Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
February 14, 2018
4:00pm

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 (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – February 14th, 2018

DATE: January 26, 2018

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/Chronic Medication Adherence Program Update – Appendix B

Action Item – Vote to Prior Authorize Zerviate™ (Cetirizine Ophthalmic Solution) – Appendix C

Action Item – Vote to Prior Authorize ArmonAir™ RespiClick® (Fluticasone Propionate), Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol), QVAR® RediHaler™ (Beclomethasone Dipropionate), AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol), and Fasenra™ (Benralizumab) and to Update Nucala® (Mepolizumab) and Xolair® (Omalizumab) Criteria – Appendix D

Action Item – Vote to Prior Authorize Emflaza® (Deflazacort) – Appendix E

Action Item – Vote to Prior Authorize Zilretta™ (Triamcinolone Acetonide Extended-Release Injectable Suspension) – Appendix F

Action Item – Vote to Prior Authorize Varubi® IV (Rolapitant) and Cinvanti™ (Aprepitant) – Appendix G

Action Item – Annual Review of Seizure Medications – Appendix H

Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Tymlos™ (Abaloparatide) – Appendix I

Annual Review of Antiviral Medications and 30-Day Notice to Prior Authorize Prevymis™ (Letermovir Tablets and Injection) – Appendix J

Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rhopressa® (Netarsudil Ophthalmic Solution) and Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution) – Appendix K

Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Xadago® (Safinamide) and Gocovri™ (Amantadine Extended-Release) – Appendix L

30-Day Notice to Prior Authorize Mepsevii™ (Vestronidase Alfa-vjbk) – Appendix M

Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Ergomar® (Ergotamine Sublingual Tablets) – Appendix N

Industry News and Updates – Appendix O

U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates – Appendix P

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – February 14, 2018 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers 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 13, 2017 DUR Minutes – Vote
B. December 13, 2017 DUR Recommendations Memorandum
C. January 10, 2018 DUR Recommendations Memorandum

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

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

A. Medication Coverage Activity for January 2018
B. Pharmacy Help Desk Activity for January 2018
C. Chronic Medication Adherence Program Update

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

5. Action Item – Vote to Prior Authorize Zerviate™ (Cetirizine Ophthalmic Solution) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize ArmonAir™ RespiClick® (Fluticasone Propionate), Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol), QVAR® RediHaler™ (Beclomethasone Dipropionate), AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol), and Fasenra™ (Benralizumab) and to Update Nucala® (Mepolizumab) and Xolair® (Omalizumab) Criteria – See Appendix D

A. Introduction
B. Nucala® (Mepolizumab) for Eosinophilic Granulomatosis with Polyangiitis (EGPA)
C. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Emflaza® (Deflazacort) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Zilretta™ (Triamcinolone Acetonide Extended-Release Injectable Suspension) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Varubi® IV (Rolapitant) and Cinvanti™ (Aprepitant) – See Appendix G

A. Introduction
B. Market News
C. College of Pharmacy Recommendations

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

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

A. Current Prior Authorization Criteria
B. Utilization of Seizure Medications
C. Prior Authorization of Seizure Medications
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Seizure Medications

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

11. Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Tymlos™ (Abaloparatide) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Osteoporosis Medications
C. Prior Authorization of Osteoporosis Medications
D. Market News and Updates
E. Tymlos™ (Abaloparatide) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Osteoporosis Medications

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

12. Annual Review of Antiviral Medications and 30-Day Notice to Prior Authorize Prevymis™ (Letermovir Tablets and Injection) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Antiviral Medications
C. Prior Authorization of Antiviral Medications
D. Market News and Updates
E. Cytomegalovirus Prevention in Hematopoietic Stem Cell Transplant Recipients
F. Prevymis™ (Letermovir) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Antiviral Medications

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

13. Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rhopressa® (Netarsudil Ophthalmic Solution) and Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Glaucoma Medications
C. Prior Authorization of Glaucoma Medications
D. Market News and Updates
E. Rhopressa® (Netarsudil Ophthalmic Solution) Product Summary
F. Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Glaucoma Medications

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

14. Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Xadago® (Safinamide) and Gocovri™ (Amantadine Extended-Release) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of PD Medications
C. Prior Authorization of PD Medications
D. Market News and Updates
E. Xadago® (Safinamide) Product Summary
F. Gocovri™ [Amantadine Extended-Release (ER)] Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of PD Medications

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

15. 30-Day Notice to Prior Authorize Mepsevii™ (Vestronidase Alfa-vjbk) – See Appendix M

A. Introduction
B. Mepsevii™ (Vestronidase Alfa-vjbk) Product Summary
C. College of Pharmacy Recommendations

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

16. Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Ergomar® (Ergotamine Sublingual Tablets) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Anti-Migraine Medications
C. Prior Authorization of Anti-Migraine Medications
D. Market News and Updates
E. Ergomar® (Ergotamine Sublingual Tablets) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Migraine Medications

Non-Presentation; Questions Only:

17. Industry News and Updates – See Appendix O

A. Introduction
B. News and Updates

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

18. U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates – See Appendix P

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

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

A. Multiple Sclerosis Medications
B. Spinraza® (Nusinersen)
C. Luxturna™ (Voretigene Neparvovec-rzyl)
D. Erythropoiesis Stimulating Agents (ESAs)
E. Chronic Lymphocytic Leukemia (CLL) Medications

**Future business subject to change.*

20. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF DECEMBER 13, 2017

BOARD MEMBERS:	PRESENT	ABSENT
Stephen Anderson, Pharm.D.	x	
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	

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	
Stephanie Nichols, Pharm.D., BCGP; 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
Melody Anthony, Deputy State Medicaid Director		x
Marlene Asmussen, R.N.; Population Care Management Director	x	
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Assistant Pharmacy Director	x	
Kelli Brodersen, Marketing Coordinator	x	
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer		x
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Thomas Nunn, D.O.; Medical 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, J.D.; Deputy General Counsel IV	x	
Kerri Wade, Pharmacy Operations Manager	x	

OTHERS PRESENT:		
Patrick Mumme, Alexion	Jeremy Franklin, Alexion	Avatar Jones, Artia Solutions
Michele Puyear, Gilead	Jim Chapman, AbbVie	Candy Vandewater, Sarepta
Frank Alvarado, Actelion	Marc Parker, Sunovion	Mark DeClerk, Lilly
Jim Dunlap, PhRMA	Jason Schwier, Amgen	Nicole Wilkerson, Novartis
Charlie Collins, Sanofi/Genzyme	Travis Tate, Health Choice	Jimmy Davis, Boehringer Ingelheim
Amber Schrantz, Lilly	Eric Gardner, Vertex	

PRESENT FOR PUBLIC COMMENT:	
Jeremy Franklin	Alexion
Michele Puyear	Gilead

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 ITEM NO. 5 SPEAKER: MICHELE PUYEAR

2B: AGENDA ITEM NO. 9 SPEAKER: DR. JEREMY FRANKLIN

ACTION: NONE REQUIRED

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

3A: NOVEMBER 8, 2017 DUR MINUTES – VOTE

3B: NOVEMBER 8, 2017 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran

Correction(s) to November minutes were discussed prior to voting. Correction(s) included the attendance noted of Kelli Brodersen from the last DUR meeting. Dr. Cothran made announcement and the DUR Board voted on the minutes with correction(s).

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR NOVEMBER 2017

4B: PHARMACY HELP DESK ACTIVITY FOR NOVEMBER 2017

4C: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE MAVYRET™ (GLECAPREVIR/ PIBRENTASVIR) AND VOSEVI® (SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR)**

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

Dr. Hardzog-Britt moved to approve; seconded by Dr. Preslar

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE BAXDELA™ (DELAFLOXACIN INJECTION AND TABLETS), OFLOXACIN 300MG TABLETS, MINOLIRA™ (MINOCYCLINE EXTENDED-RELEASE TABLETS), SOLOSEC™ (SECNIDAZOLE ORAL GRANULES), AND VABOMERE™ (MEROPENEM/ VABORBACTAM INJECTION)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nichols
Dr. Harrell moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE DUZALLO® (LESINURAD/ALLOPURINOL)
7A: INTRODUCTION
7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Ms. Varalli-Claypool moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: ANNUAL REVIEW OF PHOSPHATE BINDERS
8A: CURRENT PRIOR AUTHORIZATION CRITERIA
8B: UTILIZATION OF PHOSPHATE BINDERS
8C: PRIOR AUTHORIZATION OF PHOSPHATE BINDERS
8D: MARKET NEWS AND UPDATES
8E: COLLEGE OF PHARMACY RECOMMENDATIONS
8F: UTILIZATION DETAILS OF PHOSPHATE BINDERS
Materials included in agenda packet; presented by Dr. Abbott
Dr. Harrell moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF SOLIRIS® (ECULIZUMAB)
9A: CURRENT PRIOR AUTHORIZATION CRITERIA
9B: UTILIZATION OF SOLIRIS® (ECULIZUMAB)
9C: PRIOR AUTHORIZATION OF SOLIRIS® (ECULIZUMAB)
9D: MARKET NEWS AND UPDATES
9E: SOLIRIS® (ECULIZUMAB) FOR MYASTHENIA GRAVIS (MG) SUMMARY
9F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
Dr. Garton moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF DUCHENNE MUSCULAR DYSTROPHY (DMD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EMFLAZA® (DEFLAZACORT)
10A: CURRENT PRIOR AUTHORIZATION CRITERIA
10B: UTILIZATION OF DMD MEDICATIONS [EXONDYS 51™ (ETEPLIRSEN)]
10C: PRIOR AUTHORIZATION OF DMD MEDICATIONS [EXONDYS 51™ (ETEPLIRSEN)]
10D: MARKET NEWS AND UPDATES
10E: EMFLAZA® (DEFLAZACORT) PRODUCT SUMMARY
10F: GUIDELINE RECOMMENDATIONS
10G: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF MAINTENANCE ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ARMONAIR™ RESPICLICK® (FLUTICASONE PROPIONATE), TRELEGY™ ELLIPTA® (FLUTICASONE FUROATE/UMECLIDINIUM/VILANTEROL), QVAR® REDIHALER™ (BECLOMETHASONE DIPROPIONATE), AIRDUO™ RESPICLICK® (FLUTICASONE PROPIONATE/SALMETEROL), AND FASENRA™ (BENRALIZUMAB)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
11C: PRIOR AUTHORIZATION OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
11D: MARKET NEWS AND UPDATES

11E: ARMONAIR™ RESPICLICK® (FLUTICASONE PROPIONATE INHALATION POWDER) PRODUCT SUMMARY
11F: TRELEGY™ ELLIPTA® (FLUTICASONE FUROATE/UMECLIDINIUM/VILANTEROL INHALATION POWDER) PRODUCT SUMMARY
11G: QVAR® REDIHALER™ (BECLOMETHASONE DIPROPIONATE HFA) PRODUCT SUMMARY
11H: AIRDUO™ RESPICLICK® (FLUTICASONE PROPIONATE/SALMETEROL INHALATION POWDER) PRODUCT SUMMARY
11I: FASENRA™ (BENRALIZUMAB INJECTION) PRODUCT SUMMARY
11J: COLLEGE OF PHARMACY RECOMMENDATIONS
11K: UTILIZATION DETAILS OF MAINTENANCE ASTHMA AND COPD MEDICATIONS
11L: UTILIZATION DETAILS OF ASTHMA MONOCLONAL ANTIBODIES (PHARMACY CLAIMS)
11M: UTILIZATION DETAILS OF ASTHMA MONOCLONAL ANTIBODIES (MEDICAL CLAIMS)
11N: UTILIZATION DETAILS OF INHALED CORTICOSTEROIDS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF ANTI-EMETIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE VARUBI® IV (ROLAPITANT) AND CINVANTI™ (APREPITANT)
12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF ANTI-EMETIC MEDICATIONS
12C: PRIOR AUTHORIZATION OF ANTI-EMETIC MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: COLLEGE OF PHARMACY RECOMMENDATIONS
12F: UTILIZATION DETAILS OF ANTI-EMETIC MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE ZILRETTA™ (TRIAMCINOLONE ACETONIDE EXTENDED-RELEASE INJECTABLE SUSPENSION)
13A: INTRODUCTION
13B: ZILRETTA™ (TRIAMCINOLONE ACETONIDE EXTENDED-RELEASE INJECTABLE SUSPENSION) PRODUCT SUMMARY
13C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Nichols
Dr. Muchmore recommended that methylprednisolone be added as a trial.
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF OPHTHALMIC ALLERGY MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ZERVIATE™ (CETIRIZINE OPHTHALMIC SOLUTION)
14A: CURRENT PRIOR AUTHORIZATION CRITERIA
14B: UTILIZATION OF OPHTHALMIC ALLERGY MEDICATIONS
14C: PRIOR AUTHORIZATION OF OPHTHALMIC ALLERGY MEDICATIONS
14D: MARKET NEWS AND UPDATES
14E: ZERVIATE™ (CETIRIZINE OPHTHALMIC SOLUTION) PRODUCT SUMMARY
14F: COLLEGE OF PHARMACY RECOMMENDATIONS
14G: UTILIZATION DETAILS OF OPHTHALMIC ALLERGY MEDICATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: INDUSTRY NEWS AND UPDATES
15A: INTRODUCTION
15B: NEWS AND UPDATES
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: **NONE REQUIRED**

AGENDA ITEM NO. 17: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

No live meeting scheduled for January. January will be a packet only meeting.

17A: INJECTABLE AND VAGINAL PROGESTERONE PRODUCTS

17B: POTASSIUM BINDING MEDICATIONS

17C: DEFITELIO® (DEFIBROTIDE)

17D: KANUMA® (SEBELIPASE ALFA)

17E: ZINPLAVA™ (BEZLOTOXUMAB)

17F: LUMIZYME® (ALGLUCOSIDASE ALFA)

FUTURE BUSINESS SUBJECT TO CHANGE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: **NONE REQUIRED**

AGENDA ITEM NO. 18: **ADJOURNMENT**

The meeting was adjourned at 5:02 pm.

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

Memorandum

Date: December 14, 2017

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

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

Subject: DUR Board recommendations from meeting of December 13, 2017

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Mavyret™ (Glecaprevir/ Pibrentasvir) and Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. The prior authorization of Mavyret™ (glecaprevir/pibrentasvir) and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) with criteria similar to the other prior authorized hepatitis C medications.
2. Adding the following criteria to all prior authorized hepatitis C medications regarding short life expectancy in accordance with the hepatitis C treatment guidelines: Member must not have a limited life expectancy (less than 12 months) that cannot be remediated by treating hepatitis C virus (HCV), liver transplantation, or another directed therapy.

The following table highlights the preferred regimens for each genotype in treatment-naïve members (listed in alphabetical order). Additional regimens for treatment-experienced

members are covered, just not included in the following table. Additional regimens other than those listed may be considered based on patient-specific clinical situations. Preferred regimens are based on treatment guidelines and supplemental rebate participation and are subject to change if the manufacturer chooses not to participate in supplemental rebates.

Genotype	Patient Factors	Preferred Regimen(s)
Genotype 1		
1	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 8 or 12 weeks Mavyret™ for 8 weeks 1a: Zepatier® for 12 weeks (w/o baseline RAVs) 1a: Zepatier® + RBV for 16 weeks (w/ baseline RAVs) 1b: Zepatier® for 12 weeks
1	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (w/ RBV if decompensated) Harvoni® for 12 weeks (w/ RBV if decompensated) Mavyret™ for 12 weeks 1a: Zepatier® for 12 weeks (w/o baseline RAVs) 1a: Zepatier® + RBV for 16 weeks (w/ baseline RAVs) 1b: Zepatier® for 12 weeks
Genotype 2		
2	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks
2	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (w/ RBV if decompensated) Mavyret™ for 12 weeks
Genotype 3		
3	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks
3	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (w/ RBV if decompensated) Mavyret™ for 12 weeks
Genotype 4		
4	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Harvoni® for 12 weeks Mavyret™ for 8 weeks Technivie™ + RBV for 12 weeks Zepatier® for 12 weeks
4	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (w/ RBV if decompensated) Harvoni® for 12 weeks (w/ RBV if decompensated) Mavyret™ for 12 weeks Technivie™ + RBV for 12 weeks Zepatier® for 12 weeks
Genotype 5 or 6		
5 or 6	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Mavyret™ for 8 weeks Harvoni® for 12 weeks (w/ RBV if decompensated)
5 or 6	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (w/ RBV if decompensated) Mavyret™ for 12 weeks Harvoni® for 12 weeks (w/ RBV if decompensated)

If not specified, regimen applies to all genotypic subtypes.
w/o = without; w/ = with; RBV = ribavirin; RAV= resistance-associated variants
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.

Harvoni® (sofosbuvir/ledipasvir), Zepatier® (elbasvir/grazoprevir), Epclusa® (sofosbuvir/ velpatasvir), Mavyret™ (glecaprevir/pibrentasvir), and Vosevi® (sofosbuvir/velpatasvir/ voxilaprevir) are the preferred direct-acting antivirals (DAAs) for the treatment of chronic hepatitis C virus (HCV) genotype 1. Use of an alternative regimen including Viekira Pak™ (ombitasvir/paritaprevir/ ritonavir/dasabuvir), Viekira XR™ (ombitasvir/paritaprevir/ ritonavir/dasabuvir ER), Sovaldi® (sofosbuvir) alone, Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (daclatasvir) in combination for the treatment of HCV genotype 1 requires patient-specific, clinically significant reasoning why the preferred DAAs are not appropriate for the member. Detailed criteria for medications with no changes to the coverage criteria other than the addition of criteria regarding short life expectancy are not included in the criteria on the following pages. The criteria for each medication may include U.S. Food and Drug Administration (FDA) approved regimens or American Association for the Study of Liver Diseases (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.

