during and after application. If

accidental exposure occurs, the area should be flushed with water and the patient should seek medical care as soon as possible.

- Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis and allergic contact dermatitis, have been reported post-marketing. If anaphylactic or other clinically significant hypersensitivity reactions occur, ingenol mebutate gel should be immediately discontinued and appropriate medical therapy instituted.
- Local Skin Reactions: Severe skin reactions in the treated area, including erythema, crusting, swelling, vesiculation/pustulation, and erosion/ulceration, can occur after topical application of ingenol mebutate gel. Administration of ingenol mebutate gel is not recommended until the skin is healed from any previous drug or surgical treatment.

Adverse Reactions: The most common adverse reactions (≥2%) reported in patients treated with ingenol mebutate gel during clinical trials include the following:

- Local Skin Reactions
- Application Site Pain
- Application Site Pruritus
- Application Site Irritation
- Application Site Infection
- Periorbital Edema
- Nasopharyngitis
- Headache

Use in Special Populations:

- Pregnancy: Ingenol mebutate gel is pregnancy category C. There are no adequate and well-controlled studies in pregnant women. Ingenol mebutate gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Pediatric Use: AK is not a condition generally seen within the pediatric population. The safety and effectiveness of ingenol mebutate gel for AK in patients less than 18 years of age have not been established.
- Geriatric Use: Of the 1,165 subjects treated with ingenol mebutate gel in the clinical trials, 56% were 65 years of age and older and 21% were 75 years of age and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

Efficacy:

- Actinic Keratosis of the Face and Scalp: In two double-blind, vehicle-controlled, clinical trials, 547 adult subjects with AK on the face or scalp were randomized to treatment with either ingenol mebutate 0.015% gel or vehicle gel for three consecutive days, followed by an eight week follow-up period. The studies enrolled subjects with four to eight clinically typical, visible, discrete AK lesions within a 25cm^2 contiguous treatment area. Hypertrophic and hyperkeratotic lesions were excluded from treatment. On each scheduled dosing day, the study gel was applied to the entire treatment area. A total of 536 subjects completed these studies. Study subjects ranged from 34 to 89 years of age and 94% had Fitzpatrick skin type I, II, or III. Approximately 85% of subjects were male, and all ingenol mebutate gel-treated subjects were Caucasian. Efficacy was assessed at day 57. Complete clearance rate was defined as the proportion of subjects with no (zero) clinically visible AK lesions in the treatment area. Partial clearance rate was defined as the proportion of subjects with 75% or greater reduction in the number of AK lesions at baseline in the selected treatment area. In Study 1, 37% of patients treated

with ingenol mebutate gel 0.015% achieved a complete clearance compared to 2% for vehicle; 60% achieved a partial clearance compared to 7% for vehicle. In Study 2, 47% achieved a complete clearance versus 5% for vehicle and 68% achieved a partial clearance versus 8% for vehicle. Patients who achieved complete clearance at day 57 in Study 1 and Study 2 entered a 12-month follow-up period. Based on 108 ingenol mebutate gel-treated patients who achieved complete clearance in Study 1 and Study 2, the recurrence rate at twelve months was 54% where recurrence was defined as the percentage of subjects with any identified AK lesion in the previously treated area who achieved complete clearance at Day 57.

- Actinic Keratosis of the Trunk and Extremities: In two double-blind, vehicle-controlled clinical trials, 458 adult subjects with AK on the trunk or extremities were randomized to treatment with either ingenol mebutate 0.05% gel or vehicle gel for two consecutive days, followed by an eight week follow-up period. A total of 447 subjects completed these studies. Study subjects ranged from 34 to 89 years of age (mean 66 years) and 94% had Fitzpatrick skin type I, II, or III. All ingenol mebutate gel-treated subjects were Caucasian. In Study 3, 28% of patients treated with ingenol mebutate gel 0.05% achieved a complete clearance compared to 5% for vehicle; 44% achieved a partial clearance compared to 7% for vehicle. In Study 4, 42% achieved a complete clearance versus 5% for vehicle and 55% achieved a partial clearance versus 7% for vehicle. Subjects who achieved complete clearance at Day 57 in Study 4 entered a 12-month follow-up period. Based on 38 ingenol mebutate gel-treated subjects who achieved complete clearance in Study 4, the recurrence rate at twelve months was 50% where recurrence was defined as the percentage of subjects with any identified AK lesion in the previously treated area who achieved complete clearance at Day 57.

Cost Comparison:

Medication	Cost per Tube*	Cost per Treatment+
Picato® (ingenol mebutate 0.015% gel)	**$292.13**	**$876.39**
Picato® (ingenol mebutate 0.05% gel)	**$428.92**	**$857.84**
Diclofenac sodium gel 3%	$490.84	$490.84

Costs do not reflect rebated prices or net costs.
+Cost per treatment will vary based on patient-specific information.
*Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Picato® (ingenol mebutate gel) with the following criteria:

Picato® (Ingenol Mebutate Gel) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK); and
2. Member must be 18 years of age or older; and
3. Patient-specific information must be documented on the prior authorization form, including all of the following:
    a. Number of AK lesions being treated; and
    b. Size of each lesion being treated; and

c. Location of lesions being treated; and

4. Approval quantity and length will be based on patient-specific information provided, in accordance with Picato® prescribing information and FDA approved dosing regimen.

---

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last updated 12/2016. Last accessed 01/17/2017.

[2] Picato® Prescribing Information. LEO Pharma, Inc. Available online at: https://www.picato.com/_pdf/PrescribingInformation.pdf. Last revised 09/2016. Last accessed 01/17/2017.

Appendix O

Fiscal Year 2016 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Onzetra® Xsail® (Sumatriptan Nasal Powder) & Zembrace™ SymTouch™ (Sumatriptan Injection)

Oklahoma Health Care Authority
February 2017

Current Prior Authorization Criteria

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days.
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zecuity® (sumatriptan transdermal patch) will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual ingredients separately or lower-tiered triptan medications.
4. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.
5. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications and dihydroergotamine injection (D.H.E. 45®).

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan (Relpax®)	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)		zolmitriptan nasal spray (Zomig®)	sumatriptan injection (Imitrex®)
			sumatriptan nasal spray (Imitrex®)
			sumatriptan injection (Sumavel® DosePro®)
			sumatriptan transdermal (Zecuity®)*
			sumatriptan/naproxen (Treximet®)

*Requires a clinically significant reason why member cannot use all other available formulations of sumatriptan.