Mavyret™ (Glecaprevir/Pibrentasvir) 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. METAVIR fibrosis score or equivalent scoring with an alternative test must be indicated on prior authorization request; and
4. Mavyret™ 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 the 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, viral genotype, and treatment history will apply (new regimens will apply as approved by the FDA):

Genotype	Prior Treatment Experience	No Cirrhosis	Compensated Cirrhosis
1, 2, 3, 4, 5, or 6	Treatment Naïve	8 weeks	12 weeks
1	NS5A w/o NS3/4A PI	16 weeks	16 weeks
1	NS3/4A PI w/o NS5A	12 weeks	12 weeks
1, 2, 4, 5, or 6	PRS	8 weeks	12 weeks
3	PRS	16 weeks	16 weeks

w/o = without; PI = protease inhibitor; PRS = pegylated interferon, ribavirin, and/or sofosbuvir
Examples of NS5A inhibitors include: daclatasvir, elbasvir, ledipasvir, ombitasvir, pibrentasvir, velpatasvir
Examples of NS3/4A PIs include: boceprevir, glecaprevir, grazoprevir, paritaprevir, simeprevir, telaprevir, voxilaprevir

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 the 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 decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
14. Member must not have a limited life expectancy (less than 12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; 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
16. Member must not be taking the following medications: carbamazepine, rifampin, ethinyl estradiol-containing medications, St. John's wort, atazanavir, darunavir, lopinavir, ritonavir, efavirenz, atorvastatin, lovastatin, simvastatin, rosuvastatin doses greater than 10mg per day, cyclosporine doses greater than 100mg per day; 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; and
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Approval of the 8-week carton (in place of the 4-week carton) requires a patient-specific, clinically significant reason why the member requires the 8-week carton in place of the 4-week carton; 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; and
21. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 16 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) 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. METAVIR fibrosis score or equivalent scoring with an alternative test must be indicated on prior authorization request; and

4. Vosevi® 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 the 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 treatment history will apply:
    a. **Adult patients without cirrhosis or with compensated cirrhosis (Child-Pugh A):**
        i. **Genotype 1, 2, 3, 4, 5, or 6 patients who were previously treated with an HCV regimen containing an NS5A inhibitor** (e.g., daclatasvir, elbasvir, ledipasvir, ombitasvir, velpatasvir): Vosevi® for 12 weeks; or
        ii. **Genotype 1a or 3 patients who were previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor:** Vosevi® for 12 weeks; or
    b. New regimens will apply as approved by the FDA; and
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 the 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 decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
14. Member must not have a limited life expectancy (less than 12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; and
15. Member must not have severe renal impairment [estimated Glomerular Filtration Rate (eGFR) <30mL/min/1.73m^2]; and
16. 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
17. Member must not be taking the following medications: H_2-receptor antagonists at doses greater than 40mg famotidine twice daily equivalent, omeprazole doses greater than 20mg daily or other proton pump inhibitors, amiodarone, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, rifampin, rifabutin, rifapentine, atazanavir, lopinavir, tipranavir/ritonavir, efavirenz, St. John's wort, pravastatin doses greater than 40mg daily, rosuvastatin, pitavastatin, cyclosporine, methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine, topotecan; and

18. If member is using antacids they must agree to separate antacid and Vosevi® administration by four hours; and
19. 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
20. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
21. 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; and
22. 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.

Recommendation 3: Vote to Prior Authorize Baxdela™ (Delafloxacin Injection and Tablets), Ofloxacin 300mg Tablets, Minolira™ (Minocycline Extended-Release Tablets), Solosec™ (Secnidazole Oral Granules), and Vabomere™ (Meropenem/Vaborbactam Injection)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Baxdela™ (delafloxacin injection and tablets), Solosec™ (secnidazole oral granules), and Vabomere™ (meropenem/vaborbactam injection) with the following criteria:

Baxdela™ (Delafloxacin Injection and Tablets) Approval Criteria:

1. An FDA approved diagnosis of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, doxycycline, trimethoprim/sulfamethoxazole, or other cost effective therapeutic equivalent alternative(s).
3. Approval quantity will be based on Baxdela™ prescribing information and FDA approved dosing regimen(s).
    a. For Baxdela™ vials, an initial quantity limit of 6 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

Solosec™ (Secnidazole Oral Granules) Approval Criteria:

1. An FDA approved diagnosis of bacterial vaginosis; and
2. A patient-specific, clinically significant reason why the member cannot use metronidazole, tinidazole, or other cost effective therapeutic equivalent alternative(s).
3. A quantity limit of 1 packet per 30 days will apply.

Vabomere™ (Meropenem/Vaborbactam Injection) Approval Criteria:

1. An FDA approved diagnosis of complicated urinary tract infection (cUTI) or pyelonephritis; and
2. A patient-specific, clinically significant reason why the member cannot use piperacillin/tazobactam or other cost effective therapeutic equivalent alternative(s).
3. Approval quantity will be based on Vabomere™ prescribing information and FDA approved dosing regimen(s).

The College of Pharmacy also recommends the following changes to the Various Systemic Antibiotic Medications Prior Authorization category:

1. Add cephalexin 250mg tablets to the Antibiotic Special Formulation category based on net cost. Current special formulation criteria will apply.
2. Add Minolira™ (minocycline hydrochloride ER tablets) to the Antibiotic Special Formulation category. Current special formulation criteria will apply.
3. Add oflaxacin 300mg tablets with criteria similar to ofloxacin 400mg tablets and moxifloxacin prior authorization criteria based on net cost. Current criteria will apply.
4. Add Sivextro® (tedizolid) vial formulation with criteria similar to Sivextro® tablet formulation based on net cost. Current criteria will apply.

The proposed changes can be seen in red in the following criteria:

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.
2. The following oral antibiotics currently require prior authorization and the special formulation approval criteria will apply:
    - Amoxicillin/clavulanate potassium extended-release (ER) tablets (Augmentin XR®)
    - Amoxicillin ER 775mg tablets (Moxatag®)
    - Cephalexin 250mg and 500mg tablets
    - Cephalexin 750mg capsules
    - Ciprofloxacin 100mg tablets
    - Ciprofloxacin 500mg and 1,000mg ER tablets
    - Doxycycline hyclate 75mg capsules (Acticlate®)
    - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
    - Doxycycline monohydrate 75mg and 150mg capsules and tablets
    - Doxycycline monohydrate DR 40mg capsules (Oracea®)
    - Minocycline ER tablets (Minolira™)
    - Minocycline ER tablets (Solodyn®)
    - Minocycline immediate-release (IR) tablets
    - Tetracycline 250mg and 500mg capsules

Ofloxacin 300mg and 400mg Tablets and Moxifloxacin 400mg Tablets Approval Criteria:

1. Approval requires a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, and/or other cost effective therapeutic equivalent medication(s).

Sivextro® (Tedizolid) Tablet and Vial Approval Criteria:

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

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

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

Recommendation 4: Vote to Prior Authorize Duzallo® (Lesinurad/Allopurinol)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Duzallo® (lesinurad/ allopurinol) with criteria similar to Zurampic® (lesinurad):

Duzallo® (Lesinurad/Allopurinol) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved indication for the treatment of symptomatic hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of allopurinol alone; and
3. Failure of allopurinol or febuxostat alone defined by serum urate levels greater than 6.0mg/dL; and
4. Prior to starting treatment with Duzallo®, member must be on at least 300mg of allopurinol daily, unless creatinine clearance (CrCl) is less than 60mL/min then 200mg daily is required. Duzallo® 200mg/200mg will only be approved for members with a CrCl less than 60mL/min; and
5. Prescriber must verify that member has a CrCl greater than 45mL/min prior to initiating treatment. For continued approval, prescriber must verify CrCl is greater than 45mL/min and serum creatinine is not greater than two times baseline when Duzallo® was initiated; and
6. Prescriber must document member has no contraindications for use of Duzallo® including any of the following**:** Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl less than 30mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis.
7. A quantity limit of one tablet daily will apply.

Recommendation 5: Annual Review of Phosphate Binders

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends updating the Auryxia® (ferric citrate) prior authorization criteria based on new FDA approved indications with the following changes noted in red:

Auryxia® (Ferric Citrate) Approval Criteria:

1. An FDA approved diagnosis of hyperphosphatemia in patients with chronic kidney disease (CKD) on dialysis; and
    a. 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; or
2. An FDA approved diagnosis of iron deficiency anemia (IDA) in patients with CKD not on dialysis; and
    a. Documented lab results verifying IDA; and
    b. A documented intolerance or inadequate response to prior treatment with oral iron.
3. A quantity limit of 12 tablets per day will apply based on maximum recommended dose.

Recommendation 6: Annual Review of Soliris® (Eculizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following criteria for Soliris® (eculizumab) for a diagnosis of generalized myasthenia gravis:

Soliris® (Eculizumab) Approval Criteria [Generalized Myasthenia Gravis (gMG) Diagnosis]:

1. An FDA approved diagnosis of gMG; and
2. Positive serologic test for anti-acetylcholine receptor (AchR) antibodies; and
3. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV; and
4. Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score ≥6; and
5. Member must meet one of the following:
    a. Failed treatment over one year or more with two or more immunosuppressive therapies (ISTs) either in combination or as monotherapy; or
    b. Failed at least one IST and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG); and
6. Initial approvals will be for the duration of six months at which time an updated MG-ADL score must be provided. Continued authorization requires improvement in the MG-ADL score from baseline. Subsequent approvals will be for the duration of one year.

Recommendation 7: Annual Review of Duchenne Muscular Dystrophy (DMD) Medications and 30-Day Notice to Prior Authorize Emflaza® (Deflazacort)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications and 30-Day Notice to Prior Authorize ArmonAir™ RespiClick® (Fluticasone Propionate), Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol), QVAR® RediHaler™

(Beclomethasone Dipropionate), AirDuo™ RespiClick® (Fluticasone Propionate/ Salmeterol), and Fasenra™ (Benralizumab)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Anti-Emetic Medications and 30-Day Notice to Prior Authorize Varubi® IV (Rolapitant) and Cinvanti™ (Aprepitant)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Zilretta™ (Triamcinolone Acetonide Extended-Release Injectable Suspension)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Ophthalmic Allergy Medications and 30-Day Notice to Prior Authorize Zerviate™ (Cetirizine Ophthalmic Solution)

NO ACTION REQUIRED.

Recommendation 12: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 13: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: January 11, 2018

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

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

Subject: DUR Board recommendations from meeting packet of January 10, 2018

Recommendation 1: Long-Acting Beta$_2$ Agonist Utilization: Pediatric Members

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Potassium Binders

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Kanuma® (Sebelipase Alfa)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Defitelio® (Defibrotide)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Injectable and Vaginal Progesterone Products

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Zinplava™ (Bezlotoxumab)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Lumizyme® (Alglucosidase Alfa)

NO ACTION REQUIRED.

Recommendation 8: Industry News and Updates

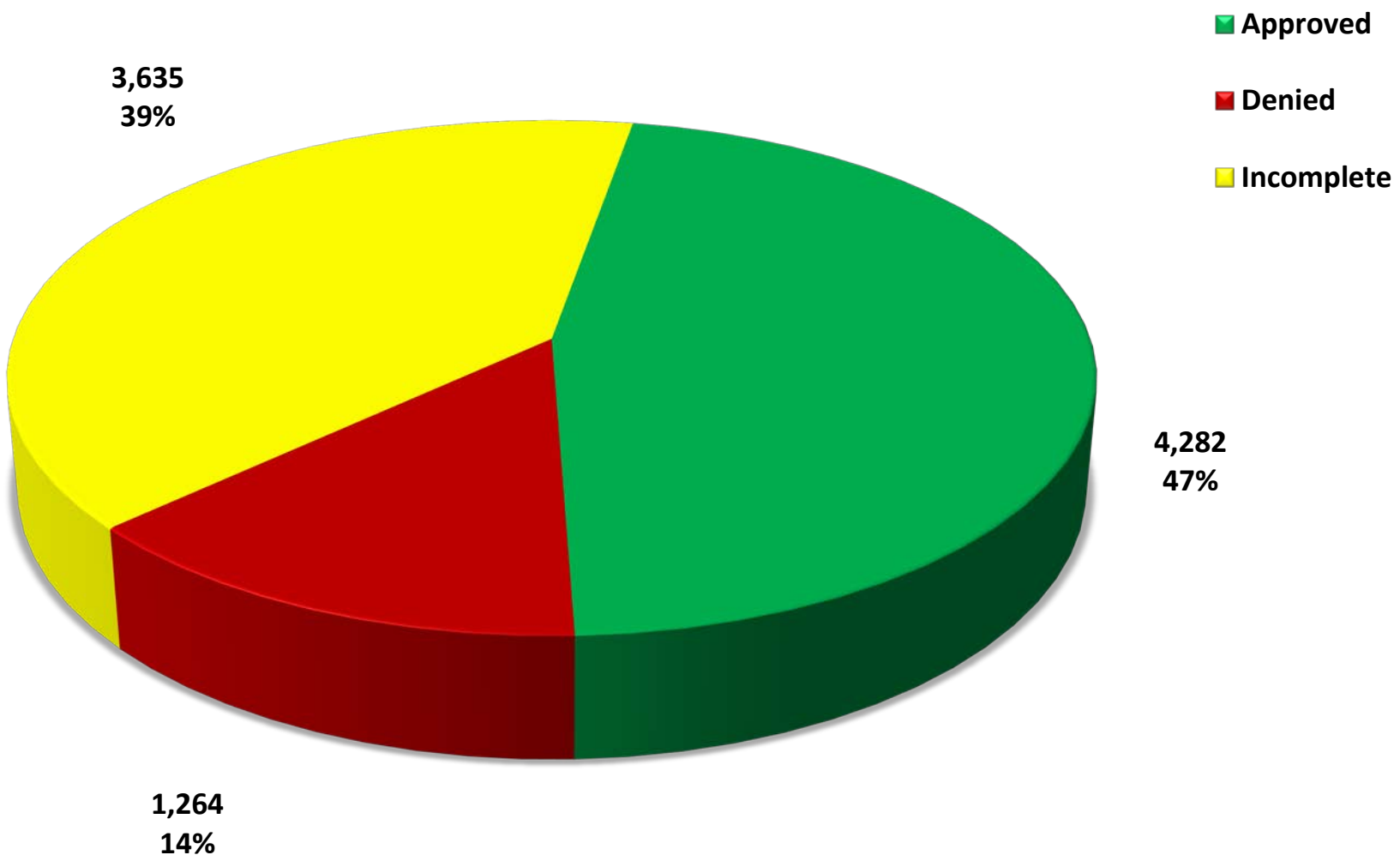
NO ACTION REQUIRED.

Recommendation 9: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

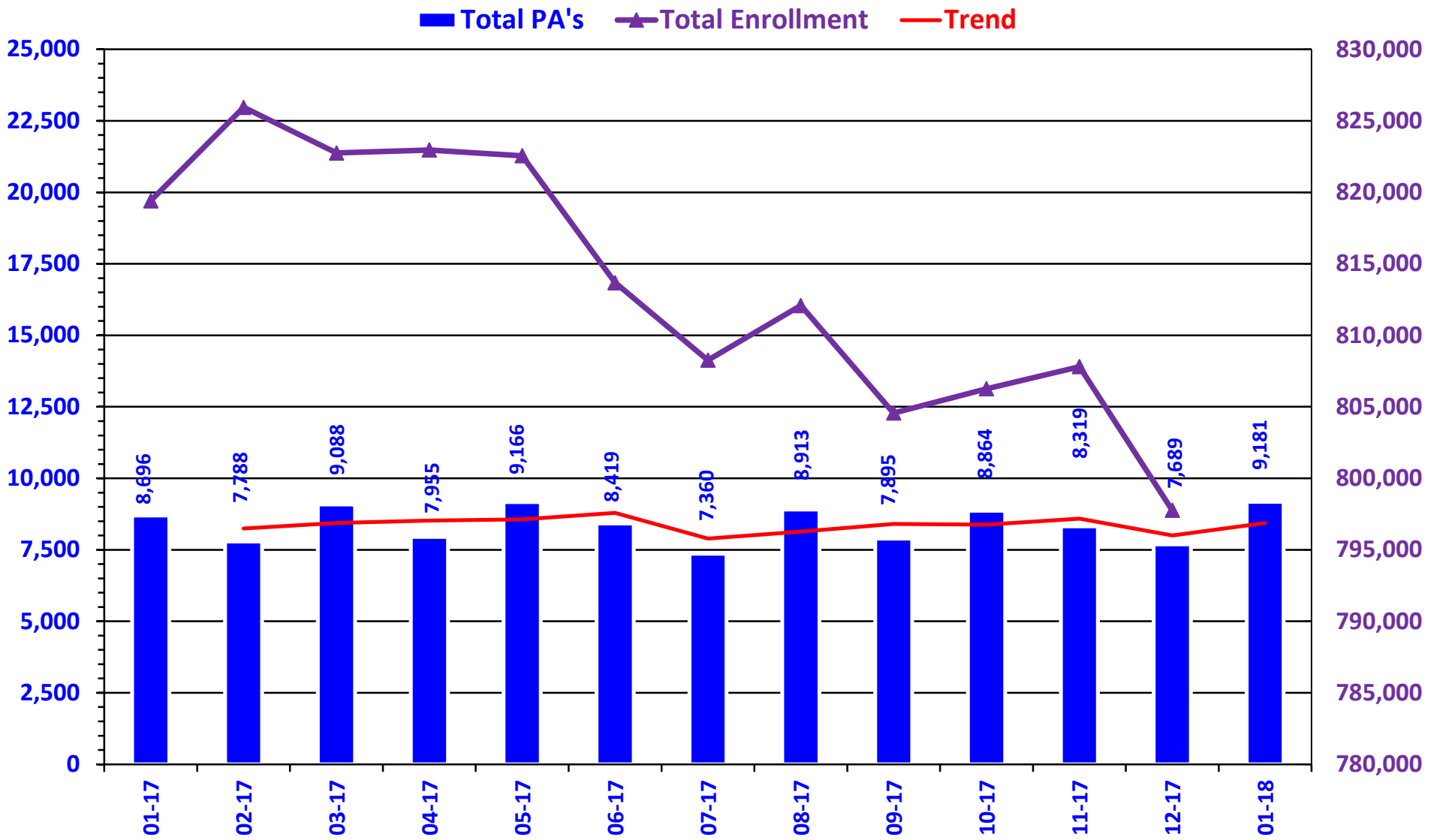
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JANUARY 2018