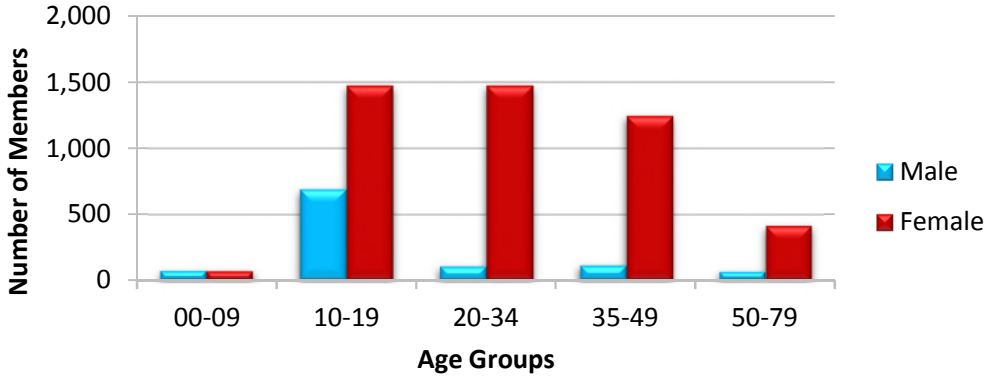
Utilization of Anti-Migraine Medications: Fiscal Year 2016

Comparison of Fiscal Years

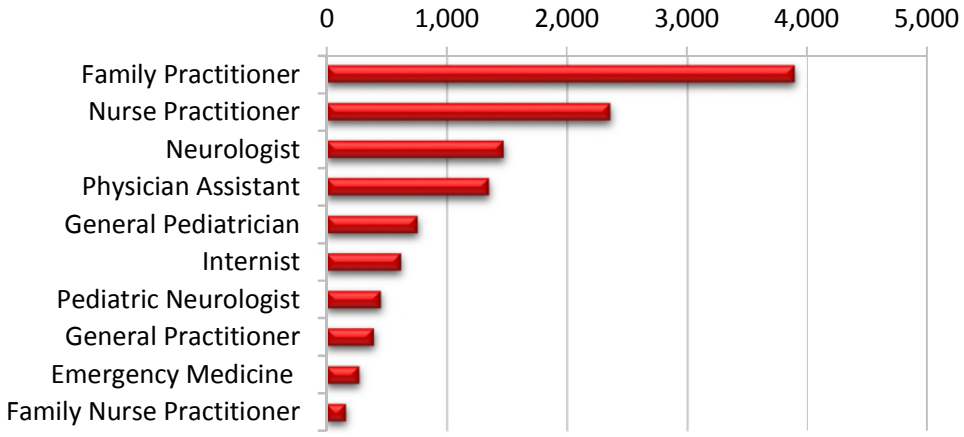
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	5,405	11,592	$317,129.38	$27.36	$1.65	120,039	192,723
2016	5,722	12,293	$429,381.14	$34.93	$2.07	129,916	206,974
% Change	**5.90%**	**6.00%**	**35.40%**	**27.70%**	**25.50%**	**8.20%**	**7.40%**
Change	**317**	**701**	**$112,251.76**	**$7.57**	**$0.42**	**9,877**	**14,251**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Anti-Migraine Medications



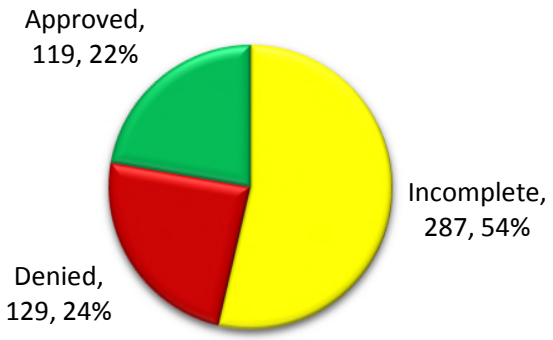
Top Prescriber Specialties of Anti-Migraine Medications by Number of Claims



Prior Authorization of Anti-Migraine Medications

There were 535 prior authorization requests submitted for anti-migraine medications during fiscal year 2016. 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



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20]

Anticipated Patent Expiration(s):

- Relpax® (eletriptan tablets): August 2017
- Zomig® (zolmitriptan nasal spray): May 2021
- Treximet® (sumatriptan/naproxen tablets): April 2026
- Sumavel® DosePro® 6mg/0.5ml (sumatriptan needle-free injection): November 2026
- Zecuity® (sumatriptan transdermal patch): November 2030

Guideline Update(s):

- **June 2016:** Management of Adults with Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies was published in *Headache: The Journal of Head and Face Pain*. Due to acute migraines

causing 1.2 million visits to U.S. emergency departments (ED) annually and lack of consistency in treatment, the American Headache Society (AHS) convened an expert panel to review the evidence and determine which medications should be considered first-line treatment for acute migraine in adults in the ED and to determine if parenteral corticosteroids prevent recurrence of migraine in adults discharged from an ED. The range of medications used in the ED includes migraine-specific drugs, anti-dopaminergics, opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, and antihistamines. Good evidence-based data for effectiveness is lacking in several of these options. The wide range of treatments is thought to be due to physician comfort and familiarity with specific medications, concern about short-term side effects, beliefs about efficacy, and response to patient request. A total of 68 studies involving 28 different medications were included in the review. The quality of each was rated according to the American Academy of Neurology's risk of bias tool: class 1 for low risk; class 2 for higher risk; and class 3 for highest risk. Based on numerous class 1 studies supporting efficacy, AHS recommends the following: metoclopramide, prochlorperazine, and sumatriptan as first-line treatment options for acute migraine in the ED, as well as dexamethasone to prevent recurrence.

News:

- **July 2015:** Teva Pharmaceutical Industries Ltd. received approval from the U.S. Food and Drug Administration (FDA) for its abbreviated new drug application (ANDA) for almotriptan malate 6.25mg and 12.5mg tablets. The ANDA contained a Paragraph IV certification. Paragraph IV certifications allow drug manufacturers to launch generic versions of brand-name medications before their patents expire. Almotriptan is generic for Axert®, which is indicated for the treatment of acute migraine headaches in adults and adolescents 12 to 17 years of age who have migraines lasting four hours or more.
- **May 2016:** Mylan® received final approval from the FDA for its ANDA for frovatriptan succinate 2.5mg tablets. Frovatriptan is the generic version of Frova®, which is indicated for the treatment of acute migraine headaches in adults.
- **June 2016:** The results of a small, retrospective chart review were published in *The Neurohospitalist* journal. Between 2008 and 2015, thirty-four patients received 10mg to 40mg of ziprasidone for the treatment of migraine. Among patients who received ziprasidone, headache severity decreased 5.68 ± 3.0 points on a 10-point scale, from admission to discharge. Ziprasidone was the last abortive medication added prior to discharge in 65% of cases. The 30-day readmission rate for migraine headache in patients who received ziprasidone was 12%. Ziprasidone was well tolerated, with side effects limited to a mild dystonic reaction (n = 1), rhinorrhea (n = 1), and a prolonged QTc of 495 milliseconds (n = 1). The author discusses several limitations of this study including its retrospective nature, the lack of a control group, and lack of a systematic collection of adverse events. However, the findings suggest that ziprasidone may be an effective abortive medication for migraines and warrants further studies comparing ziprasidone to the standard of care.
- **June 2016:** Upsher-Smith Laboratories, Inc. announced that the FDA has granted tentative approval for its supplemental new drug application (sNDA) for Qudexy® XR

(topiramate extended-release) capsules for use as prophylaxis of migraine headache in adults. There are currently no extended-release topiramate formulations approved for migraine prophylaxis in the U.S. Qudexy® XR has been available in the U.S. since June 2014, and is indicated for initial monotherapy in patients 2 years of age and older with partial-onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 2 years of age or older with partial-onset or primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome.

- **June 2016:** Teva Pharmaceuticals issued a letter informing health care providers of the voluntary suspension of the sale, marketing, and distribution of Zecuity® (sumatriptan iontophoretic transdermal system). Teva received post-marketing reports of application site reactions described as burns and scars in patients treated with Zecuity®. Descriptions of these reactions included severe redness, cracked skin, blistering or welts, and burns or scars where the patch was worn. Patients described severe pain, itching, or burning. Although many cases resolved within hours to weeks, there are reports of cases with unresolved skin reactions, typically skin discoloration, after several months. Teva reported working in full cooperation with the FDA to better understand these adverse events. Prescribers were advised to stop prescribing Zecuity®, instruct patients to discontinue use, and evaluate patients and application site reactions as needed.
- **August 2016:** The FDA granted tentative approval to Supernus Pharmaceuticals' sNDA for Trokendi XR® (topiramate extended-release) to expand the label to include prophylaxis of migraine headache in adults. The sNDA is tentative because while the FDA has determined that the drug meets all the required quality, safety, and efficacy standards for approval, it is subject to pediatric exclusivity, which expires March 28, 2017. Final approval may not be made effective until this exclusivity period has expired. Trokendi XR® is indicated for initial monotherapy in patients 6 years of age and older with partial-onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients 6 years of age and older with partial onset, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome.
- **October 2016:** A business decision was made by Endo Pharmaceuticals, Inc. to discontinue Sumavel® DosePro® 4mg/0.5mL. According to the FDA website, this decision is not related to quality, safety or efficacy concerns. The alternate strength of this product, Sumavel® DosePro® 6mg/0.5mL, is still available.

Pipeline:

- **ALD403:** At the American Headache Society 58th Annual Scientific Meeting in June 2016, Alder Biopharmaceuticals released the results of their Phase 2b clinical trial investigating the efficacy of a new drug, ALD403. This medication is a monoclonal antibody targeted to calcitonin gene-related peptide (CGRP) for migraine prevention. In the Phase 2b clinical trial, 33% and 31% of chronic migraine patients dosed intravenously with single 300mg and 100mg doses, respectively, of ALD403 experienced a 75% decrease in their migraines from an average of 16 or more migraine days per month. These results met the primary efficacy end-point for the first 12-week period. After 24 weeks, these numbers stayed fairly consistent, at 29% and 31%, respectively. The study was part of

Alder's PROMISE 1 (Prevention of Migraine via Intravenous ALD403 Safety and Efficacy 1) initiative, and results will be reported again at the 48-week mark, which will conclude the study. The results from all three checkpoints will inform and guide researchers as the PROMISE 2 initiative is started.

- **Erenumab:** In November 2016, Amgen announced positive results for erenumab from a global Phase 3, randomized, double-blind, placebo-controlled STudy to evaluate the efficacy and safety of erenumab in migRaIne preVEntion (STRIVE). The data showed the STRIVE study met the primary endpoint at 24 weeks. That is, demonstrating statistically significant reductions from baseline in monthly migraine days in patients with episodic migraine treated with a once-monthly subcutaneous injection of either 70mg or 140mg erenumab compared with placebo. The safety profile of erenumab was comparable to placebo. Erenumab is a monoclonal antibody specifically designed for the prevention of migraine. It targets and blocks the CGRP receptor thought to be involved in migraines.
- **Galcanezumab:** Eli Lilly's monoclonal antibody, galcanezumab, which binds and inhibits CGRP is currently in Phase 3 trials. In June 2015, Eli Lilly announced that it met the primary endpoint in a Phase 2b study in episodic migraine. Galcanezumab demonstrated a statistically significant reduction in migraine headache days and a safety and tolerability profile confirming the previous results. In addition to the migraine program, Lilly has initiated two Phase 3 trials with galcanezumab in patients suffering from cluster headache.
- **Lasmiditan:** CoLucid Pharmaceuticals, Inc. announced in September 2016, that its Phase 3 pivotal study evaluating lasmiditan, the SAMURAI study, achieved both the primary and key secondary efficacy endpoints with statistical significance ($p < 0.001$). The primary endpoint was the efficacy of lasmiditan (100mg and 200mg) in comparison to placebo based on freedom from migraine headache pain two hours after dosing. The key secondary endpoint was the efficacy of lasmiditan based on freedom from the most bothersome associated symptom (MBS) of migraine (nausea, phonophobia, or photophobia) two hours after dosing. Lasmiditan is the first in a new class of migraine therapies called "ditans." These are agents designed specifically to act through non-vasoconstrictive mechanisms to serve the needs of different subgroups of patients, including those who have cardiovascular risk factors or stable cardiovascular disease, and those who are dissatisfied with their current therapies. Lasmiditan selectively targets 5-HT1F receptors expressed in the trigeminal pathway without vasoconstriction for the acute treatment of migraine in adults, with or without aura.
- **Semprana™ (dihydroergotamine):** Allergan received a complete response letter (CRL) from the FDA in June 2014 for the new drug application for Semprana™. The two specific items listed in the CRL are related to specifications around content uniformity on the improved canister filling process and on standards for device actuation. There were no issues related to the clinical safety and efficacy of the product and Allergan received draft labeling from the FDA for the product. Allergan plans to meet with the FDA and work to fully address these issues to the satisfaction of the FDA. Semprana™ is expected to launch in the U.S. in 2017. Semprana™ is an orally inhaled dihydroergotamine product indicated for the acute treatment of migraine in adults.