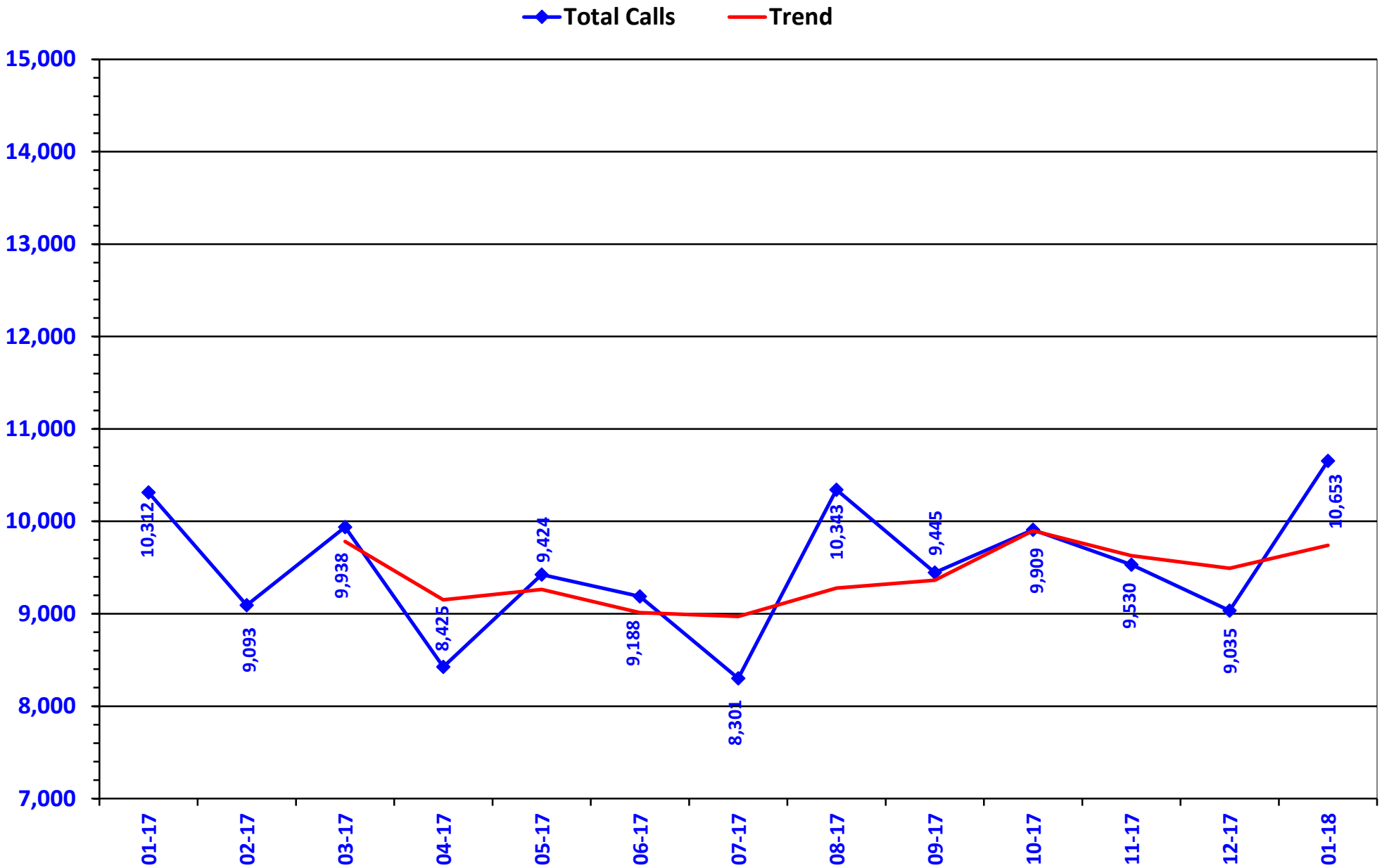
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JANUARY 2017 – JANUARY 2018



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JANUARY 2017 – JANUARY 2018



Prior Authorization Activity

1/1/2018 Through 1/31/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	135	11	24	100	342
Analgesic - NonNarcotic	13	0	4	9	0
Analgesic - Narcotic	486	236	61	189	158
Angiotensin Receptor Antagonist	15	5	4	6	358
Antiasthma	68	19	16	33	269
Antibiotic	34	17	0	17	208
Anticonvulsant	143	70	10	63	309
Antidepressant	172	44	23	105	316
Antidiabetic	186	69	28	89	344
Antihistamine	25	3	11	11	354
Antimigraine	39	6	14	19	124
Antineoplastic	94	73	8	13	170
Antiparasitic	22	1	5	16	15
Antiulcers	117	29	30	58	152
Antiviral	31	9	1	21	7
Anxiolytic	84	47	8	29	278
Atypical Antipsychotics	190	84	17	89	331
Biologics	111	53	16	42	306
Bladder Control	55	14	15	26	338
Blood Thinners	225	146	11	68	334
Botox	30	20	5	5	344
Buprenorphine Medications	425	282	31	112	75
Cardiovascular	87	37	15	35	293
Chronic Obstructive Pulmonary Disease	176	24	35	117	295
Constipation/Diarrhea Medications	109	18	33	58	267
Contraceptive	23	18	1	4	307
Dermatological	362	128	89	145	193
Diabetic Supplies	471	270	20	181	205
Endocrine & Metabolic Drugs	101	66	8	27	139
Erythropoietin Stimulating Agents	24	11	7	6	110
Fibric Acid Derivatives	12	3	2	7	359
Fibromyalgia	504	240	115	149	349
Fish Oils	13	1	5	7	357
Gastrointestinal Agents	87	21	26	40	95
Growth Hormones	86	58	13	15	141
Hepatitis C	220	148	17	55	9
HFA Rescue Inhalers	44	1	10	33	17
Insomnia	29	4	6	19	173
Insulin	89	32	19	38	332
Miscellaneous Antibiotics	21	1	3	17	357
Multiple Sclerosis	55	28	8	19	146
Muscle Relaxant	48	5	18	25	26
Nasal Allergy	44	4	14	26	151
Neurological Agents	129	18	48	63	282
NSAIDs	186	25	55	106	247
Ocular Allergy	21	5	6	10	72
Ophthalmic Anti-infectives	13	0	4	9	0
Osteoporosis	22	9	5	8	336
Other*	316	70	81	165	245
Otic Antibiotic	26	7	1	18	12

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Respiratory Agents	17	13	0	4	218
Statins	23	6	5	12	309
Stimulant	1,086	386	87	613	340
Synagis	103	44	21	38	82
Testosterone	57	10	17	30	334
Topical Antifungal	31	2	5	24	185
Topical Corticosteroids	88	1	29	58	23
Vitamin	56	11	25	20	296
Pharmacotherapy	84	76	0	8	298
Emergency PAs	1	1	0	0	
Total	**7,564**	**3,040**	**1,195**	**3,329**	
Overrides					
Brand	124	101	3	20	81
Compound	10	10	0	0	151
Diabetic Supplies	4	1	1	2	24
Dosage Change	290	268	2	20	11
High Dose	5	3	0	2	32
Ingredient Duplication	12	11	0	1	10
Lost/Broken Rx	106	99	0	7	11
NDC vs Age	317	226	14	77	238
Nursing Home Issue	48	43	0	5	21
Opioid Quantity	21	20	0	1	150
Other*	46	41	1	4	11
Prescriber Temp Unlock	1	1	0	0	358
Quantity vs. Days Supply	595	403	43	149	239
STBS/STBSM	26	18	0	8	92
Stolen	6	2	1	3	10
Temporary Unlock	1	0	1	0	0
Third Brand Request	41	27	4	10	20
Overrides Total	**1,617**	**1,242**	**69**	**306**	
Total Regular PAs + Overrides	**9,181**	**4,282**	**1,264**	**3,635**	

Denial Reasons	
Unable to verify required trials.	2,653
Does not meet established criteria.	1,299
Lack required information to process request.	929
Other PA Activity	
Duplicate Requests	670
Letters	11,070
No Process	6
Changes to existing PAs	678
Helpdesk Initiated Prior Authorizations	655
PAs Missing Information	30

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

Chronic Medication Adherence Program Update

Oklahoma Health Care Authority
February 2018

Prescriber Mailing: Maintenance Diabetes and Cardiovascular Medications

The Chronic Medication Adherence (CMA) educational mailing is processed quarterly and sent to prescribers with members on chronic maintenance medications for diabetes, blood pressure, or cholesterol. The purpose of these mailings is to encourage medication adherence and improve the quality of care for SoonerCare members on these medications.

Previously, prescribers were selected randomly to receive letters if they met the inclusion criteria for the mailing module. In February 2016, the CMA mailing changed to sending the educational letters to the same consistent prescribers. Included prescribers will receive four letters per year that alternate between diabetes and cardiovascular medications, to better inform them of their SoonerCare patients using maintenance medications and to make their patients' adherence more convenient to track over time including any improvements or changes. Inclusion criteria required the prescriber to have two or more SoonerCare patients taking diabetes, blood pressure, and cholesterol medications. A total of 231 prescribers were selected for inclusion in the consistent mailings. The review period for each mailing is one year and patients are assigned to prescribers if they are the last prescriber of record for a maintenance medication on paid pharmacy claims.

Each mailing includes a prescriber summary report with a "star rating" based on their overall percentage of patients considered adherent to chronic maintenance medications. Adherence is estimated by measuring the Proportion of Days Covered (PDC), or percent of days in the past year covered by prescription claims. A patient is considered adherent if their PDC is greater than or equal to 80%. A patient is considered non-adherent if their PDC is less than 80%. A higher percentage (and corresponding star rating) is better and indicates that more of their patients are adherent to their maintenance medications. Each mailing also includes a list of medication adherence patient resources intended to offer prescribers methods to improve their patients' adherence.

Cardiovascular Mailing Summary

- Addresses adherence to maintenance renin angiotensin system (RAS) antagonists [e.g., angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), direct renin inhibitors] and HMG-CoA reductase inhibitors (i.e., statins)

Date Letter Processed	Total Letters Mailed	Total Members Included
February 2015	345	6,672
August 2015	259	4,497
February 2016	231	3,835
August 2016	221	4,588

Date Letter Processed	Total Letters Mailed	Total Members Included
February 2017	207	4,025
August 2017	192	3,334

Adherence is shown in the Provider Summary Report as a percentage for RAS antagonists and as a percentage for statins, with a corresponding star rating for each category. The star ratings for the percentage of patients that are adherent to RAS antagonists or statins are based on the 2017 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. The following key is shown to illustrate the star ratings and adherence percentages for each star rating.

RAS antagonists:

5 Stars: Excellent (≥ 85%)

4 Stars: Above Average (≥ 83% to < 85%)

3 Stars: Average (≥ 80% to < 83%)

2 Stars: Below Average (≥ 77% to < 80%)

1 Star: Poor (≥ 60% to < 77%)

0 Stars: Very Poor (< 60%)

Statins:

5 Stars: Excellent (≥ 84%)

4 Stars: Above Average (≥ 80% to < 84%)

3 Stars: Average (≥ 74% to < 80%)

2 Stars: Below Average (≥ 70% to < 74%)

1 Star: Poor (≥ 60% to < 70%)

0 Stars: Very Poor (< 60%)

Diabetes Mailing Summary

- Addresses adherence to maintenance medications for diabetes excluding insulin and Symlin® (pramlintide)

Date Letter Processed	Total Letters Mailed	Total Members Included
November 2014	457	2,894
May 2015	177	975
November 2015	378	2,288
May 2016	224	2,127
November 2016	212	1,633
May 2017	192	1,484
November 2017	172	1,341

Adherence is shown in the Provider Summary Report as a percentage and corresponding star rating for all diabetes medications (excluding insulin and Symlin®). The star ratings for the percentage of patients that are adherent to diabetes medications are based on the 2017 Medicare Star Ratings. However, a rating of zero stars is exclusive to SoonerCare. The following key is shown to illustrate the star ratings and adherence percentages for each star rating.

Diabetes Medications:

5 Stars: Excellent (≥ 86%)

4 Stars: Above Average (≥ 82% to < 86%)

3 Stars: Average (≥ 78% to < 82%)

2 Stars: Below Average (≥ 74% to < 78%)

1 Star: Poor (≥ 60% to < 74%)

0 Stars: Very Poor (< 60%)

Example Star Rating[1]

Report date: <Report Date>
NPI: <Prescriber NPI>

Provider: <Provider Name>
SoonerCare Provider ID: <Provider ID>

Percentage of patients adherent to RAS antagonists: 66.67%

1 out of 5 stars

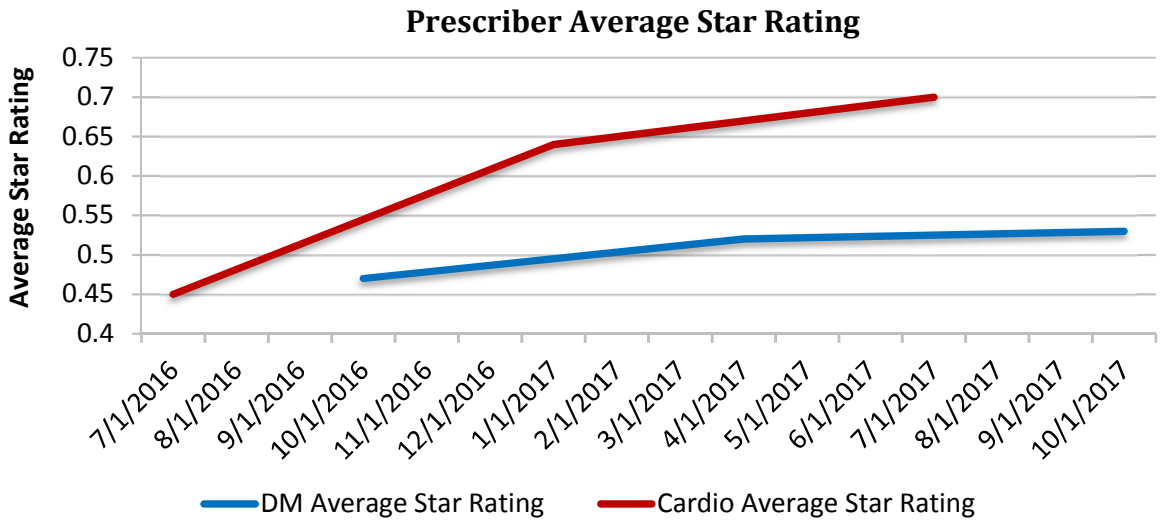
Percentage of patients adherent to statins: 60.00%

1 out of 5 stars

Trends Specific to Prescribers and Members Included in the Mailings

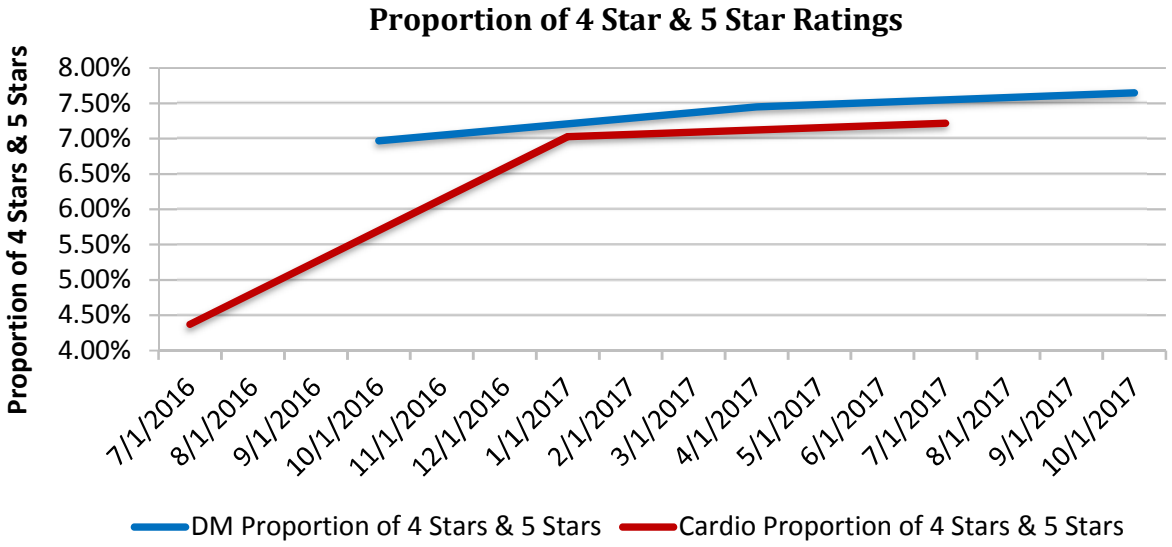
The following line graph shows trends in the average star rating for prescribers included in the mailing since July 2016. This graph is specific to those prescribers included in the mailings and differentiates between diabetes (DM) and cardiovascular (cardio; i.e., statins and RAS antagonists) modules. Please note, the vertical axis starts at a star rating of 0.4 in order to reflect small changes.

Prescribers selected for initial inclusion in the mailing were those prescribers with a 0 star rating and two or more patients in all categories (DM, statins, and RAS antagonists). An increase in the average star rating was seen for both mailing modules with a larger increase in the cardiovascular star ratings. Despite favorable increases in the average star ratings, opportunities for further enhancements continue to exist.