- **TEV-48125:** The results of Teva Pharmaceuticals Phase 2b study of TEV-48125 were published in the July 2016 issue of the journal *Neurology*. Participants were dosed with monthly injections of either 900mg, a 675mg loading dose followed by 225mg, or placebo. TEV-48125 demonstrated a significant improvement within one week of therapy initiation in patients with chronic migraine (CM). The primary endpoint for the study was the mean change from baseline in the number of headache hours of any severity during the 28-day post-treatment period ending with month three. For headache hours, the 675/225mg dose separated from placebo on day seven and the 900mg dose separated from placebo after three days of therapy. For both the 675/225mg and 900mg doses, the improvement was sustained through the second and third weeks of therapy and throughout the study. TEV-48125 is a fully humanized monoclonal antibody that potently and selectively binds to CGRP, and is indicated for preventive treatment of CM and high-frequency episodic migraine.
- **TI-001:** Trigemina Inc. is currently in Phase 2 clinical trials for TI-001, an intranasally administered formulation of oxytocin. TI-001 passes through the nasal mucosa to the trigeminal nerve where its uptake can provide both an analgesic effect and reduce the frequency of migraines. The Phase 2 clinical study is evaluating efficacy, tolerability, and safety in patients with chronic and high frequency episodic migraine. If approved by the FDA, TI-001 could be the first non-invasive treatment approved for both chronic and high frequency episodic migraine. In open label data from its current trial, TI-001 has provided significantly superior relief to patients compared to any approved therapy with a high level of safety. Headache day reductions seen so far outpace that of other therapies studied, and the frequency of secondary symptoms and the use of rescue medications for acute pain are also both significantly reduced.
- **Ubrogepant:** At the American Headache Society 58th Annual Scientific Meeting in June 2016, Allergan's oral CGRP receptor blocker Phase 2b study results were presented. Patients were randomly assigned to treat a single migraine attack with ubrogepant (1, 10, 25, 50, or 100mg) or placebo. The co-primary endpoints were pain freedom and headache response (reduction in headache severity from severe or moderate to mild or none) at two hours. The study uncovered a positive response trend across ubrogepant doses, as measured by the proportion of participants who achieved two-hour pain freedom ($P<0.001$ for trend test). The 100mg dose was significantly superior to placebo for two-hour pain freedom (25.8% vs 8.9%), but not for the two-hour headache response endpoint. Ubrogepant appears to be free of known cardiovascular liability. This may allow it to become an acute migraine treatment option for patients with cardiovascular disease.

Onzetra® Xsail® (Sumatriptan Nasal Powder) Product Summary

FDA Approved: January 2016

Indications: Onzetra® Xsail® is a serotonin 5-HT1B/1D receptor agonist indicated for the acute treatment of migraine with or without aura in adults.

Dosing:

- The recommended dose is 22mg of sumatriptan nasal powder (two 11mg nosepieces), administered using the Xsail® breath-powered delivery device.
- It is supplied as a disposable nosepiece containing a capsule and a reusable breath-powered delivery device body. Each capsule contains 11mg sumatriptan base (equivalent to 15.4mg of sumatriptan succinate nasal powder) in a clear, hypromellose capsule.
- Onzetra® Xsail® is available in kits containing 8 doses (16 nosepieces).
- A disposable nosepiece containing 11mg of sumatriptan powder is placed on the delivery device, the piercing button is used to pierce the inner capsule, and the nosepiece is inserted into the nostril while the mouthpiece is inserted between the lips. The patient blows forcefully through the mouthpiece to deliver the sumatriptan powder to the nasal cavity. This is repeated in the other nostril for the second 11mg dose (22mg total dose).
- If the migraine has not resolved in two hours, or returns after a transient improvement, a second dose of 22mg may be administered at least two hours after the first dose.
- The maximum recommended dose is two doses (44mg/4 nosepieces) in 24 hours or one dose of Onzetra® Xsail® and one dose of another sumatriptan product, separated by at least two hours.
- The safety of treating an average of more than four headaches in a 30 day period has not been established.

Zembrace™ SymTouch™ (Sumatriptan Injection) Product Summary

FDA Approved: January 2016

Indications: Zembrace™ SymTouch™ is a serotonin (5-HT1B/1D) receptor agonist indicated for acute treatment of migraine with or without aura in adults.

Dosing:

- The recommended dose is 3mg of sumatriptan injected subcutaneously.
- One 3mg injection may be given up to four times a day with each injection at least one hour apart.
- The maximum cumulative dose that may be given in 24 hours is 12mg.
- Zembrace™ SymTouch™ is available as a prefilled, ready-to-use, single dose, disposable auto-injector containing 3mg sumatriptan. The attached needle penetrates approximately ¼ inch (6mm) for subcutaneous use.
- It is available in cartons containing four auto-injectors.

Cost Comparison

Medication	Cost per unit	Cost per Month*
Zembrace™ SymTouch™ (sumatriptan injection)	**$599.00/box**	**$2,396.00**
Onzetra® Xsail® (sumatriptan nasal powder)	**$500.64/box**	**$500.64**
Imitrex® (sumatriptan nasal spray)	$286.26/box	$572.52
Imitrex® (sumatriptan injection)	$47.70/vial	$381.60
Imitrex® (sumatriptan tablets)	$0.75/tablet	$13.50

Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per month based on current quantity limits for 30 day supply for triptan products, as the safety and efficacy of treating more than four headaches per month has not been established.

Recommendations

The College of Pharmacy recommends the placement of Onzetra® Xsail® and Zembrace™ SymTouch™ into the Special PA Tier of the Anti-Migraine Medications Product Based Prior Authorization (PBPA) category with the following criteria, shown in red:

Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days.
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower-tiered triptan medications.
2. Use of Zecuity®, Onzetra® Xsail®, and Zembrace™ SymTouch™ will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower-tiered triptan medications.
3. Use of Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual ingredients separately or lower-tiered triptan medications.
4. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications.

5. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications and dihydroergotamine injection (D.H.E. 45®).

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
eletriptan (Relpax®)	naratriptan (Amerge®)	almotriptan (Axert®)	dihydroergotamine injection (D.H.E. 45®)
rizatriptan (Maxalt®, Maxalt MLT®)	zolmitriptan (Zomig®, Zomig-ZMT®)	frovatriptan (Frova®)	dihydroergotamine nasal spray (Migranal®)
sumatriptan (Imitrex®)		zolmitriptan nasal spray (Zomig®)	sumatriptan injection (Imitrex®)
			sumatriptan injection (Sumavel® DosePro®)
			sumatriptan injection (Zembrace™ SymTouch™)*
			sumatriptan nasal powder (Onzetra® Xsail®)*
			sumatriptan nasal spray (Imitrex®)
			sumatriptan transdermal (Zecuity®)*
			sumatriptan/naproxen (Treximet®)

*Requires a clinically significant reason why member cannot use all other available formulations of sumatriptan.

Utilization Details of Anti-Migraine Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
SUMATRIPTAN TAB 100MG	3,672	1,584	$45,101.91	$0.83	$12.28	10.50%
SUMATRIPTAN TAB 50MG	3,552	1,967	$42,999.01	$0.77	$12.11	10.01%
SUMATRIPTAN TAB 25MG	2,382	1,340	$32,519.81	$0.92	$13.65	7.57%
RIZATRIPTAN TAB 10MG	912	454	$15,868.54	$0.75	$17.40	3.70%
RIZATRIPTAN TAB 10MG ODT	706	359	$14,579.97	$0.89	$20.65	3.40%
RIZATRIPTAN TAB 5MG ODT	335	190	$7,001.16	$0.91	$20.90	1.63%
RIZATRIPTAN TAB 5MG	300	184	$5,711.61	$0.77	$19.04	1.33%
MAXALT-MLT TAB 10MG	4	3	$53.40	$0.51	$13.35	0.02%
MAXALT-MLT TAB 5MG	1	1	$15.12	$0.50	$15.12	0.01%
TIER-1 SUBTOTAL	**11,864**	**6,082**	**$163,850.53**	**$0.83**	**$13.81**	**38.17%**
TIER-2 PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
NARATRIPTAN TAB 2.5MG	91	28	$4,035.49	$2.77	$44.35	0.94%
ZOLMITRIPTAN TAB 5MG	45	15	$2,522.89	$1.93	$56.06	0.59%
ZOLMITRIPTAN TAB 5MG	17	5	$990.29	$1.94	$58.25	0.23%
NARATRIPTAN TAB 1MG	14	7	$782.22	$3.08	$55.87	0.18%
ZOLMITRIPTAN TAB 2.5MG	13	6	$685.63	$1.76	$52.74	0.16%
TIER-2 SUBTOTAL	**180**	**61**	**$9,016.52**	**$2.30**	**$50.09**	**2.10%**
TIER-3 PRODUCTS						
RELPAX TAB 40MG	29	7	$10,653.22	$30.52	$367.35	2.48%
ZOMIG NASAL SPR 5MG	17	8	$5,677.01	$11.13	$333.94	1.32%
FROVA TAB 2.5MG	10	2	$4,966.24	$48.69	$496.62	1.16%
RELPAX TAB 20MG	8	2	$4,117.05	$25.41	$514.63	0.96%
ALMOTRIPTAN TAB 12.5MG	3	1	$563.85	$51.26	$187.95	0.13%
ZOMIG SPR 2.5MG	3	2	$1,088.87	$12.10	$362.96	0.25%
AXERT TAB 6.25MG	2	1	$1,040.67	$20.01	$520.34	0.24%
TIER-3 SUBTOTAL	**72**	**23**	**$28,106.91**	**$22.03**	**$390.37**	**6.54%**
SPECIAL PA PRODUCTS						
SUMATRIPTAN INJ 6MG/0.5	43	7	$23,685.50	$29.57	$550.83	5.52%
MIGRANAL SPR 4MG/ML	34	17	$114,825.86	$180.26	$3,377.23	26.74%
SUMATRIPTAN SPR 20MG/ACT	28	10	$8,490.41	$12.13	$303.23	1.98%
DIHYDROERGOT SPR 4MG/ML	19	12	$58,322.60	$129.03	$3,069.61	13.58%
TREXIMET TAB 85-500MG	11	2	$7,692.28	$23.31	$699.30	1.79%
SUMATRIPTAN INJ 6MG/0.5	10	1	$3,823.74	$12.75	$382.37	0.89%
SUMATRIPTAN SPR 5MG/ACT	9	2	$2,409.54	$16.06	$267.73	0.56%
SUMATRIPTAN INJ 6MG/0.5	9	3	$1,261.05	$6.71	$140.12	0.29%
DIHYDROERGOT INJ 1MG/ML	6	2	$3,349.71	$49.26	$558.29	0.78%
SUMATRIPTAN INJ 4MG/0.5	6	1	$3,299.31	$22.00	$549.89	0.77%
SUMAVEL DOSE INJ 6MG/0.5	1	1	$953.66	$31.79	$953.66	0.22%
SUMATRIPTAN INJ 6MG/0.5	1	1	$293.52	$9.78	$293.52	0.07%
SPECIAL PA SUBTOTAL	**177**	**59**	**$228,407.18**	**$59.54**	**$1,290.44**	**53.19%**
TOTAL	**12,293**	**5,722***	**$429,381.14**	**$2.07**	**$34.93**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Relpax® (eletriptan) moved to Tier-1 on 01/01/2017, during fiscal year 2017. It is shown in Tier-3 of the utilization details to reflect its status and usage for fiscal year 2016.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 11/2016. Last accessed 12/29/2016.

[2] Orr SL, Friedman BW, Christie S, et al. Management of Adults with Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies. *Headache: The Journal of Head and Face Pain* 2016; 56(6): 911-940.
[3] Rodriguez, T. New Guidelines for Migraine Treatment in the Emergency Department. *Neurology Advisor*. Available online at: http://www.neurologyadvisor.com/migraine-and-headache/new-guidelines-for-migraine-treatment-in-the-emergency-department/article/504319/. Issued 06/20/2016. Last accessed 01/10/2017.
[4] Teva Pharmaceutical Industries, Ltd. Teva First to Receive Approval and Launch Generic Axert® Tablets in the United States. Available online at: http://www.tevapharm.com/news/teva_first_to_receive_approval_and_launch_generic_axert_tablets_in_the_united_states_07_15.aspx. Issued 07/08/2015. Last accessed 01/10/2017.
[5] Mylan®. Mylan Launches Generic Frova® Tablets. Available online at: http://newsroom.mylan.com/2016-05-12-Mylan-Launches-Generic-Frova-Tablets. Issued 05/12/2016. Last accessed 01/10/2017.
[6] Landsness EC, Leo HW, Bucelli RC. Ziprasidone as a Potential Abortive Therapy for Status Migrainosus. *The Neurohospitalist* 2016; 6(4): 151-156.
[7] Upsher-Smith Laboratories, Inc. Upsher-Smith Granted Tentative FDA Approval For Qudexy® XR (topiramate) Extended-Release Capsules for Prophylaxis of Migraine Headache in Adults. Available online at: http://www.prnewswire.com/news-releases/upsher-smith-granted-tentative-fda-approval-for-qudexy-xr-topiramate-extended-release-capsules-for-prophylaxis-of-migraine-headache-in-adults-300282668.html. Issued 06/09/2016. Last accessed 12/2016.
[8] Teva Pharmaceuticals. Urgent – Zecuity® (Sumatriptan Iontophoretic Transdermal System) Suspension Of Marketing. Available online at: https://www.zecuity.com/hcp/ZecuityDHCPLetter-MarketSuspensionJune102016.pdf. Issued 06/10/2016. Last accessed 12/2016.
[9] Anderson, P. 'Tentative' FDA Nod to Trokendi XR® for Migraine Prevention. *Medscape*. Available online at: http://www.medscape.com/viewarticle/867721. Issued 08/22/2016. Last accessed 12/2016.
[10] U.S. Food and Drug Administration (FDA): Current and Resolved Drug Shortages and Discontinuations Reported to FDA. Sumatriptan (Sumavel DosePro) Injection. Available online at: https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Sumatriptan+(Sumavel+DosePro)+Injection&st=d&tab=tabs-2. Issued 10/17/2016. Last accessed 01/10/2017.
[11] Alder Biopharmaceuticals. Pipeline: ALD403. Available online at: http://www.alderbio.com/therapeutics/pipeline/. Last accessed 12/2016.
[12] Migraine News: New Migraine Drug ALD403 Continues to Show Promise. Available online at: https://migraine.com/news/new-drug-continues-to-show-promise/. Issued 07/27/2016. Last accessed 12/2016.
[13] Amgen® News Releases: Amgen® Announces Erenumab Significantly Reduces Monthly Migraine Days In Patients With Episodic Migraine In Second Phase 3 Study. Available online at: https://www.amgen.com/media/news-releases/2016/11/amgen-announces-erenumab-significantly-reduces-monthly-migraine-days-in-patients-with-episodic-migraine-in-second-phase-3-study/. Issued 11/16/2016. Last accessed 01/03/2017.
[14] Eli Lilly and Company Press Release: Lilly's Investigational Medicine For Prevention Of Migraine Met Primary Endpoint In A Phase 2b Study. Available online at: http://lilly.mediaroom.com/index.php?s=9042&item=137444. Issued 06/17/2015. Last accessed 12/2016.
[15] CoLucid Pharmaceuticals, Inc. CoLucid Pharmaceuticals Announces Achievement of Both Primary and Key Secondary Endpoints in the SAMURAI Phase 3 Pivotal Trial of Lasmiditan in Migraine. Available online at: http://www.colucid.com/colucid-pharmaceuticals-announces-achievement-primary-key-secondary-endpoints-samurai-phase-3-pivotal-trial-lasmiditan-migraine/. Issued 09/06/2016. Last accessed 01/03/2017.
[16] The Pharma Letter: U.S. FDA delays Allergan's Semprana decision, approves Ozurdex. Available online at: http://www.thepharmaletter.com/article/us-fda-delays-allergan-s-semprana-decision-approves-ozurdex. Issued 01/07/2014. Last accessed 01/03/2017.
[17] Decision Resources Group: First-in-Class Anti-CGRP Monoclonal Antibodies for Migraine Prevention from Eli Lilly, Teva, Amgen/Novartis, and Alder will Drive Market Growth Through 2025. Available online at: http://www.prnewswire.com/news-releases/first-in-class-anti-cgrp-monoclonal-antibodies-for-migraine-prevention-from-eli-lilly-teva-amgennovartis-and-alder-will-drive-market-growth-through-2025-300333186.html. Issued 09/27/2016. Last accessed 01/10/2017.
[18] Bigal ME, Dodick DW, Krymchantowski AV, et al. TEV-48125 for the Preventive Treatment of Chronic Migraine: Efficacy at Early Time Points. *Neurology* 2016; 87(1): 41-48.
[19] Trigemina, Inc. Product Pipeline: TI-001 for High Frequency Migraine. Available online at: http://trigemina.com/product-pipeline/. Last accessed 01/10/2017.
[20] Anderson P. Drugs Targeting CGRP Show Promise in Migraine. *Medscape*. Available online at: http://www.medscape.com/viewarticle/865233#vp_2. Issued 06/22/2016. Last accessed 01/10/2017.