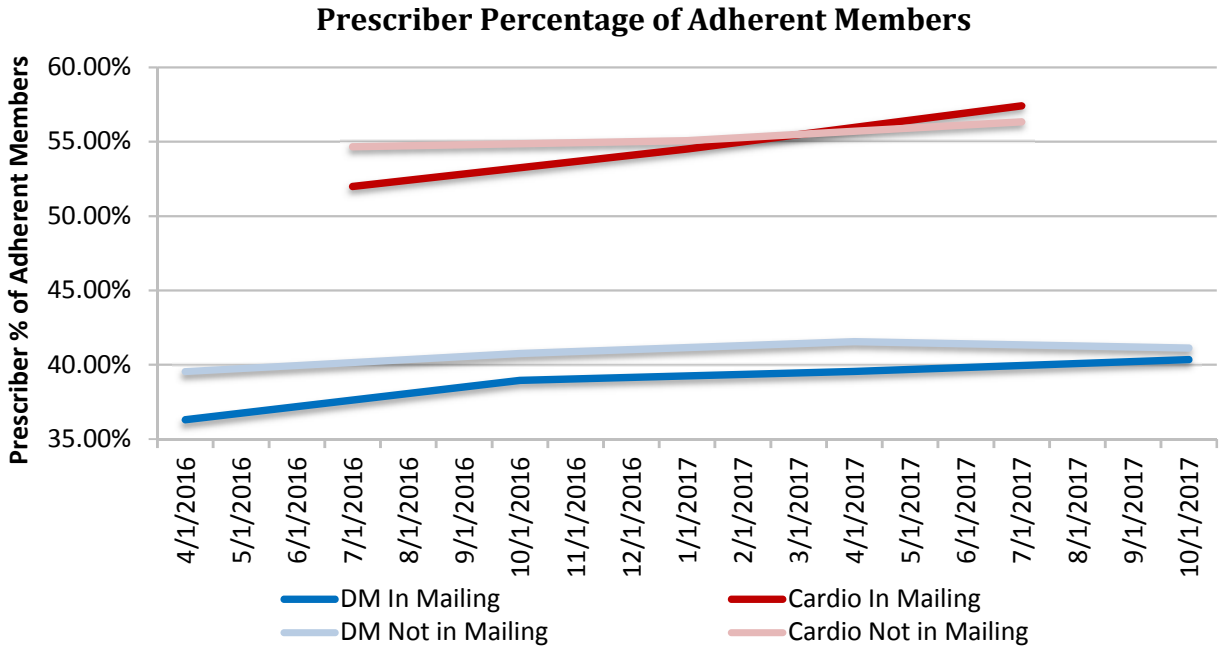
The following line graph shows trends in the proportion of prescribers with 4 star and 5 star ratings included in the mailing since July 2016. This graph is specific to those prescribers included in the mailings and differentiates between diabetes and cardiovascular modules. Please note, the vertical axis starts at a percentage of 4.0% in order to reflect small changes.

An increase in the proportion of 4 star and 5 star ratings was seen for both mailing modules with a larger increase in the cardiovascular module. The proportion of 0 star ratings has consistently declined since July 2016 with a 25% decline seen in the cardiovascular module and an 18% decline seen in the diabetes module. Similar to the average star rating, while favorable increases were seen, opportunities for further enhancements continue to exist.



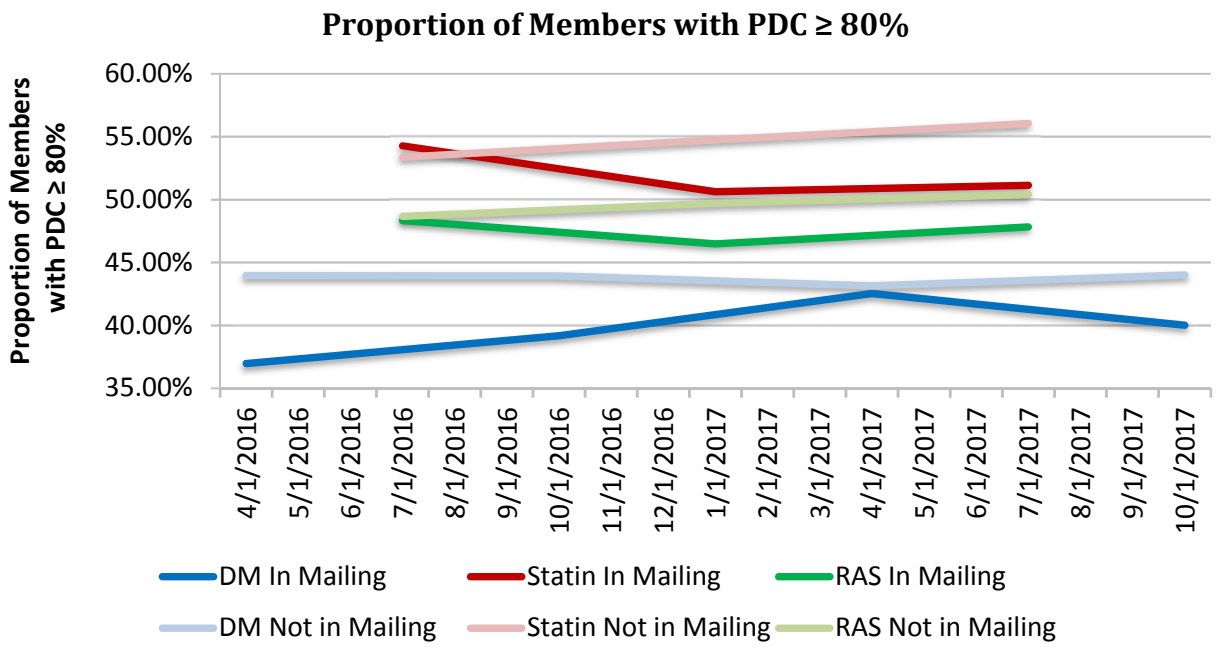
The following line graph shows trends in the average prescriber percentage of adherent members for prescribers included in the mailing compared to those not included in the mailing for both modules since April 2016. Those considered adherent had a PDC of greater than or equal to 80%. Please note, the vertical axis starts at a percentage of 35% in order to reflect small changes.

An increase in the prescriber percentage of adherent members was seen for both modules for those prescribers included in the mailing compared to a relatively linear trend for prescribers not included in the mailing. This indicates prescriber mailings may have a positive impact on the percentage of adherent members for prescribers.



The following line graph shows trends in the proportion of members with a PDC greater than or equal to 80% for those with prescribers included in the mailing compared to those with prescribers not included in the mailing since April 2016. Please note, the vertical axis starts at a percentage of 35% in order to reflect small changes.

Unlike prescribers included in the mailings, members included in the mailings are not consistent and may change over time due to medication discontinuations or changing to a prescriber not included in the mailing. Only 54.9% of members in the October 2017 mailing were in the original diabetes mailing conducted in April 2016. The changes in member inclusion may account for some of the variability seen in member PDC for those with prescribers included in the mailing, particularly the diabetes module. Despite member variability, overall trends show an immediate increase in PDC after a mailing followed by a steady decline. These results indicate including both modules on each mailing might be a more effective intervention to reduce waning effects.



Conclusions

Data specific to prescribers in the mailing shows an overall trend towards higher average star ratings and an increase in the prescriber percentage of adherent members using maintenance diabetes and cardiovascular medications. Trends in prescriber specific measures continue to show improvement and while favorable increases were seen, opportunities for further enhancements continue to exist. Member specific trends were less promising with inconsistency in member PDC for those with prescribers included in the mailing. This is likely a result of variability in the members included in the mailings as they can change prescribers or discontinue medications and no longer be included in the analysis. The College of Pharmacy will continue to monitor member adherence with the goal of achieving a member PDC of 80% or greater and a five star rating of prescriber percentage of adherent members. New interventions will be implemented where appropriate, and results will be reported to the Drug Utilization Review (DUR) Board when available.

[1] Centers for Medicare & Medicaid Services (CMS): Medicare 2017 Part C & D Star Rating Technical Notes. Available online at: https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovgenin/performancedata.html. Last updated 09/26/2016. Last accessed 01/10/2018.

Appendix C

Vote to Prior Authorize Zerviate™ (Cetirizine Ophthalmic Solution)

Oklahoma Health Care Authority
February 2018

Introduction[1,2]

Zerviate™ (cetirizine ophthalmic 0.24% solution) is a histamine-1 (H_1) receptor antagonist indicated for the treatment of ocular itching associated with allergic conjunctivitis. Zerviate™ is supplied as a sterile, aqueous ophthalmic solution containing cetirizine 0.24% (equivalent to cetirizine hydrochloride 0.29%) in a 7.5mL or 10mL multi-dose ophthalmic bottle with a dropper tip. The recommended dose of cetirizine ophthalmic solution is one drop in each affected eye twice daily. Cost and launch information for Zerviate™ are not yet available.

Recommendations

The College of Pharmacy recommends the following:

- The placement of Zerviate™ (cetirizine ophthalmic solution) into Tier-3 of the Ophthalmic Allergy Product Based Prior Authorization category. Current Tier-3 criteria would apply.
- Moving Elestat® (epinastine) from Tier-3 to Tier-2 based on net cost. Current Tier-2 criteria would apply.

Ophthalmic Allergy Medications		
Tier-1	**Tier-2**	**Tier-3**
cromolyn (Crolom®)	azelastine (Optivar®)	alcaftadine (Lastacaft®)
ketotifen (Alaway®, Zaditor® OTC)	**epinastine (Elestat®)**	bepotastine (Bepreve®)
	olopatadine (Patanol®)	**cetirizine (Zerviate™)**
	olopatadine (Pazeo®)	emedastine (Emadine®)
		lodoxamide (Alomide®)
		loteprednol (Alrex®)
		nedocromil (Alocril®)
		olopatadine (Pataday®)

OTC = over-the-counter
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Ophthalmic Allergy Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of one Tier-1 product for a minimum of two weeks in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. A contraindication to all lower tiered medications.

Ophthalmic Allergy Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 product and all available Tier-2 medications for a minimum of two weeks each that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. A contraindication to all lower tiered medications.

[1] Han DH. FDA Approves Zerviate for Allergic Conjunctivitis. *MPR*. Available online at: http://www.empr.com/news/cetirizine-ophthalmic-solution-ocular-itching-zerviate/article/665808/. Issued 06/01/2017. Last accessed 01/18/2018.

[2] Zerviate™ Prescribing Information. Akorn, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208694s000lbl.pdf. Last revised 05/2017. Last accessed 01/18/2018.

Appendix D

Vote to Prior Authorize ArmonAir™ RespiClick® (Fluticasone Propionate), Trelegy™ Ellipta® (Fluticasone Furoate/ Umeclidinium/Vilanterol), QVAR® RediHaler™ (Beclomethasone Dipropionate), AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol), and Fasenra™ (Benralizumab) and to Update Nucala® (Mepolizumab) and Xolair® (Omalizumab) Criteria

Oklahoma Health Care Authority
February 2018

Introduction[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15]

- **ArmonAir™ RespiClick® (fluticasone propionate inhalation powder)** is an inhaled corticosteroid (ICS) indicated for maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older. ArmonAir™ RespiClick® is supplied as an inhalation powder aerosol containing 55mcg, 113mcg, or 232mcg of fluticasone propionate per actuation. The recommended dose is one oral inhalation twice daily. The wholesale acquisition cost (WAC) per inhaler ranges from $169.28 to $226.66 depending on strength.
- **Trelegy™ Ellipta® (fluticasone furoate/umeclidinium/vilanterol inhalation powder)** is a combination of fluticasone furoate, an ICS, umeclidinium, a long-acting muscarinic antagonist (LAMA), and vilanterol, a long-acting beta$_2$ agonist (LABA). It is indicated for the long-term, once-daily, maintenance treatment of patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema, who are on a fixed-dose combination of fluticasone furoate and vilanterol for airflow obstruction and reducing exacerbations in whom additional treatment of airflow obstruction is desired or for patients who are already receiving umeclidinium and a fixed-dose combination of fluticasone furoate and vilanterol. Trelegy™ Ellipta® is supplied as an inhalation powder containing two foil blister strips of powder for oral inhalation. One strip contains fluticasone furoate 100mcg per blister and the other contains umeclidinium/vilanterol 62.5mcg/25mcg per blister. The recommended regimen is one oral inhalation once daily. The WAC per inhaler is $529.80.
- **QVAR® RediHaler™ (beclomethasone dipropionate HFA)** is an ICS indicated for maintenance treatment of asthma as prophylactic therapy in patients 4 years of age and older. QVAR® RediHaler™ is supplied as a breath-actuated inhalation aerosol containing either 40mcg or 80mcg per actuation. The recommended dose for patients 4 to 11 years of age is 40mcg or 80mcg twice daily. The recommended dose in patients 12 years of age and older is 40mcg, 80mcg, 160mcg, or 320mcg twice daily. QVAR® MDI (beclomethasone dipropionate HFA), the currently available form of QVAR® approved by the U.S. Food and Drug Administration (FDA) in 2014, will be discontinued upon the

launch of QVAR® RediHaler™. The national average drug acquisition cost (NADAC) per inhaler ranges from $156.77 to $216.99.

- **AirDuo™ RespiClick® (fluticasone propionate/salmeterol inhalation powder)** is a fixed dose combination product containing an ICS and a LABA indicated for the treatment of asthma in patients 12 years of age and older. AirDuo™ RespiClick® is supplied as an inhalation powder containing fluticasone propionate 55mcg, 113mcg, or 232mcg and salmeterol 14mcg per actuation. The recommended dose is one inhalation twice daily. Teva simultaneously launched AirDuo™ RespiClick® and an authorized generic fluticasone propionate/salmeterol inhalation powder and expects that sales of the authorized generic will represent most of the sales of the two products. The WAC per AirDuo™ RespiClick® inhaler is $302.10; the NADAC per authorized generic fluticasone propionate/salmeterol inhaler is $83.51.
- **Fasenra™ (benralizumab injection)** is an interleukin-5 receptor alpha-directed cytolytic monoclonal antibody (IgG1, kappa) indicated for the add-on maintenance treatment of patients with severe asthma 12 years of age and older, and with an eosinophilic phenotype. Fasenra™ is not for the treatment of other eosinophilic conditions. Fasenra™ is supplied as a single-dose prefilled syringe containing 30mg benralizumab per 1mL. Fasenra™ should be administered via subcutaneous (SC) injection. The recommended dose is 30mg every 4 weeks for the first three doses, followed by 30mg every 8 weeks thereafter. The WAC per dose is $4,752.11.

Nucala® (Mepolizumab) for Eosinophilic Granulomatosis with Polyangiitis (EGPA)[16,17,18,19,20]

EGPA Summary

EGPA, previously known as Churg-Strauss syndrome, is a systemic necrotizing vasculitis characterized by allergic rhinitis, asthma, and blood and tissue eosinophilia. In 1990, the American College of Rheumatology (ACR) outlined the following six criteria for the diagnosis of Churg-Strauss syndrome: asthma, eosinophilia of more than 10% in peripheral blood, paranasal sinusitis, pulmonary infiltrates, vasculitis with extravascular eosinophils, and polyneuropathy. The presence of four or more criteria yields a sensitivity of 85% and a specificity of 99.7%.

Asthma is the cardinal clinical feature of EGPA and is present in more than 90% of patients. Although largely characterized as a lung disease, patients often suffer from additional systemic effects including skin lesions, heart failure, pericarditis, thromboembolic disease, neuropathy, and renal insufficiency. The incidence of EGPA is estimated to be 1 to 3 cases per 100,000 adults per year; the age of onset varies from 15 to 70 years, with a mean age of approximately 38 years.

The mainstay of EGPA treatment is systemic glucocorticoids. An estimated 20% of patients will require additional treatment with cytotoxic medications such as cyclophosphamide, azathioprine, methotrexate, or rituximab. In December 2017, the FDA approved Nucala® (mepolizumab) for the treatment of adult patients with EGPA. Nucala® (mepolizumab) was previously approved for add-on maintenance treatment of patients with severe asthma 12

years of age and older, and with an eosinophilic phenotype. This new indication provides the first FDA-approved therapy specifically to treat EGPA.

Phase 3 MIRRA Study:
The efficacy of mepolizumab for the treatment of EGPA was established in a 52-week randomized placebo-controlled trial. A total of 136 subjects with EGPA received mepolizumab or placebo SC once every four weeks. Subjects enrolled had a diagnosis of EGPA for at least six months prior to enrollment with a history of relapsing or refractory disease and were on a stable dosage of oral corticosteroid (OCS) therapy (prednisolone or prednisone) of ≥7.5mg/day (but not >50mg/day) for at least four weeks prior to enrollment. Starting at week 4, OCS was tapered during the treatment period at the discretion of the investigator. The co-primary endpoints were the total accrued duration of remission over the 52-week treatment period, defined as Birmingham Vasculitis Activity Score (BVAS) = 0 (no active vasculitis) plus prednisolone or prednisone dose ≤4mg/day, and the proportion of subjects in remission at both week 36 and week 48 of treatment. The BVAS is a clinician-completed tool to assess clinically active vasculitis; the score includes both general symptoms (arthralgia, arthritis, and fever) and involvement of eight major organ systems (skin, mucous membranes, ear/nose/throat, cardiovascular, pulmonary, gastrointestinal, renal, and nervous system). At each site, persistent symptoms or manifestations are given one point and new or worse symptoms are given two points. The score ranges from 0 (complete remission) to a maximum of 68. Subjects receiving 300mg of mepolizumab achieved a significantly greater accrued time in remission compared with placebo [odds ratio (OR): 5.9; 95% confidence interval (CI) (2.7, 13.0)]. A significantly higher proportion of subjects receiving 300mg of mepolizumab achieved remission at both week 36 and week 48 compared with placebo [OR: 16.7; 95% CI (3.6, 77.6)].

Dosing:
- Nucala® (mepolizumab) is supplied as a single-dose 100mg vial.
- The recommended dose of mepolizumab for a diagnosis of EGPA is 300mg as three separate 100mg injections administered SC every four weeks.

Cost:

Medication	Cost per Month	Cost per Year
Nucala® (mepolizumab) 100mg	**$8,606.01**	**$111,878.13**

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Costs (SMAC) if NADAC unavailable.
Mepolizumab is dosed every four weeks; cost per year based on 13 doses.

Recommendations

The College of Pharmacy recommends the prior authorization of ArmonAir™ RespiClick® (fluticasone propionate), Trelegy™ Ellipta® (fluticasone furoate/umeclidinium/vilanterol), Qvar® RediHaler™ (beclomethasone dipropionate), AirDuo™ RespiClick® (fluticasone propionate/salmeterol), and Fasenra™ (benralizumab) with the following criteria:

Arnuity® Ellipta® (Fluticasone Furoate) and ArmonAir™ RespiClick® (Fluticasone Propionate) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 12 years of age or older; and
3. A patient-specific, clinically significant reason why Flovent® (fluticasone propionate) is not an option for the member.