Appendix P

Fiscal Year 2016 Annual Review of Xuriden™ (Uridine Triacetate)

Oklahoma Health Care Authority
February 2017

Hereditary Orotic Aciduria Overview[1,2,3,4]

Hereditary orotic aciduria (HOA) or Type I hereditary orotic aciduria is a rare autosomal recessive disorder characterized by anemia and developmental delays. The prevalence of this disorder is less than one in one million with approximately twenty known cases worldwide.

HOA is caused by a defect or a deficiency in uridine 5'-monophosphate (UMP) synthase, an enzyme in the pyrimidine pathway. It is coded by a single gene localized to chromosome 3q13. Lack of UMP synthase impacts two enzyme activities, orotic phosphoribosyltransferase and orotidine monophosphate decarboxylase, which reside in a single protein. This results in the body being unable to synthesize the enzyme uridine. This enzyme is necessary for the production of RNA and DNA. The interruption in this pathway leads to excessive production of orotic acid as there is no feedback inhibition from the products normally produced. The overproduction of orotic acid leads to accumulation which is excreted in the urine in large quantities. Additionally, the inability to form nucleic acids leads to decreased erythrocyte formation, which leads to anemia.

The symptoms of HOA include blood abnormalities (megaloblastic anemia), developmental delays (physical and intellectual), urinary tract obstruction due to the formation of orotic acid crystals in the urinary tract, and failure to thrive. Additionally, marked susceptibility to infection is seen in individuals with HOA. There are two known cases in which the patients exhibited orotic aciduria, but did not have megaloblastic anemia. It is thought that these individuals had sufficient UMP synthase to prevent anemia. Additionally there is one reported individual with only orotidylic decarboxylase deficiency with normal expression of phosphoribosyltransferase. This condition is referred to as Type II hereditary orotic aciduria.

Treatment of HOA includes taking supplements of uridine and ingesting high dietary levels of uridine (broccoli, yeast, tomatoes, organ meat). In September 2015, the U.S. Food and Drug Administration (FDA) approved Xuriden™ (uridine triacetate), the first FDA-approved treatment for patients with HOA. Xuriden™ (uridine triacetate) delivers 4- to 6-fold more uridine into the systemic circulation compared to equivalent doses of uridine itself. In clinical trials, patients switched from oral uridine to Xuriden™ (uridine triacetate) had hematological parameters that continued to be stable and growth parameters showed an increase in weight and continued stability in height. Additionally, continued normal levels of urine orotic acid and orotidine were noted.

Current Prior Authorization Criteria

Xuriden™ (Uridine Triacetate) Approval Criteria:

1. An FDA approved diagnosis of Hereditary Orotic Aciduria defined by at least one of the following:

    a. Assay of the orotate phosphoribosyltransferase and orotidylic acid decarboxylase enzymes in the patients erythrocytes showing deficiency in both enzymes or deficiency in orotidylic acid decarboxylase alone; or
    b. Evidence of megaloblastic anemia; or
        i. Shown not to improve with iron supplements
        ii. Normal serum folate and vitamin B12 levels and no evidence of transcobalamine II deficiency
    c. Orotic acid crystals visualized in the urine via microscopy; and
2. Current weight of member must be provided on the prior authorization request; and
    a. Weights should be reassessed every six months to ensure proper dosing and effectiveness; or
    b. Prescriber can indicate urine orotic acid levels are within normal ranges and dosing remains appropriate; and
3. The prescriber must verify that the patient/caregiver is able to properly measure and administer medication; and
4. A quantity limit of four packets per day will apply.

Utilization of Xuriden™ (Uridine Triacetate): Fiscal Year 2016

There was no utilization of Xuriden™ (uridine triacetate) during fiscal year 2016.

Prior Authorization of Xuriden™ (Uridine Triacetate)

There were no prior authorization requests submitted for Xuriden™ (uridine triacetate) during fiscal year 2016.

Market News and Updates[5]

Anticipated Patent Expiration(s):

- Xuriden™ (uridine triacetate): July 2018

Recommendations

The College of Pharmacy does not recommend any changes to the Xuriden™ (uridine triacetate) prior authorization criteria at this time.

---

[1] Xuriden™ Prescribing Information. Wellstat Therapeutics Corporation. Available online at: http://www.xuriden.com/FPI.pdf. Last revised 08/2016. Last accessed 12/2016.
[2] OMIM® Online Mendelian Inheritance in Man®: #258900 Orotic Aciduria. Available online at: http://www.omim.org/entry/258900?search=hereditary%20orotic%20aciduria&highlight=orotic%20aciduria%20hereditary. Last revised 10/17/2016. Last accessed 12/2016.
[3] Biochemistry for Medics©. Available online at: http://www.namrata.co/orotic-aciduria-causes-clinical-manifestations-diagnosis-and-treatment/. Issued 02/19/2013. Last accessed 12/2016.
[4] Orphanet: Hereditary Orotic Aciduria. Available online at: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=30. Last revised 06/2006. Last accessed 12/2016.
[5] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1. Last revised 11/2016. Last accessed 12/2016.