QVAR® RediHaler™ (Beclomethasone Dipropionate HFA) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be 4 years of age or older; and
3. A patient-specific, clinically significant reason why QVAR® (beclomethasone dipropionate HFA) is not an option for the member; and
4. A trial of all available Tier-1 inhaled corticosteroids or a patient-specific, clinically significant reason why they are not appropriate for the member.

AirDuo™ RespiClick® (Fluticasone Propionate/Salmeterol) Approval Criteria:

1. An FDA approved diagnosis of asthma; and
2. Member must be at or above the minimum age indicated; and
3. Failure of both Advair® (fluticasone/salmeterol) and Dulera® (mometasone/formoterol) or a reason why Advair® and Dulera® are not appropriate for the member; and
4. Member must have used an inhaled corticosteroid for at least one month immediately prior; and
5. Member must be considered uncontrolled by provider [required rescue medication >2 days a week (not for prevention of exercise induced bronchospasms) and/or needed oral systemic corticosteroids]; or
6. A clinical situation warranting initiation with combination therapy due to severity of asthma.

Inhaled Corticosteroids and Combination Products	
Tier-1	**Tier-2**
beclomethasone dipropionate (QVAR®)	**beclomethasone dipropionate (QVAR® RediHaler™)**
budesonide (Pulmicort®)	budesonide/formoterol (Symbicort®)
ciclesonide (Alvesco®)	fluticasone furoate (Arnuity® Ellipta®)
flunisolide (Aerospan®)	fluticasone furoate/vilanterol (Breo® Ellipta®)
fluticasone propionate (Flovent®)	**fluticasone propionate (ArmonAir™ RespiClick®)**
fluticasone/salmeterol (Advair®)	**fluticasone propionate/salmeterol (AirDuo™ RespiClick®)**
mometasone/formoterol (Dulera® HFA)	
mometasone furoate (Asmanex®)	

Tier-1 products are covered with no prior authorization required.
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Trelegy™ Ellipta® (Fluticasone Furoate/Umeclidinium/Vilanterol) Approval Criteria:

1. An FDA approved diagnosis of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema; and

2. A four week trial of at least one long-acting beta$_2$ agonist (LABA) and a four week trial of one long-acting muscarinic antagonist (LAMA) within the past 90 days used concomitantly with an inhaled corticosteroid (ICS); and
3. A patient-specific, clinically significant reason why the member requires the triple combination therapy in place of the individual components or use of a LABA/ICS combination with a LAMA.

Fasenra™ (Benralizumab Injection) Approval Criteria:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be age 12 years or older; and
3. Member must have a baseline blood eosinophil count of 300 cell/µL or greater within the last six weeks of initiation 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 (≥880mcg/day fluticasone propionate or equivalent daily dose or ≥440mcg/day in ages 12 to 17 years) 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. Fasenra™ must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
8. Fasenra™ 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. A quantity limit of 1 prefilled syringe per 56 days will apply.

Additionally, the College of Pharmacy recommends the following criteria for Nucala® (mepolizumab) for a diagnosis of Eosinophilic Granulomatosis with Polyangiitis (EGPA):

Nucala® (Mepolizumab Injection) Approval Criteria [Eosinophilic Granulomatosis with Polyangiitis (EGPA) Diagnosis]:

1. An FDA approved indication for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA); and
2. Member meets one of the following:
    a. Member must have a past history of at least one confirmed EGPA relapse [requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy, or hospitalization] with in the past twelve months; or

    b. Member must have refractory disease within the last six months following induction of standard treatment regimen administered compliantly for at least three months; and
3. Diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) will not be approved; and
4. Failure to achieve remission despite glucocorticoid therapy (oral prednisone equivalent equal to or greater than 7.5mg/day) for a minimum of 4 weeks duration; and
5. Nucala® must be prescribed by an allergist, pulmonologist, pulmonary specialist, or rheumatologist or the member must have been evaluated by an allergist, pulmonologist, pulmonary specialist, or rheumatologist within the last twelve months (or be an advanced care practitioner with a supervising physician who is an allergist, pulmonologist, pulmonary specialist, or rheumatologist); and
6. Nucala® must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
7. A quantity limit of 3 vials per 28 days will apply.
8. Initial approvals will be for the duration of six months after which time compliance will be evaluated for continued approval. For continued approval, member must be compliant and prescriber must verify the member is responding to Nucala® as demonstrated by a Birmingham Vasculitis Activity Score (BVAS) of zero, fewer EGPA relapses from baseline, or a decrease in daily OCS dose regimen from baseline.

Lastly, the College of Pharmacy recommends updating the Nucala® (mepolizumab) and Xolair® (omalizumab) asthma criteria regarding administration and anaphylaxis with criteria similar to the other medications in the class. Changes can be seen in red in the following criteria:

Nucala® (Mepolizumab Injection) Approval Criteria [Severe Eosinophilic Phenotype Asthma Diagnosis]:

1. An FDA approved indication for add-on maintenance treatment of patients with severe eosinophilic phenotype asthma; and
2. Member must be age 12 years or older; and
3. Member must have a baseline blood eosinophil count of 150 cell/mcL or greater within the last six weeks of initiation of dosing; and
4. Member must have had at least two asthma exacerbations requiring systemic corticosteroids within the last twelve 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 (≥880mcg/day fluticasone propionate or equivalent daily dose or ≥440mcg/day in ages 12 to 17 years) used compliantly for at least the past twelve months (for ICS/LABA combination products, 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. Nucala® must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and

8. Nucala® 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; and
10. A quantity limit of 1 vial per 28 days will apply.

Xolair® (Omalizumab) Approval Criteria [Asthma Diagnosis]:

1. Member must have a diagnosis of severe persistent asthma [as per National Asthma Education and Prevention Program (NAEPP) guidelines]; and
2. Member must be between 6 and 75 years of age; and
3. Member must have a positive skin test to at least one perennial aeroallergen. Positive perennial aeroallergens must be listed on the prior authorization request; and
4. Member must have a pretreatment serum IgE level between 30 and 1,300 IU/mL (depending on member age); and
5. Member's weight must be between 20kg and 150kg; and
6. Member must have been on high-dose inhaled corticosteroids (ICS) (≥880mcg/day fluticasone propionate or equivalent daily dose or ≥440mcg/day in ages 12 to 17 years) for at minimum the past three months; and
7. Prescribed Xolair® dose must be an FDA approved regimen per Xolair® prescribing information; and
8. Xolair® must be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis; and
9. Xolair® 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
10. Member must have been in the emergency room (ER) or hospitalized, due to an asthma exacerbation, twice in the past twelve months (date of visits must be listed on the prior authorization request), or member must have been determined to be dependent on systemic corticosteroids to prevent serious exacerbations; and
11. Both the prior authorization request form and statement of medical necessity form must be submitted for processing; and
12. Initial approvals will be for the duration of six months after which time compliance will be evaluated for continued approval.

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Appendix E

Vote to Prior Authorize Emflaza® (Deflazacort)

Oklahoma Health Care Authority
February 2018

Introduction[1,2]

Emflaza® (deflazacort) is a corticosteroid indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older. It is supplied as 6mg, 18mg, 30mg, and 36mg oral tablets. It is also supplied as a 22.75mg/mL oral suspension in a 13mL bottle with two 1mL dosing syringes. The recommended dose is approximately 0.9mg/kg by mouth once daily. It is recommended to round up to the nearest possible dose when using tablets, and to the nearest tenth of a milliliter (mL) when using suspension. Deflazacort tablets can be administered whole or crushed. If crushed, the tablets should be taken immediately after mixing with applesauce. It is recommended that the appropriate dose of deflazacort suspension be added to 3 to 4 ounces of juice or milk and mixed well. The dose should then be administered immediately.

In 2016, the American Academy of Neurology (AAN) published a practice guideline update on corticosteroid treatment of DMD. Prednisone is recommended to improve strength and pulmonary function. Prednisone and deflazacort may be used to improve timed motor function, reducing the need for scoliosis surgery, and delaying cardiomyopathy onset by 18 years of age. Deflazacort may also be used to delay age at loss of ambulation by 1.4 to 2.5 years and increasing survival at 5 to 15 years of follow-up. The AAN found that prednisone may be associated with increased weight gain in the first years of treatment compared with deflazacort. Deflazacort may be associated with increased risk of cataracts compared with prednisone. The AAN guidelines do not recommend one corticosteroid over the other.

Cost Comparison:

Medication	Cost Per 30 Days*	Cost Per Year*
Emflaza® (deflazacort) tablet	**$4,290.00 - $15,936.00**	**$51,480.00 - $191,232.00**
Emflaza® (deflazacort) suspension	**$5,797.20 - $22,464.30**	**$69,566.40 - $269,571.60**
prednisone tablet 20mg	$3.90 - $11.70	$46.80 - $140.40

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 given as a range based on average weight for males 5 to 19 years of age at recommended dosing using historically available costs which may not reflect current costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Emflaza® (deflazacort) with the following criteria:

Emflaza® (Deflazacort) Approval Criteria:

1. An FDA approved diagnosis of Duchenne muscular dystrophy (DMD); and

2. Member must be 5 years of age or older; and
3. Emflaza® must be prescribed by or in consultation with a prescriber who specializes in the treatment of DMD; and
4. A patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed must be provided; and
5. Patients already established on deflazacort via the ACCESS DMD Program must also document a patient-specific, clinically significant reason why the member cannot use prednisone even when the tablets are crushed; and
6. For Emflaza® suspension, a patient-specific, clinically significant reason why the member cannot use the tablet formulation in the place of oral suspension even when the tablets are crushed must be provided; and
7. For continued authorization, the member's recent weight must be provided in order to authorize the appropriate amount of drug required according to package labeling.
8. For the tablets, a quantity limit of 30 tablets per 30 days will apply and for the suspension, a quantity limit of 39mL (3 bottles) per 30 days will apply. Quantity limit requests will be based on the member's recent weight taken within the last 30 days.

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Appendix F

Vote to Prior Authorize Zilretta™ (Triamcinolone Acetonide Extended-Release Injectable Suspension)

Oklahoma Health Care Authority
February 2018

Introduction[1]

Zilretta™ [triamcinolone extended-release (ER) injection] is a synthetic corticosteroid for intra-articular injection for the management of osteoarthritis (OA) pain of the knee. The recommended dosing of Zilretta™ is a single dose of 32mg/5mL via intra-articular injection into the effected knee(s). Zilretta™ is only approved for treatment of OA pain of the knee and has not been evaluated for management of OA pain of the shoulder or hip and may not be suitable for use in small joints, such as the hand. The efficacy and safety of repeat administration of Zilretta™ for the management of OA pain of the knee has not been evaluated.

Cost Comparison:

Medication	Cost Per Vial
Zilretta™ (triamcinolone acetonide ER 32mg/5mL injection)	**$570.00**
triamcinolone acetonide 40mg/mL injection	$8.76
methylprednisolone 40mg/mL injection	$5.87

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

Recommendations

The College of Pharmacy recommends the prior authorization of Zilretta™ (triamcinolone acetonide ER injection) with the following criteria:

Zilretta™ [Triamcinolone Acetonide Extended-Release (ER) Injection] Approval Criteria:

1. An FDA approved diagnosis of osteoarthritis (OA) pain of the knee; and
2. Zilretta™ will only be approvable for use in the knee(s) for OA pain; and
3. A patient-specific, clinically significant reason why the member cannot use Kenalog-40® (triamcinolone acetonide 40mg injection) or Depo-Medrol® (methylprednisolone injection) must be provided.
4. A quantity limit of 1 injection per knee per 12 weeks will apply.

[1] Zilretta™ Prescribing Information. Flexion Therapeutics, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208845s000lbl.pdf. Issued 10/2017. Last accessed 01/18/2018.

Appendix G

Vote to Prior Authorize Varubi® IV (Rolapitant) and Cinvanti™ (Aprepitant)

Oklahoma Health Care Authority
February 2018

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

- **Varubi® IV [rolapitant for intravenous (IV) use]** was approved by the U.S. Food and Drug Administration (FDA) in October 2017 for use in combination with other anti-emetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy (HEC). Varubi® (rolapitant) oral tablets were first FDA approved in 2015 for the same indication. Rolapitant is a substance P/neurokinin 1 (NK1) receptor antagonist and is available as 90mg oral tablets and as an injectable emulsion for IV use in a single-dose, ready-to-use vial (166.5mg/92.5mL). Varubi® IV was FDA approved based on data demonstrating the bioequivalence of IV rolapitant to oral rolapitant. The recommended dosage of rolapitant is to administer one dose (180mg orally as a single dose or 166.5mg infused IV over 30 minutes) on day 1 of the chemotherapy cycle (within two hours prior to initiation of chemotherapy), in combination with dexamethasone and a 5-HT_3 receptor antagonist (e.g., ondansetron, granisetron, palonosetron). The wholesale acquisition cost (WAC) of Varubi® IV is $295.08 per dose (one 166.5mg/92.5mL vial).
- **Cinvanti™ (aprepitant for IV use)** was FDA approved in November 2017 for use in combination with other anti-emetic agents in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of HEC, including high-dose cisplatin, and prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC). Aprepitant is an NK1 receptor antagonist, and Cinvanti™ is available as an injectable emulsion for IV use in a single-dose vial (130mg/18mL). Other FDA approved formulations of aprepitant include aprepitant oral capsules (brand Emend® and generic formulations), aprepitant powder for oral suspension (brand Emend®), and IV fosaprepitant (brand Emend®), which is the prodrug of aprepitant and is available as a powder for IV solution. Emend® (oral aprepitant and IV fosaprepitant) has the same FDA approved indications as Cinvanti™. Cinvanti™ was FDA approved based on data demonstrating the bioequivalence of Cinvanti™ to Emend® IV. The recommended dosage of Cinvanti™ for HEC is to administer one dose (130mg aprepitant infused IV over 30 minutes) on day 1 of the chemotherapy cycle (administered within 30 minutes prior to initiation of chemotherapy), in combination with dexamethasone and a 5-HT_3 receptor antagonist. The WAC of Cinvanti™ is $295.02 per dose (one 130mg/18mL vial).

Market News[7]

News:

- **January 2018:** A warning about anaphylaxis, anaphylactic shock, and other hypersensitivity reactions occurring with the use of rolapitant in patients with cancer has been highlighted by the FDA in a MedWatch bulletin. Anaphylactic and hypersensitivity reactions to the drug, some of which required hospitalization, have been reported in the postmarketing setting. These reactions occurred during or soon after the infusion of rolapitant injectable emulsion (for IV use), and most reactions occurred within the first few minutes of administration. If anaphylaxis or any other serious hypersensitivity/infusion reaction occurs, rolapitant should be stopped immediately, appropriate medical management should be initiated, and rolapitant should not be used in that patient again.

Recommendations

The College of Pharmacy recommends the prior authorization of Varubi® IV (rolapitant for IV use) and Cinvanti™ (aprepitant for IV use) with the following criteria:

Varubi® and Varubi® IV (Rolapitant) Approval Criteria:

1. An FDA approved indication for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy; and
2. For oral Varubi® (rolapitant oral tablets), a previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. For Varubi® IV [rolapitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
4. Approval length will be based on duration of need.
5. A quantity limit of two tablets or two vials per chemotherapy cycle will apply.

Kytril® and Sancuso® (Granisetron), Anzemet® (Dolasetron), Emend® and Cinvanti™ (Aprepitant), and Emend® IV (Fosaprepitant) Approval Criteria:

1. An FDA approved diagnosis; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in an inadequate response is required for authorization in members receiving moderately emetogenic chemotherapy; and
3. No ondansetron trial is required for authorization of Emend® (aprepitant) in members receiving highly emetogenic chemotherapy; and
4. For Emend® (aprepitant) oral suspension, 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 the oral capsule formulation cannot be used; and
5. For Cinvanti™ [aprepitant intravenous (IV) emulsion], a previously failed trial of IV fosaprepitant (Emend® IV) that resulted in an inadequate response, or a patient-specific, clinically significant reason why IV fosaprepitant cannot be used must be provided; and
6. Approval length will be based on duration of need.

Additionally, based on the current low net cost of Akynzeo® (netupitant/palonosetron), the College of Pharmacy recommends making Akynzeo® available without a prior authorization for members with cancer; however, Akynzeo® will follow the original criteria and require a previously failed trial of aprepitant if the net cost increases compared to other available products. The changes to the current criteria are shown in red:

Akynzeo® (Netupitant/Palonosetron) Approval Criteria:

1. An FDA approved diagnosis for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. A previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. Approval length will be based on duration of need.
4. A quantity limit of one capsule per chemotherapy cycle will apply.
5. Akynzeo® will not require a prior authorization for members with cancer and claims will pay at the point of sale if the member has a reported oncology diagnosis within the past six months of claims history.
    a. Based on the current low net cost, Akynzeo® will not require a prior authorization for members with cancer; however, Akynzeo® will follow the original criteria and require a previously failed trial of aprepitant if the net cost increases compared to other available products.

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[3] Varubi® (Rolapitant) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/varubi/. Last revised 10/24/2017. Last accessed 01/04/2018.

[4] Heron Therapeutics, Inc. Heron Therapeutics Announces U.S. FDA Approval of Cinvanti™ (Aprepitant) Injectable Emulsion for the Prevention of Acute and Delayed Chemotherapy-Induced Nausea and Vomiting (CINV). *Business Wire*. Available online at: http://www.businesswire.com/news/home/20171109006358/en/Heron-Therapeutics-Announces-U.S.-FDA-Approval-CINVANTI%E2%84%A2. Issued 11/09/2017. Last accessed 01/04/2018.

[5] Cinvanti™ (Aprepitant) Prescribing Information. Heron Therapeutics, Inc. Available online at: http://www.cinvanti.com/pdfs/CINVANTI_PI_11.9.17.pdf. Last revised 11/2017. Last accessed 01/04/2018.

[6] Emend® (Aprepitant) Package Insert. MedLibrary.org. Available online at: https://medlibrary.org/lib/rx/meds/emend-1/. Last revised 02/23/2012. Last accessed 01/04/2018.

[7] Chustecka Z. FDA Warning on Anaphylaxis with Rolapitant for CINV. *Medscape*. Available online at: https://www.medscape.com/viewarticle/891382?nlid=120070_3901&src=wnl_newsalrt_180116_MSCPEDIT&uac=163910MN&impID=1535282&faf=1. Issued 01/16/2018. Last accessed 01/17/2018.

Appendix H

Fiscal Year 2017 Annual Review of Seizure Medications

Oklahoma Health Care Authority
February 2018

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.

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 three 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.

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.

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 must be provided.
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 one* other medications commonly used for seizures. (*The manufacturer of 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 must be provided.
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 must be provided.
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 adjunctive therapy in the treatment of 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 one* other medications commonly used for seizures. (*The manufacturer of 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® oral suspension, a patient-specific, clinically significant reason why Fycompa® oral tablets cannot be used must be provided.
5. Members currently stable on Fycompa® 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 (LGS); 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 indication of one of the following:
    a. Partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
    b. Adjunctive therapy in seizures associated with Lennox-Gastaut Syndrome (LGS); or
    c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate), must be provided.
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 indication of one of the following:
   a. Partial-onset or primary generalized tonic-clonic (PGTC) seizures; or
   b. Adjunctive therapy in seizures associated with Lennox-Gastaut Syndrome (LGS); or
   c. Prophylaxis of migraine headaches; and
2. A patient-specific, clinically significant reason why the member cannot use the short-acting formulation, Topamax® (topiramate), must be provided.
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 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 SABRIL REMS program and maintain enrollment throughout therapy.

Utilization of Seizure Medications: Fiscal Year 2017

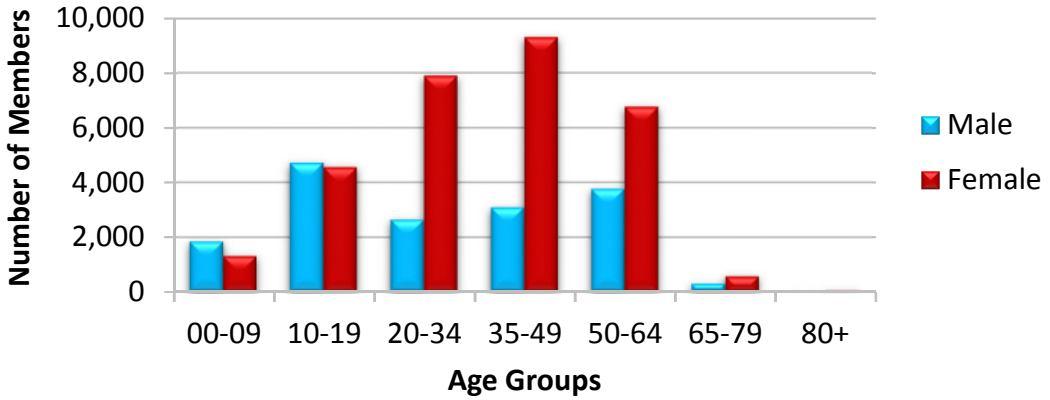
The following utilization data includes seizure medications used for all diagnoses and does not differentiate between epilepsy diagnoses and other diagnoses, for which use may be appropriate.

Comparison of Fiscal Years: Seizure Medications

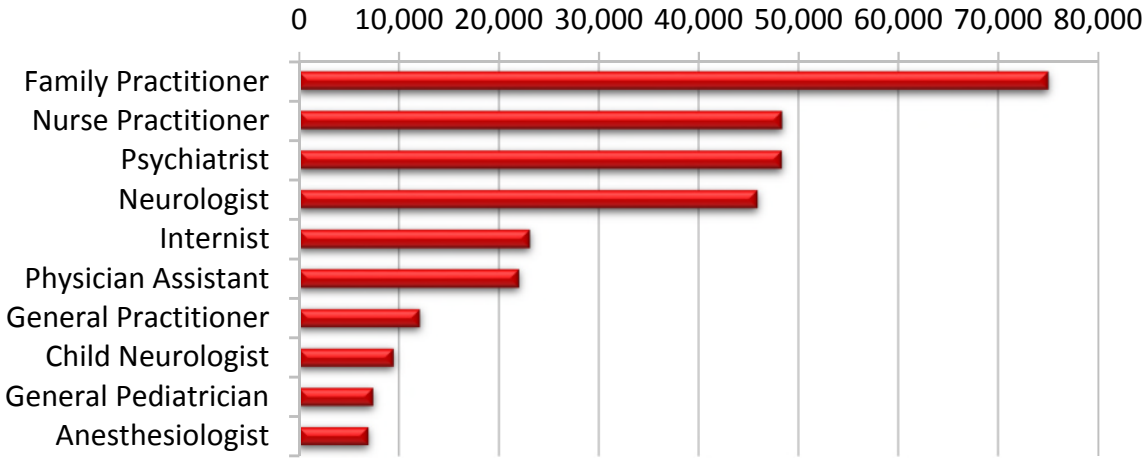
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	45,883	324,958	$22,844,154.76	$70.30	$2.33	30,833,720	9,806,478
2017	46,730	332,721	$25,109,540.98	$75.47	$2.50	31,755,013	10,062,267
% Change	**1.80%**	**2.40%**	**9.90%**	**7.40%**	**7.30%**	**3.00%**	**2.60%**
Change	**847**	**7,763**	**$2,265,386.22**	**$5.17**	**$0.17**	**921,293**	**255,789**

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

Demographics of Members Utilizing Seizure Medications



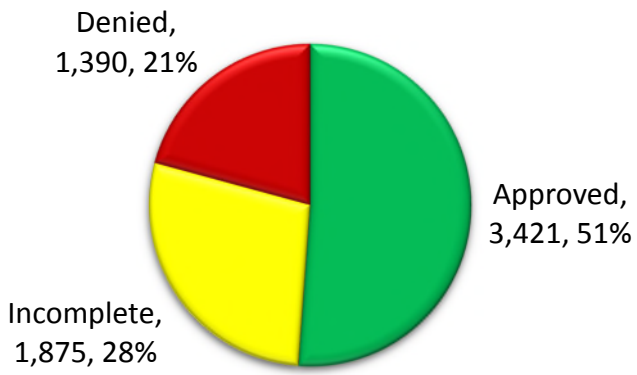
Top Prescriber Specialties of Seizure Medications by Number of Claims



Prior Authorization of Seizure Medications

There were 6,686 prior authorization requests submitted for seizure medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23]

Anticipated Patent Expiration(s):

- Lyrica® (pregabalin): December 2018
- Briviact® (brivaracetam): February 2021
- Vimpat® (lacosamide): March 2022
- Banzel® (rufinamide): May 2023
- Fycompa® (perampanel): May 2026
- Oxtellar XR® [oxcarbazepine extended-release (ER)]: April 2027
- Trokendi XR® (topiramate ER): April 2028
- Aptiom® (eslicarbazepine): August 2032
- Carnexiv™ (carbamazepine): February 2033
- Qudexy® XR (topiramate ER): March 2033
- Spritam® (levetiracetam): March 2034

New U.S. Food and Drug Administration (FDA) Approval(s):

- **March 2017:** The FDA approved a supplemental New Drug Application (sNDA) for Qudexy® XR (topiramate ER capsules) for use as prophylaxis of migraine headaches in adults and in adolescents 12 years of age and older. Qudexy® XR was first FDA approved in 2014 for the treatment of partial-onset seizures, primary generalized tonic-clonic (PGTC) seizures, and Lennox-Gastaut Syndrome (LGS). The current prior authorization (PA) criteria for Qudexy® XR has been updated to reflect the new indication for prophylaxis of migraine headaches (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **April 2017:** The FDA approved an sNDA for Trokendi XR® (topiramate ER capsules) for use as prophylaxis of migraine headaches in adults and in adolescents 12 years of age and older. Trokendi XR® was first FDA approved in 2013 for the treatment of partial-onset seizures, PGTC seizures, and LGS. The current PA criteria for Trokendi XR® has been updated to reflect the new indication for prophylaxis of migraine headaches (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **July 2017:** The FDA approved an sNDA for Fycompa® (perampanel) for use as monotherapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients 12 years of age and older with epilepsy. Perampanel was first FDA approved in 2012 as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients 12 years of age and older with epilepsy. Perampanel is also indicated as adjunctive therapy for the treatment of PGTC seizures in patients 12 years of age and older with epilepsy. The current PA criteria for Fycompa® has been updated to reflect the updated indication for monotherapy in the treatment of partial-onset seizures (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **September 2017:** The FDA approved an sNDA for Aptiom® (eslicarbazepine) to expand the indication for the treatment of partial-onset seizures to include children and adolescents 4 to 17 years of age. Eslicarbazepine was first FDA approved in 2013 for use

as adjunctive treatment of partial-onset seizures in adults, followed by FDA approval for use as monotherapy in adults in 2015.

- **September 2017:** The FDA approved an sNDA for Briviact® (brivaracetam) for use as monotherapy for the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy. Brivaracetam was first FDA approved in 2016 as adjunctive therapy for the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy. The current PA criteria for Briviact® has been updated to reflect the updated indication for monotherapy in the treatment of partial-onset seizures (shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report).
- **October 2017:** The FDA approved a New Drug Application (NDA) for Lyrica® CR (pregabalin ER tablets) as once-daily therapy for the management of neuropathic pain associated with diabetic peripheral neuropathy and the management of postherpetic neuralgia. Lyrica® CR did not receive FDA approval for the management of fibromyalgia or as adjunctive therapy for adult patients with partial-onset seizures. A full review of Lyrica® CR will be completed within the annual review of special formulations.
- **November 2017:** The FDA approved an sNDA for Vimpat® (lacosamide) to expand the indication for the treatment of partial-onset seizures to include children and adolescents 4 to 16 years of age. Lacosamide was first FDA approved in 2008 for use as adjunctive treatment of partial-onset seizures in patients 17 years of age and older, followed by FDA approval for use as monotherapy in patients 17 years of age and older in 2014.

News:

- **June 2017:** GlaxoSmithKline (GSK) discontinued the manufacture of Potiga® (ezogabine), citing commercial reasons, specifically due to very limited use and declining numbers of patients initiating therapy on the drug. GSK stated that the drug withdrawal was not due to safety or efficacy reasons. Ezogabine was FDA approved in 2011 as adjunctive treatment for partial-onset seizures in adults. The labeling for ezogabine was updated in 2013 to include a boxed warning regarding the risk of permanent retinal abnormalities, potential vision loss, and skin discoloration.

Pipeline:

- **May 2017:** The FDA approved Elepsia XR™ (levetiracetam ER 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 issued a Complete Response Letter (CRL) to the pharmaceutical company, withdrawing their approval of Elepsia XR™ due to regulatory issues at the manufacturing plant. In July 2016, the research company licensed Elepsia XR™ to its parent company as a way to speed up U.S. market entry following the manufacturing issues. However, in May 2017, the FDA issued a second CRL, denying the NDA for Elepsia XR™ after an inspection of the manufacturing facility. The pharmaceutical company stated that satisfactory resolution of the deficiencies identified during the inspection is required before the final approval of Elepsia XR™ can be granted. The novel once-daily formulation of levetiracetam is expected to improve convenience and compliance for patients who currently take multiple levetiracetam tablets every day. Keppra XR® (levetiracetam ER) was FDA

approved in 2008, is also dosed once daily, and is available as 500mg and 750mg tablets (brand name and generic).

- **August 2017:** The FDA granted Orphan Drug designation for Epygenix Therapeutics' product, EPX-300, for the treatment of patients with Dravet syndrome. Dravet syndrome, a lifelong form of epilepsy, begins in the first year of life with frequent or prolonged seizures. Intellectual disability, behavioral abnormalities, gait and motor dysfunction, and increased mortality are commonly observed as the disease progresses, and patients with Dravet syndrome also suffer from life-threatening seizures that cannot be adequately controlled by available medications. The effectiveness of EPX-300 was discovered using a proprietary phenotype-based zebrafish drug screening platform. The zebrafish harbors 82% of human disease-associated genes and shares many physiological and metabolic pathways with humans. Epygenix previously received Orphan Drug designations from the FDA for two other products, EPX-100 and EPX-200, for the treatment of Dravet syndrome. EPX-100 is currently in Phase 1 clinical trials, while EPX-200 and EPX-300 are both currently in Phase 2 clinical trials.
- **September 2017:** Zogenix reported top-line results from a pivotal Phase 3 clinical trial of ZX008 in Dravet syndrome. The trial met its primary objective of demonstrating that ZX008, at a dose of 0.8mg/kg/day, is superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on the change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period ($p<0.001$). ZX008 also demonstrated statistically significant improvements vs. placebo in all key secondary measures, including the proportion of patients with clinically meaningful reductions in seizure frequency and longest seizure-free interval. ZX008 is low-dose fenfluramine hydrochloride, and was generally well-tolerated in the study with the adverse effects consistent with the known safety profile of fenfluramine. Zogenix is anticipating top-line results from its second pivotal Phase 3 clinical trial in the first half of 2018 and remains on track to submit an NDA to the FDA for ZX008 in the second half of 2018. ZX008 has received both Fast Track and Orphan Drug designations from the FDA for the treatment of Dravet syndrome.
- **September 2017:** Sage Therapeutics reported results from its Phase 3 STATUS Trial of brexanolone (SAGE-547) in the treatment of super-refractory status epilepticus (SRSE). The study did not meet the primary endpoint, comparing success in weaning of third-line agents and resolution of potentially life-threatening status epilepticus with brexanolone vs. placebo (43.9% vs. 42.4%; $p=0.8775$) when added to standard-of-care. SRSE is a life-threatening, persistent state of seizure that does not respond to first-, second-, or third-line treatments, and is a neurological emergency that may cause death or life-altering outcomes. SRSE is a complicated condition that is poorly understood, and there are no treatments for SRSE currently approved by the FDA. Despite failing to meet the primary endpoint, Sage is hopeful that the information from the STATUS Trial will inform current treatments and aid in the development of future treatments for patients with SRSE. This first-ever trial in a highly variable and complex patient population confirms that research in a critical care unit is possible and deepens the understanding of GABA mechanisms and their effect on brain circuitry. Brexanolone has

been granted both Fast Track and Orphan Drug designations from the FDA for the treatment of SRSE. Sage is also currently evaluating brexanolone in a Phase 3 development program for the treatment of postpartum depression, for which they have received Breakthrough Therapy designation from the FDA.

- **December 2017:** The FDA granted Greenwich Biosciences' lead cannabinoid product candidate, Epidiolex®, Priority Review status, which accelerates the timing of the FDA review process compared to a standard review. Priority Review status is designated for drugs that may offer major advances in treatment or provide a treatment where no adequate therapies exist. Epidiolex® is a proprietary oral solution of pure plant-derived cannabidiol (CBD). CBD lacks the psychotropic effects of tetrahydrocannabinol (THC), which is found in many cannabis products. Greenwich submitted an NDA to the FDA in October 2017 for Epidiolex® as adjunctive treatment of seizures associated with LGS and Dravet syndrome, two highly treatment-resistant forms of childhood-onset epilepsy. The FDA also granted Epidiolex® Rare Pediatric Disease and Orphan Drug designations in the treatment of both LGS and Dravet syndrome, and Fast Track designation for the treatment of Dravet syndrome. The Prescription Drug User Fee Act (PDUFA) goal date for completion of the FDA review of the NDA for Epidiolex® is June 27, 2018. Greenwich is currently evaluating additional clinical development programs in other orphan seizure disorders, including Phase 3 clinical trials in tuberous sclerosis complex (TSC) and infantile spasms (IS). Epidiolex® has received Orphan Drug designation from the FDA for the treatment of TSC and IS.

Recommendations

The College of Pharmacy recommends the changes shown in red in the *Current Prior Authorization Criteria* section at the beginning of this report, based on new or updated FDA-approved indications for Qudexy® XR, Trokendi XR®, Briviact®, and Fycompa® (details found in the *Market News* section of this report).