Appendix Q

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

FDA NEWS RELEASE

For Immediate Release: December 14th, 2016
FDA approves Eucrisa for eczema

The U.S. Food and Drug Administration approved Eucrisa (crisaborole) ointment to treat mild to moderate eczema (atopic dermatitis) in patients two years of age and older.
Atopic dermatitis, a chronic inflammatory skin disease, is often referred to as "eczema," which is a general term for the several types of inflammation of the skin. Atopic dermatitis is the most common of the many types of eczema and onset typically begins in childhood and can last through adulthood. The cause of atopic dermatitis is a combination of genetic, immune and environmental factors. In atopic dermatitis, the skin develops red, scaly and crusted bumps, which are extremely itchy. Scratching leads to swelling, cracking, "weeping", and finally, coarsening and thickening of the skin.
Eucrisa, applied topically twice daily, is a phosphodiesterase 4 (PDE-4) inhibitor, although its specific mechanism of action in atopic dermatitis is not known.
The safety and efficacy of Eucrisa were established in two placebo-controlled trials with a total of 1,522 participants ranging in age from two years of age to 79 years of age, with mild to moderate atopic dermatitis. Overall, participants receiving Eucrisa achieved greater response with clear or almost clear skin after 28 days of treatment.
Serious side effects of Eucrisa include hypersensitivity reactions. Eucrisa should not be used in patients who have had a hypersensitivity reaction to Eucrisa's active ingredient, crisaborole. The most common side effect of Eucrisa is application site pain, including burning or stinging.
Eucrisa is manufactured by Palo Alto, California-based Anacor Pharmaceuticals, Inc.

FDA NEWS RELEASE

For Immediate Release: December 23rd, 2016
FDA approves first drug for spinal muscular atrophy

The U.S. Food and Drug Administration approved Spinraza (nusinersen), the first drug approved to treat children and adults with spinal muscular atrophy (SMA), a rare and often fatal genetic disease affecting muscle strength and movement. Spinraza is an injection administered into the fluid surrounding the spinal cord.
SMA is a hereditary disease that causes weakness and muscle wasting because of the loss of lower motor neurons controlling movement. There is wide variability in age of onset, symptoms and rate of progression. Spinraza is approved for use across the range of spinal muscular atrophy patients.
The FDA worked closely with the sponsor during development to help design and implement the analysis upon which this approval was based. The efficacy of Spinraza was demonstrated in a clinical trial in 121 patients with infantile-onset SMA who were diagnosed before 6 months of age and who were less than 7 months old at the time of their first dose. Patients were randomized to receive an injection of Spinraza, into the fluid surrounding the spinal cord, or undergo a mock procedure without drug injection (a skin prick). Twice the number of patients received Spinraza compared to those who underwent the mock procedure. The trial assessed the percentage of patients with improvement in motor milestones, such as head control, sitting, ability to kick in supine position, rolling, crawling, standing and walking.
The FDA asked the sponsor to conduct an interim analysis as a way to evaluate the study results as early as possible; 82 of 121 patients were eligible for this analysis. Forty percent of patients treated with Spinraza achieved improvement in motor milestones as defined in the study, whereas none of the control patients did. Additional open-label uncontrolled clinical studies were conducted in symptomatic patients who ranged in age from 30 days to 15 years at the time of the first dose, and in presymptomatic patients who ranged in age from 8 days to 42 days at the time of first dose. These studies lacked control groups and therefore were more difficult to interpret than the controlled study, but the findings appeared generally supportive of the clinical efficacy demonstrated in the controlled clinical trial in infantile-onset patients.

The most common side effects found in participants in the clinical trials on Spinraza were upper respiratory infection, lower respiratory infection and constipation. Warnings and precautions include low blood platelet count and renal toxicity. Toxicity in the nervous system (neurotoxicity) was observed in animal studies.
The FDA granted this application fast track designation and priority review. The drug also received orphan drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.
The sponsor is receiving a rare pediatric disease priority review voucher under a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases. A voucher can be redeemed by a sponsor at a later date to receive priority review of a subsequent marketing application for a different product. This is the eighth rare pediatric disease priority review voucher issued by the FDA since the program began.
Spinraza is marketed by Biogen of Cambridge, Massachusetts and was developed by Ionis Pharmaceuticals of Carlsbad, California.

FDA NEWS RELEASE

For Immediate Release: January 17th, 2017
FDA approves a generic of Xyrem with a REMS Program

The U.S. Food and Drug Administration (FDA) has approved the first generic version of Xyrem (sodium oxybate) Oral Solution, to treat cataplexy and excessive daytime sleepiness in patients with narcolepsy, which is a potentially debilitating disease. Cataplexy is a primary symptom of narcolepsy where patients suddenly lose muscle tone, including voluntary muscle control, while awake. Muscle weakness or paralysis associated with cataplexy may cause a person to collapse. Approximately 70 percent of people with narcolepsy have cataplexy. Sodium oxybate is the only medication approved to treat cataplexy in patients with narcolepsy.
The use of Xyrem has been associated with serious side effects including seizures, trouble breathing, changes in alertness, coma, and death. Additionally, the active ingredient in Xyrem (and in the newly approved generic) is sodium oxybate. Sodium oxybate is the sodium salt of gamma hydroxybutyrate (GHB). GHB has not been approved for any medical use and has the potential for abuse, such as in cases of sexual assault.
Because of the potential risks associated with Xyrem, it is subject to strict safety controls on prescribing and dispensing under a program called a Risk Evaluation and Mitigation Strategy (REMS). FDA's approval of generic sodium oxybate is subject to a REMS with strict safety controls that are comparable to those currently required for Xyrem.
Specifically, under both the Xyrem REMS and the generic sodium oxybate REMS, sodium oxybate can be prescribed only by a certified prescriber, and dispensed only to an enrolled patient by a certified pharmacy. Only a certified pharmacy that ships directly to patients can dispense sodium oxybate. Sodium oxybate will not be available in retail pharmacies.
In approving this generic version of Xyrem, the FDA is maintaining strict safety requirements for sodium oxybate, while providing patients with access to a generic medication option for narcolepsy.

Safety Announcements

Updated FDA review concludes that use of type 2 diabetes medicine pioglitazone may be linked to an increased risk of bladder cancer

[12/12/16] As a result of an updated review, the U.S. Food and Drug Administration (FDA) has concluded that use of the type 2 diabetes medicine pioglitazone (Actos, Actoplus Met, Actoplus Met XR, Duetact, Oseni) may be linked to an increased risk of bladder cancer. The labels of pioglitazone-containing medicines already contain warnings about this risk, and the FDA has now approved label updates to describe the additional studies they reviewed.
They alerted the public about the possible risk of bladder cancer in September 2010 and June 2011 based on interim results from a 10-year epidemiologic study. They changed the labels of pioglitazone-containing medicines in August 2011 to include warnings about this risk, and required the manufacturer to modify and continue the 10-year study.

Pioglitazone is approved to improve blood sugar control, along with diet and exercise, in adults with type 2 diabetes. Pioglitazone works by increasing the body's sensitivity to insulin, a natural hormone that helps control blood sugar levels. Untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease.

Health care professionals should not use pioglitazone in patients with active bladder cancer, and should carefully consider the benefits and risks before using pioglitazone in patients with a history of bladder cancer.

Patients should contact their health care professionals if they experience any of the following signs or symptoms after starting pioglitazone, as these may be due to bladder cancer:

- Blood or a red color in the urine
- New or worsening urge to urinate
- Pain when urinating

The FDA reviewed additional published studies evaluating the risk of bladder cancer in patients treated with pioglitazone. Results varied among the reviewed studies. For instance, the 10-year epidemiologic study did not find an increased risk of bladder cancer with pioglitazone use, whereas another study did. In addition, a randomized controlled trial found an increased risk during the trial period; however the risk did not persist when patients were followed after the trial was completed. Furthermore, findings of these and other reviewed studies conflicted about whether the duration of use and/or total dose over time of pioglitazone influenced the risk of bladder cancer. They also previously communicated in 2010 that bladder tumors were seen with pioglitazone exposure in animal studies. Overall, the data suggest that pioglitazone use may be linked to an increased risk of bladder cancer.

Safety Announcements

FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women

[12/14/16] The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains.

Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

To better inform the public about this potential risk, we are requiring warnings to be added to the labels of general anesthetic and sedation drugs. We will continue to monitor the use of these drugs in children and pregnant women and will update the public if additional information becomes available.

Anesthetic and sedation drugs are necessary for infants, children, and pregnant women who require surgery or other painful and stressful procedures, especially when they face life-threatening conditions requiring surgery that should not be delayed. In addition, untreated pain can be harmful to children and their developing nervous systems.

Health care professionals should balance the benefits of appropriate anesthesia in young children and pregnant women against the potential risks, especially for procedures that may last longer than 3 hours or if multiple procedures are required in children under 3 years. Discuss with parents, caregivers, and pregnant women the benefits, risks, and appropriate timing of surgery or procedures requiring anesthetic and sedation drugs.

Parents and caregivers should discuss with their child's health care professional the potential adverse effects of anesthesia on brain development, as well as the appropriate timing of procedures that can be delayed without jeopardizing their child's health. **Pregnant women** should have similar conversations with their health care professionals. Also talk with them about any questions or concerns.

Published studies in pregnant animals and young animals have shown the use of general anesthetic and sedation drugs for more than 3 hours caused widespread loss of nerve cells in the brain. Studies in young animals suggest these changes result in long-term effects on the animals' behavior or learning. Studies have also been conducted in children, some of which support findings from previous animal studies, particularly after repeated or prolonged exposure to these drugs early in life. All the studies in children had limitations, and it is unclear whether any negative effects seen in children's learning or behavior were due to the drugs or to other factors, such as the underlying medical condition that led to the need for the surgery or procedure.

FDA has been investigating the potential adverse effects of general anesthetic and sedation drugs on children's brain development since the first animal study on this topic was published in 1999. We held advisory committee meetings in 2007, 2011, and 2014. To coordinate and fund research in this area, we also formed a partnership with the International Anesthesia Research Society (IARS) called SmartTots (Strategies for Mitigating Anesthesia-Related neuroToxicity in Tots). More research is still needed to provide additional information about the safe use of these drugs in young children and pregnant women.

Safety Announcements

FDA revises description of mental health side effects of the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) to reflect clinical trial findings

[12-16-2016] Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion)* is lower than previously suspected. The risk of these mental health side effects is still present, especially in those currently being treated for mental illnesses such as depression, anxiety disorders, or schizophrenia, or who have been treated for mental illnesses in the past. However, most people who had these side effects did not have serious consequences such as hospitalization. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines.

As a result of our review of the large clinical trial, we are removing the *Boxed Warning* for serious mental health side effects from the Chantix drug label. The language describing the serious mental health side effects seen in patients quitting smoking will also be removed from the *Boxed Warning* in the Zyban label. We are also updating the existing warning section in both labels that describes the side effects on mood, behavior, or thinking to include the results from the clinical trial. This decision is consistent with the recommendations of external experts at a September 2016 FDA Advisory Committee meeting. The patient Medication Guide that explains the risks associated with the use of the medicines will continue to be provided with every patient prescription; however, the risk evaluation and mitigation strategy (REMS) that formally required the Medication Guide will be removed.

Our review of the clinical trial results also confirmed that Chantix, Zyban, and nicotine replacement patches were all more effective for helping people quit smoking than placebo. These medicines were found to better help people quit smoking regardless of whether or not they had a history of mental illness.

The health benefits of quitting smoking are substantial, including decreasing the chances of developing lung disease, heart disease, and some cancers. There are also benefits that are nearly immediate or occur after a short time as a nonsmoker such as improvements in circulation, breathing, and the senses of taste and smell. Millions of Americans have serious health problems caused by smoking that can be reduced by quitting. Smoking has been found to harm many organs in the body and diminishes a person's overall health. Chantix and Zyban are prescription medicines that are FDA-approved to help adults quit smoking.

Health care professionals should counsel patients about the benefits of stopping smoking and how they can get help to quit, and discuss the benefits and risks of using medicines to help them quit smoking.

Patients should stop taking Chantix or Zyban and call their health care professionals right away if they notice any side effects on mood, behavior, or thinking. Patients should also talk to their health care professionals for help and information about stopping smoking, including about whether stop-smoking medicines may help or if they have any questions or concerns about taking a medicine.

FDA continues to evaluate the safety and effectiveness of drugs after they go on the market. In the case of Chantix and Zyban, we received and assessed case reports of serious changes in mood and behavior in patients taking the medicines, which led us to require that a *Boxed Warning* be added to the labels in 2009. At the time, we required the drug companies to conduct a large clinical trial to evaluate these side effects, and we have now reviewed the findings. Based on these results, we now have a better idea about the frequency and severity of these side effects on mood, behavior, or thinking, and have confirmed that the benefits of taking Chantix or Zyban to help quit smoking outweigh these risks.

Current Drug Shortages Index (as of January 30th, 2017):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Alitretinoin (Panretin) Gel	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Ceftazidime and Avibactam (AVYCAZ) for Injection, 2.5g	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin Lyophilized Powder for Injection	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Estradiol Valerate Injection, USP	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Hydroxyamphetamine Hydrobromide/Tropicamide (Paremyd)	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigotindisulfonate Sodium (Indigo Carmine) Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Nitrous Oxide, Gas	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Scopolamine (Transderm Scop) Transdermal System Patch	***Currently in Shortage***
Sodium Acetate Injection, USP	***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***
Sumatriptan (Imitrex) Nasal Spray	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tigecycline (Tygacil) Injection	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***