Utilization Details of Seizure Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
GABAPENTIN PRODUCTS						
GABAPENTIN CAP 300MG	36,395	11,136	$374,779.31	$10.30	$0.31	1.49%
GABAPENTIN TAB 600MG	23,220	4,974	$459,374.97	$19.78	$0.64	1.83%
GABAPENTIN TAB 800MG	14,891	2,641	$340,297.29	$22.85	$0.76	1.36%
GABAPENTIN CAP 100MG	9,194	3,605	$79,054.57	$8.60	$0.29	0.31%
GABAPENTIN CAP 400MG	5,738	1,652	$69,413.19	$12.10	$0.40	0.28%
GABAPENTIN SOL 250MG/5ML	674	132	$38,873.20	$57.68	$1.93	0.15%
NEURONTIN CAP 300MG	12	1	$4,610.17	$384.18	$12.81	0.02%
NEURONTIN TAB 800MG	12	1	$10,557.59	$879.80	$29.33	0.04%
GABAPENTIN SOL 300MG/6ML	2	2	$145.82	$72.91	$2.43	0.00%
SUBTOTAL	**90,138**	**24,144**	**$1,377,106.11**	**$15.28**	**$0.49**	**5.48%**
CLONAZEPAM PRODUCTS						
CLONAZEPAM TAB 1MG	18,212	3,898	$134,729.77	$7.40	$0.25	0.54%
CLONAZEPAM TAB 0.5MG	13,500	3,731	$94,972.99	$7.04	$0.25	0.38%
CLONAZEPAM TAB 2MG	5,345	1,031	$43,665.00	$8.17	$0.28	0.17%
CLONAZEP ODT TAB 0.25MG	814	264	$37,838.33	$46.48	$1.86	0.15%
CLONAZEP ODT TAB 0.5MG	461	138	$21,332.47	$46.27	$1.80	0.08%
CLONAZEP ODT TAB 0.125MG	399	130	$17,180.35	$43.06	$1.96	0.07%
CLONAZEP ODT TAB 1MG	215	64	$8,664.33	$40.30	$1.74	0.03%
CLONAZEP ODT TAB 2MG	50	16	$1,487.56	$29.75	$1.88	0.01%
KLONOPIN TAB 2MG	12	1	$2,866.16	$238.85	$7.96	0.01%
KLONOPIN TAB 1MG	11	1	$2,780.91	$252.81	$8.43	0.01%
SUBTOTAL	**39,019**	**9,274**	**$365,517.87**	**$9.37**	**$0.33**	**1.46%**
TOPIRAMATE PRODUCTS						
TOPIRAMATE TAB 50MG	9,665	2,869	$95,244.87	$9.85	$0.32	0.38%
TOPIRAMATE TAB 100MG	9,183	1,943	$101,516.07	$11.05	$0.36	0.40%
TOPIRAMATE TAB 25MG	8,692	3,387	$77,088.04	$8.87	$0.29	0.31%
TOPIRAMATE TAB 200MG	3,636	610	$49,881.01	$13.72	$0.44	0.20%
TOPIRAMATE CAP 15MG	550	163	$20,546.85	$37.36	$1.24	0.08%
TOPIRAMATE CAP 25MG	472	106	$32,242.85	$68.31	$2.40	0.13%
TOPAMAX TAB 100MG	52	5	$43,344.53	$833.55	$27.52	0.17%
TROKENDI XR CAP 200MG	46	12	$37,264.86	$810.11	$27.00	0.15%
TROKENDI XR CAP 100MG	35	9	$27,893.39	$796.95	$26.57	0.11%
TROKENDI XR CAP 50MG	33	8	$10,159.04	$307.85	$10.26	0.04%
TOPAMAX TAB 200MG	25	2	$24,217.86	$968.71	$32.29	0.10%
TOPAMAX TAB 25MG	19	2	$2,156.72	$113.51	$3.78	0.01%
TOPAMAX SPR CAP 25MG	11	1	$30,821.25	$2,801.93	$82.41	0.12%
TROKENDI XR CAP 25MG	11	3	$2,858.21	$259.84	$8.66	0.01%
TOPIRAMATE CAP ER 200MG	10	3	$3,444.24	$344.42	$11.48	0.01%
TOPAMAX TAB 50MG	6	2	$2,553.70	$425.62	$14.19	0.01%
TOPIRAMATE CAP ER 100MG	5	1	$0.00^	$0.00^	$0.00^	0.00%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
TOPIRAMATE CAP ER 150MG	4	1	$1,575.72	$393.93	$13.13	0.01%
SUBTOTAL	**32,455**	**9,127**	**$562,809.21**	**$17.34**	**$0.57**	**2.24%**
LEVETIRACETAM PRODUCTS						
LEVETIRACETA SOL 100MG/ML	10,604	1,644	$223,234.19	$21.05	$0.68	0.89%
LEVETIRACETA TAB 500MG	8,824	1,962	$125,140.43	$14.18	$0.47	0.50%
LEVETIRACETA TAB 1000MG	5,284	873	$149,972.21	$28.38	$0.94	0.60%
LEVETIRACETA TAB 750MG	3,803	683	$80,142.02	$21.07	$0.69	0.32%
LEVETIRACETA TAB 250MG	1,560	368	$19,079.38	$12.23	$0.41	0.08%
LEVETIRACETA TAB 750MG ER	621	96	$31,809.36	$51.22	$1.66	0.13%
LEVETIRACETA TAB 500MG ER	586	116	$18,437.66	$31.46	$1.05	0.07%
KEPPRA XR TAB 500MG	101	11	$80,736.30	$799.37	$26.66	0.32%
KEPPRA SOL 100MG/ML	89	9	$57,916.41	$650.75	$21.55	0.23%
KEPPRA XR TAB 750MG	87	8	$83,715.36	$962.25	$30.03	0.33%
KEPPRA TAB 1000MG	67	8	$71,965.43	$1,074.11	$34.19	0.29%
KEPPRA TAB 750MG	61	7	$58,541.62	$959.70	$25.02	0.23%
KEPPRA TAB 500MG	50	5	$33,446.67	$668.93	$22.30	0.13%
LEVETIRACETM INJ 500MG/5ML	17	2	$1,892.91	$111.35	$16.75	0.01%
KEPPRA TAB 250MG	9	1	$8,366.30	$929.59	$30.99	0.03%
SUBTOTAL	**31,763**	**5,793**	**$1,044,396.25**	**$32.88**	**$1.08**	**4.16%**
DIVALPROEX, VALPROATE, AND VALPROIC ACID PRODUCTS						
DIVALPROEX TAB 500MG DR	8,068	1,526	$130,941.04	$16.23	$0.54	0.52%
DIVALPROEX TAB 500MG ER	6,862	1,329	$412,172.00	$60.07	$1.99	1.64%
DIVALPROEX TAB 250MG DR	5,730	1,354	$76,517.82	$13.35	$0.44	0.30%
DIVALPROEX TAB 250MG ER	3,427	797	$222,327.16	$64.88	$2.14	0.89%
DIVALPROEX CAP 125MG	2,229	340	$222,602.21	$99.87	$3.40	0.89%
VALPROIC ACD SOL 250MG/5ML	2,085	297	$52,585.63	$25.22	$0.87	0.21%
DIVALPROEX TAB 125MG DR	1,549	379	$15,870.50	$10.25	$0.34	0.06%
VALPROIC ACD CAP 250MG	1,041	210	$27,682.54	$26.59	$0.89	0.11%
DEPAKOTE SPR CAP 125MG	187	18	$63,666.10	$340.46	$10.79	0.25%
DEPAKOTE ER TAB 500MG	70	8	$35,630.96	$509.01	$17.47	0.14%
DEPAKOTE TAB 500MG DR	62	8	$40,114.14	$647.00	$20.89	0.16%
DEPAKOTE ER TAB 250MG	50	5	$18,294.16	$365.88	$12.24	0.07%
DEPAKOTE TAB 250MG DR	44	5	$8,810.43	$200.24	$6.38	0.04%
DEPAKOTE TAB 125MG DR	14	2	$1,470.84	$105.06	$3.50	0.01%
VALPROATE INJ 500MG/5ML	7	1	$3,417.40	$488.20	$16.92	0.01%
VALPROATE INJ 100MG/ML	5	1	$2,577.65	$515.53	$17.18	0.01%
SUBTOTAL	**31,430**	**6,280**	**$1,334,680.58**	**$42.47**	**$1.41**	**5.32%**
LAMOTRIGINE PRODUCTS						
LAMOTRIGINE TAB 100MG	10,644	2,279	$101,918.91	$9.58	$0.32	0.41%
LAMOTRIGINE TAB 25MG	7,554	2,729	$88,330.80	$11.69	$0.39	0.35%
LAMOTRIGINE TAB 200MG	7,472	1,343	$82,561.88	$11.05	$0.34	0.33%
LAMOTRIGINE TAB 150MG	4,122	844	$44,964.61	$10.91	$0.35	0.18%
LAMOTRIGINE CHW 25MG	450	74	$20,662.01	$45.92	$1.50	0.08%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
LAMICTAL TAB 200MG	130	14	$111,759.52	$859.69	$28.74	0.45%
LAMOTRIGINE TAB 300MG ER	111	21	$41,738.29	$376.02	$11.45	0.17%
LAMOTRIGINE TAB 200MG ER	110	15	$51,422.26	$467.48	$15.68	0.20%
LAMICTAL TAB 150MG	103	10	$84,107.95	$816.58	$29.05	0.33%
LAMOTRIGINE CHW 5MG	102	36	$3,197.04	$31.34	$1.05	0.01%
LAMICTAL TAB 100MG	65	7	$57,866.10	$890.25	$28.37	0.23%
LAMOTRIGINE TAB 50MG ER	63	15	$9,570.22	$151.91	$5.20	0.04%
LAMOTRIGINE TAB 50MG ODT	49	12	$13,863.77	$282.93	$9.44	0.06%
LAMOTRIGINE TAB 100MG ER	45	10	$9,275.63	$206.13	$6.87	0.04%
LAMICTAL XR TAB 200MG	33	4	$35,377.45	$1,072.04	$35.73	0.14%
LAMOTRIGINE TAB 250MG ER	26	4	$29,724.95	$1,143.27	$38.11	0.12%
LAMOTRIGINE TAB 25MG ODT	23	9	$8,707.15	$378.57	$12.44	0.03%
LAMOTRIGINE TAB 100MG	23	6	$8,590.01	$373.48	$12.45	0.03%
LAMICTAL ODT TAB 100MG	14	2	$5,171.10	$369.36	$12.31	0.02%
LAMICTAL ODT TAB 200MG	13	1	$9,607.55	$739.04	$25.62	0.04%
LAMICTAL ODT TAB 25MG	13	2	$7,210.73	$554.67	$18.49	0.03%
LAMICTAL ODT TAB 50MG	13	1	$7,553.23	$581.02	$20.14	0.03%
LAMICTAL XR TAB 300MG	13	2	$27,172.34	$2,090.18	$69.67	0.11%
LAMOTRIG ODT TAB 100MG	10	1	$4,959.61	$495.96	$16.53	0.02%
LAMOTRIGINE TAB 25MG ER	9	1	$936.88	$104.10	$3.47	0.00%
LAMICTAL TAB 25MG	6	1	$8,256.30	$1,376.05	$45.87	0.03%
LAMOTRIGINE TAB 200MG	3	1	$1,280.22	$426.74	$14.22	0.01%
LAMOTRIGINE KIT ODT 25/50/100MG	1	1	$374.95	$374.95	$12.50	0.00%
LAMICTAL XR TAB 50MG	1	1	$848.49	$848.49	$28.28	0.00%
SUBTOTAL	**31,221**	**7,446**	**$877,009.95**	**$28.09**	**$0.91**	**3.49%**
OXCARBAZEPINE PRODUCTS						
OXCARBAZEPIN TAB 300MG	11,057	2,379	$209,297.44	$18.93	$0.63	0.83%
OXCARBAZEPIN TAB 600MG	8,300	1,404	$256,629.33	$30.92	$1.03	1.02%
OXCARBAZEPIN TAB 150MG	6,884	1,841	$103,942.97	$15.10	$0.51	0.41%
OXCARBAZEPIN SUS 300MG/5ML	2,673	444	$485,418.96	$181.60	$5.81	1.93%
TRILEPTAL SUS 300MG/5ML	225	28	$132,202.20	$587.57	$19.29	0.53%
OXTELLAR XR TAB 600MG	107	20	$95,391.34	$891.51	$28.02	0.38%
TRILEPTAL TAB 600MG	94	11	$128,493.50	$1,366.95	$45.36	0.51%
OXTELLAR XR TAB 300MG	37	9	$8,711.20	$235.44	$8.03	0.03%
OXTELLAR XR TAB 150MG	20	5	$3,353.54	$167.68	$5.59	0.01%
TRILEPTAL TAB 300MG	16	2	$8,127.61	$507.98	$16.93	0.03%
SUBTOTAL	**29,413**	**6,143**	**$1,431,568.09**	**$48.67**	**$1.62**	**5.70%**
PREGABALIN PRODUCTS						
LYRICA CAP 150MG	3,089	540	$1,323,406.22	$428.43	$14.51	5.27%
LYRICA CAP 100MG	1,808	350	$831,636.53	$459.98	$15.31	3.31%
LYRICA CAP 75MG	1,637	400	$698,412.34	$426.64	$14.15	2.78%
LYRICA CAP 300MG	1,060	158	$409,625.29	$386.44	$12.87	1.63%
LYRICA CAP 200MG	856	130	$333,170.91	$389.22	$13.17	1.33%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
LYRICA CAP 50MG	752	224	$326,078.84	$433.62	$14.53	1.30%
LYRICA CAP 225MG	325	53	$143,822.17	$442.53	$14.75	0.57%
LYRICA CAP 25MG	83	28	$31,983.21	$385.34	$13.13	0.13%
LYRICA SOL 20MG/ML	2	1	$805.95	$402.98	$13.43	0.00%
SUBTOTAL	**9,612**	**1,884**	**$4,098,941.46**	**$426.44**	**$14.30**	**16.32%**
CARBAMAZEPINE PRODUCTS						
CARBAMAZEPIN TAB 200MG	4,313	812	$253,938.58	$58.88	$1.95	1.01%
CARBAMAZEPIN CHW 100MG	844	132	$42,580.61	$50.45	$1.69	0.17%
CARBAMAZEPIN TAB 400MG ER	572	86	$114,275.88	$199.78	$6.50	0.46%
EPITOL TAB 200MG	497	124	$26,903.95	$54.13	$1.80	0.11%
CARBAMAZEPIN TAB 200MG ER	482	100	$56,240.59	$116.68	$3.74	0.22%
CARBAMAZEPIN CAP 300MG ER	432	53	$39,423.02	$91.26	$3.01	0.16%
CARBAMAZEPIN CAP 200MG ER	297	50	$25,051.31	$84.35	$2.79	0.10%
CARBAMAZEPIN SUS 100MG/5ML	272	36	$29,859.09	$109.78	$3.99	0.12%
CARBAMAZEPIN TAB 100MG ER	165	39	$10,280.94	$62.31	$2.13	0.04%
CARBAMAZEPIN CAP 100MG ER	147	30	$10,870.50	$73.95	$2.49	0.04%
TEGRETOL-XR TAB 400MG	102	10	$34,573.13	$338.95	$10.88	0.14%
TEGRETOL TAB 200MG	86	8	$29,100.58	$338.38	$11.25	0.12%
TEGRETOL SUS 100MG/5ML	73	7	$24,074.72	$329.79	$10.79	0.10%
CARBATROL CAP 200MG	50	5	$9,875.47	$197.51	$6.79	0.04%
TEGRETOL-XR TAB 200MG	47	6	$13,962.44	$297.07	$8.56	0.06%
TEGRETOL-XR TAB 100MG	32	6	$3,929.56	$122.80	$4.24	0.02%
CARBATROL CAP 300MG	20	4	$3,253.39	$162.67	$5.41	0.01%
CARBATROL CAP 100MG	3	1	$347.79	$115.93	$3.86	0.00%
SUBTOTAL	**8,434**	**1,509**	**$728,541.55**	**$86.38**	**$2.87**	**2.90%**
PHENYTOIN AND FOSPHENYTOIN PRODUCTS						
PHENYTOIN EX CAP 100MG	5,065	812	$170,202.79	$33.60	$1.11	0.68%
DILANTIN CAP 100MG	439	56	$58,451.54	$133.15	$4.21	0.23%
PHENYTOIN SUS 125MG/5ML	264	35	$9,203.37	$34.86	$1.24	0.04%
PHENYTOIN CHW 50MG	241	37	$9,319.70	$38.67	$1.30	0.04%
DILANTIN CAP 30MG	78	13	$3,517.24	$45.09	$1.42	0.01%
DILANTIN CHW 50MG	70	11	$6,483.42	$92.62	$2.68	0.03%
PHENYTOIN EX CAP 200MG	62	23	$5,143.59	$82.96	$2.77	0.02%
PHENYTEK CAP 200MG	52	10	$4,959.69	$95.38	$3.18	0.02%
PHENYTEK CAP 300MG	46	13	$5,609.83	$121.95	$3.78	0.02%
PHENYTOIN EX CAP 300MG	41	21	$4,270.90	$104.17	$3.24	0.02%
CEREBYX INJ 100MG/2ML	11	1	$2,921.73	$265.61	$76.89	0.01%
DILANTIN-125 SUS 125MG/5ML	10	2	$1,364.27	$136.43	$4.55	0.01%
SUBTOTAL	**6,379**	**1,034**	**$281,448.07**	**$44.12**	**$1.46**	**1.12%**
LACOSAMIDE PRODUCTS						
VIMPAT TAB 200MG	2,051	240	$1,481,133.29	$722.15	$24.60	5.90%
VIMPAT TAB 100MG	1,343	231	$893,654.68	$665.42	$22.41	3.56%
VIMPAT SOL 10MG/ML	777	102	$513,479.49	$660.85	$22.69	2.04%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
VIMPAT TAB 150MG	730	116	$517,229.66	$708.53	$23.71	2.06%
VIMPAT TAB 50MG	620	116	$237,216.13	$382.61	$13.10	0.94%
SUBTOTAL	**5,521**	**805**	**$3,642,713.25**	**$659.79**	**$22.40**	**14.51%**
ZONISAMIDE PRODUCTS						
ZONISAMIDE CAP 100MG	3,031	427	$58,821.27	$19.41	$0.65	0.23%
ZONISAMIDE CAP 50MG	933	171	$15,130.65	$16.22	$0.53	0.06%
ZONISAMIDE CAP 25MG	397	98	$5,852.72	$14.74	$0.49	0.02%
ZONEGRAN CAP 100MG	32	3	$56,282.23	$1,758.82	$58.63	0.22%
SUBTOTAL	**4,393**	**699**	**$136,086.87**	**$30.98**	**$1.04**	**0.54%**
PHENOBARBITAL PRODUCTS						
PHENOBARB TAB 64.8MG	759	90	$33,135.17	$43.66	$1.44	0.13%
PHENOBARB TAB 32.4MG	536	74	$25,231.71	$47.07	$1.58	0.10%
PHENOBARB SOL 20MG/5ML	513	119	$26,389.43	$51.44	$1.77	0.11%
PHENOBARB ELX 20MG/5ML	512	107	$34,769.97	$67.91	$2.34	0.14%
PHENOBARB TAB 97.2MG	258	35	$12,413.68	$48.12	$1.42	0.05%
PHENOBARB TAB 30MG	167	28	$3,287.90	$19.69	$0.71	0.01%
PHENOBARB TAB 60MG	102	18	$1,754.36	$17.20	$0.58	0.01%
PHENOBARB TAB 16.2MG	75	12	$1,631.22	$21.75	$0.75	0.01%
PHENOBARB TAB 100MG	57	10	$821.60	$14.41	$0.43	0.00%
PHENOBARB TAB 15MG	51	11	$908.51	$17.81	$0.57	0.00%
PHENOBARB INJ 65MG/ML	1	1	$91.46	$91.46	$91.46	0.00%
SUBTOTAL	**3,031**	**505**	**$140,435.01**	**$46.33**	**$1.55**	**0.56%**
CLOBAZAM PRODUCTS						
ONFI TAB 10MG	912	135	$827,671.58	$907.53	$30.59	3.30%
ONFI TAB 20MG	907	103	$1,517,778.90	$1,673.41	$56.22	6.04%
ONFI SUS 2.5MG/ML	617	88	$965,762.62	$1,565.26	$52.29	3.85%
SUBTOTAL	**2,436**	**326**	**$3,311,213.10**	**$1,359.28**	**$45.66**	**13.19%**
DIAZEPAM PRODUCTS						
DIAZEPAM GEL 10MG	1,311	755	$470,186.72	$358.65	$57.94	1.87%
DIAZEPAM GEL 20MG	342	92	$159,067.44	$465.11	$54.07	0.63%
DIASTAT ACDL GEL 5-10MG	148	85	$85,488.57	$577.63	$50.44	0.34%
DIAZEPAM GEL 2.5MG	114	89	$60,113.58	$527.31	$47.30	0.24%
DIASTAT ACDL GEL 12.5-20MG	80	36	$43,453.23	$543.17	$77.73	0.17%
DIASTAT PED GEL 2.5MG	38	24	$12,693.36	$334.04	$47.36	0.05%
SUBTOTAL	**2,033**	**1,081**	**$831,002.90**	**$408.76**	**$55.96**	**3.31%**
ETHOSUXIMIDE PRODUCTS						
ETHOSUXIMIDE CAP 250MG	663	129	$65,725.78	$99.13	$3.17	0.26%
ETHOSUXIMIDE SOL 250MG/5ML	493	90	$41,450.60	$84.08	$2.77	0.17%
ZARONTIN CAP 250MG	32	6	$9,300.27	$290.63	$9.05	0.04%
SUBTOTAL	**1,188**	**225**	**$116,476.65**	**$98.04**	**$3.18**	**0.46%**
PRIMIDONE PRODUCTS						
PRIMIDONE TAB 50MG	651	138	$7,338.32	$11.27	$0.35	0.03%
PRIMIDONE TAB 250MG	288	44	$4,869.03	$16.91	$0.52	0.02%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
MYSOLINE TAB 250MG	21	2	$70,158.92	$3,340.90	$111.36	0.28%
SUBTOTAL	**960**	**184**	**$82,366.27**	**$85.80**	**$2.65**	**0.33%**
ACETAZOLAMIDE PRODUCTS						
ACETAZOLAMID TAB 250MG	489	135	$65,386.41	$133.71	$4.51	0.26%
ACETAZOLAMID CAP 500MG ER	295	92	$38,817.52	$131.58	$4.36	0.15%
ACETAZOLAMID TAB 125MG	71	26	$11,277.05	$158.83	$5.56	0.04%
SUBTOTAL	**855**	**253**	**$115,480.98**	**$135.07**	**$4.54**	**0.46%**
RUFINAMIDE PRODUCTS						
BANZEL TAB 400MG	379	48	$891,008.30	$2,350.95	$78.48	3.55%
BANZEL SUS 40MG/ML	271	33	$526,444.70	$1,942.60	$64.86	2.10%
BANZEL TAB 200MG	101	14	$85,203.87	$843.60	$28.55	0.34%
SUBTOTAL	**751**	**95**	**$1,502,656.87**	**$2,000.87**	**$66.92**	**5.98%**
FELBAMATE PRODUCTS						
FELBAMATE TAB 600MG	234	27	$79,039.33	$337.77	$10.91	0.31%
FELBAMATE SUS 600MG/5ML	134	14	$103,814.50	$774.74	$26.85	0.41%
FELBAMATE TAB 400MG	74	10	$11,183.83	$151.13	$4.97	0.04%
FELBATOL TAB 400MG	37	4	$37,733.97	$1,019.84	$33.99	0.15%
FELBATOL TAB 600MG	23	3	$25,905.89	$1,126.34	$37.54	0.10%
SUBTOTAL	**502**	**58**	**$257,677.52**	**$513.30**	**$17.00**	**1.03%**
PERAMPANEL PRODUCTS						
FYCOMPA TAB 8MG	154	27	$89,564.98	$581.59	$19.45	0.36%
FYCOMPA TAB 6MG	98	26	$52,709.01	$537.85	$18.03	0.21%
FYCOMPA TAB 10MG	75	11	$42,284.95	$563.80	$18.79	0.17%
FYCOMPA TAB 4MG	53	17	$29,257.50	$552.03	$18.83	0.12%
FYCOMPA TAB 12MG	38	5	$28,641.34	$753.72	$25.12	0.11%
FYCOMPA TAB 2MG	26	8	$9,281.23	$356.97	$11.90	0.04%
FYCOMPA SUS 0.5MG/ML	8	2	$7,628.60	$953.58	$31.79	0.03%
SUBTOTAL	**452**	**96**	**$259,367.61**	**$573.82**	**$19.22**	**1.03%**
BRIVARACETAM PRODUCTS						
BRIVIACT TAB 50MG	160	47	$138,772.54	$867.33	$29.38	0.55%
BRIVIACT TAB 100MG	93	26	$88,503.08	$951.65	$32.04	0.35%
BRIVIACT SOL 10MG/ML	23	6	$16,461.45	$715.72	$24.79	0.07%
BRIVIACT TAB 75MG	13	4	$11,798.26	$907.56	$30.25	0.05%
BRIVIACT TAB 10MG	4	2	$3,981.98	$995.50	$33.18	0.02%
BRIVIACT TAB 25MG	3	1	$308.07	$102.69	$3.42	0.00%
SUBTOTAL	**296**	**86**	**$259,825.38**	**$877.79**	**$29.69**	**1.03%**
VIGABATRIN PRODUCTS						
SABRIL POW 500MG	120	16	$1,662,088.23	$13,850.74	$461.95	6.62%
SABRIL TAB 500MG	25	6	$470,984.14	$18,839.37	$641.67	1.88%
SUBTOTAL	**145**	**22**	**$2,133,072.37**	**$14,710.84**	**$492.40**	**8.50%**
ESLICARBAZEPINE PRODUCTS						
APTIOM TAB 800MG	65	12	$60,285.85	$927.47	$30.42	0.24%
APTIOM TAB 600MG	49	9	$77,189.96	$1,575.31	$54.74	0.31%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	COST/ DAY	% COST
APTIOM TAB 400MG	21	5	$17,318.94	$824.71	$27.49	0.07%
APTIOM TAB 200MG	4	2	$3,231.68	$807.92	$26.93	0.01%
SUBTOTAL	**139**	**28**	**$158,026.43**	**$1,136.88**	**$38.15**	**0.63%**
TIAGABINE PRODUCTS						
TIAGABINE TAB 4MG	58	8	$29,084.58	$501.46	$17.29	0.12%
GABITRIL TAB 16MG	27	3	$7,832.47	$290.09	$9.67	0.03%
GABITRIL TAB 12MG	23	3	$9,761.71	$424.42	$14.15	0.04%
TIAGABINE TAB 2MG	9	2	$2,732.98	$303.66	$10.12	0.01%
SUBTOTAL	**117**	**16**	**$49,411.74**	**$422.32**	**$14.31**	**0.20%**
METHSUXIMIDE PRODUCTS						
CELONTIN CAP 300MG	38	4	$11,708.89	$308.13	$10.25	0.05%
SUBTOTAL	**38**	**4**	**$11,708.89**	**$308.13**	**$10.25**	**0.05%**
TOTAL	**332,721**	**46,730***	**$25,109,540.98**	**$75.47**	**$2.50**	**100%**

^SoonerCare was not the primary coverage on claims for this medication; therefore, costs do not reflect actual drug costs.
*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.

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Appendix I

Fiscal Year 2017 Annual Review of Osteoporosis Medications and 30-Day Notice to Prior Authorize Tymlos™ (Abaloparatide)

Oklahoma Health Care Authority
February 2018

Current Prior Authorization Criteria

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax® + D)	alendronate effervescent tabs (Binosto®)
calcium + vitamin D*	ibandronate tabs (Boniva®)	alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)	risedronate tabs (Actonel®)	alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		teriparatide inj (Forteo®)

*Must be used in combination with a bisphosphonate to count as a Tier-1 trial.
tabs = tablets; inj = injection; soln = solution; DR = delayed-release
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Osteoporosis Medications Tier-2 Approval Criteria:

1. A trial of at least one Tier-1 medication, compliantly used for at least 6 months concomitantly with calcium + vitamin D, that failed to prevent fracture or improve bone mineral density (BMD) scores; or
2. Hypersensitivity to or intolerable adverse effects with all Tier-1 medications.
3. Quantity limits apply based on FDA approved maximum doses.

Osteoporosis Medications Special Prior Authorization (PA) Approval Criteria:

1. **Forteo® (Teriparatide):**
    a. A Bone Mineral Density test (T-score at or below -2.5) within the last month; and
    b. One of the following (if a 12-month bisphosphonate trial is inappropriate for the member, the member must have trial of Prolia® or a patient-specific, clinically significant reason why Prolia® is not appropriate):
        i. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D; or
        ii. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or
    c. The diagnosis of non-healing fracture may be approved for 6 months.
    d. Approval will be for a maximum of 2 years of therapy.
2. **Prolia® (Denosumab) and Boniva® IV (Ibandronate Injection):**
    a. A minimum of a 12-month trial with a Tier-1 or Tier-2 bisphosphonate plus adequate calcium and vitamin D; or

b. Contraindication to or intolerable adverse effects with Tier-1 and Tier-2 medications.
c. Clinical exceptions may apply for members with:
    i. Severe esophageal disease (e.g., ulcerations, strictures); or
    ii. Inability to take anything by mouth; or
    iii. Inability to sit or stand for prolonged periods; or
    iv. Inability to take bisphosphonates orally or other special medical circumstances that justify this method of administration.

3. **Atelvia® (Risedronate Delayed-Release Tablets), Binosto® (Alendronate Effervescent Tablets), and Actonel® (Risedronate 30mg Tablets):**
    a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 medications.
    b. Members with diagnosis in history of Paget's disease will not require prior authorization.
4. **Fosamax® (Alendronate Oral Solution):**
    a. An FDA approved diagnosis of osteoporosis or Paget's disease; and
    b. A patient-specific, clinically significant reason the member cannot use the oral tablet formulation.
5. **Fosamax® (Alendronate 40mg Tablets):**
    a. A patient-specific, clinically significant reason why the member cannot use all other available Tier-1 and Tier-2 products including a 35mg alendronate tablet in combination with a 5mg alendronate tablet to achieve a 40mg dose.
6. **Quantity Limits apply based on U.S. Food and Drug Administration (FDA) approved maximum doses.**

Utilization of Osteoporosis Medications: Fiscal Year 2017

Comparison of Fiscal Years: Pharmacy Claims

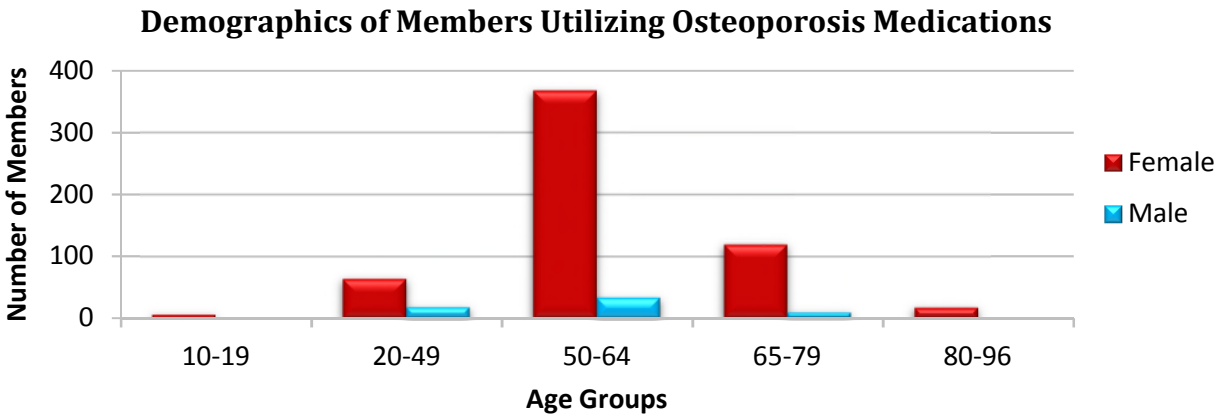
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	636	3,268	$422,766.97	$129.37	$4.24	21,414	99,792
2017	632	3,165	$305,865.24	$96.64	$3.11	19,992	98,315
% Change	**-0.60%**	**-3.20%**	**-27.70%**	**-25.30%**	**-26.70%**	**-6.60%**	**-1.50%**
Change	**-4**	**-103**	**-$116,901.73**	**-$32.73**	**-$1.13**	**-1,422**	**-1,477**

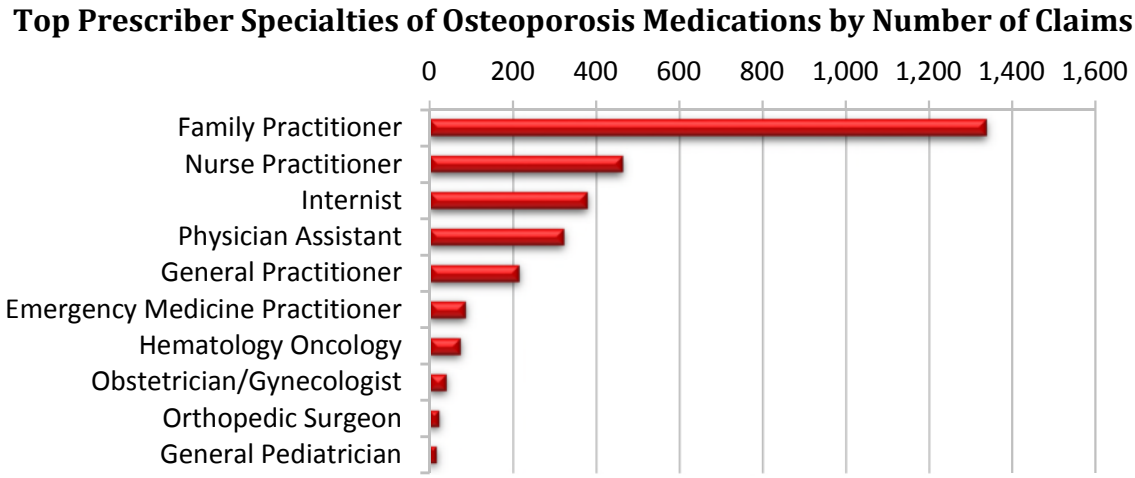
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Fiscal Year 2017 Utilization: Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Claims/Member
92	309	$537,353.39	$1,739.01	3.4

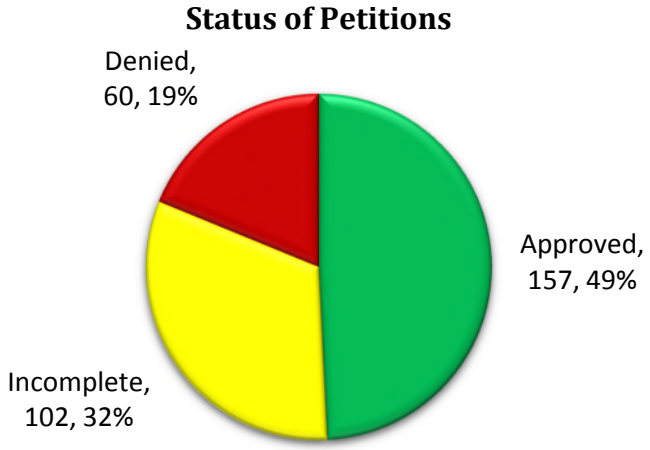
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Osteoporosis Medications

There were 319 prior authorization requests submitted for osteoporosis medications during fiscal year 2017. Computer edits are in place to detect lower tiered medications or diagnosis information in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2017.



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

Anticipated Patent Expiration(s):

- Fosamax® Plus D (alendronate/vitamin D tablets): January 2019
- Binosto® (alendronate effervescent tablets): August 2023
- Forteo® (teriparatide injection): March 2025
- Reclast® (zoledronic acid injection): August 2028

New U.S. Food and Drug Administration (FDA) Approval(s):

- Tymlos™ (abaloparatide): April 2017
- Xgeva® (denosumab): January 2018 (expanded indication)
    - The FDA expanded the approved indication of denosumab for the prevention of skeletal-related events in patients with bone metastases from solid tumors to include patients with multiple myeloma.

Guideline Update(s):

- **April 2017:** The *Journal of Bone Oncology* published a joint position statement by seven international and European organizations identifying fracture-related risk factors in patients treated by aromatase-inhibitors (AI). Women receiving adjuvant AI therapy for breast cancer experience a two-to-four-fold increase in bone loss compared to the normal rate of bone loss with menopause, and as a result are at heightened risk of fracture. The conclusions of the joint position statement include:
    - In all patients initiating AI treatment, fracture risk should be assessed and recommendations given in regard to exercise and calcium/vitamin D supplementation.
    - Bone-directed therapy should be recommended for the duration of AI treatment to all patients with a T-score <-2.0, or with a T-score of <-1.5 with one additional risk factor, or with two or more risk factors [without low bone mineral density (BMD)].
    - Patients with a T-score >-1.5 and no risk factors should be managed based on BMD loss during the first year, and based on local guidelines for postmenopausal osteoporosis.
    - Based on current evidence, twice yearly denosumab or once yearly zoledronate for the duration of AI therapy is recommend for the prevention of aromatase inhibitor-associated bone loss (AIBL).
- **June 2017:** The American College of Physicians (ACP) published updated guideline recommendations on the treatment of low bone density and osteoporosis to prevent fractures in men and women. The recommendations do not include use of ibandronate, raloxifene, or hormone replacement therapy (HRT). Additionally, anabolic agents, such as teriparatide, are not recommended as first-line treatment. The guideline authors also concluded that evidence is insufficient to recommend calcium and vitamin D or physical activity to prevent fracture in any group of patients.
    - <u>Recommendation 1:</u> Prescribers should offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis.

- Recommendation 2: Osteoporotic women should be treated with pharmacologic therapy for 5 years.
- Recommendation 3: Pharmacologic treatment with bisphosphonates should be offered to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis.
- Recommendation 4: ACP recommends against bone density monitoring during the 5-year pharmacologic treatment period for osteoporosis in women.
- Recommendation 5: ACP recommends against using menopausal estrogen therapy or menopausal estrogen plus progestin therapy or raloxifene for the treatment of osteoporosis in women.
- Recommendation 6: The decision to treat osteopenic women 65 years of age or older who are at a high risk for fracture should be based on a discussion of patient preferences, fracture risk profile, benefits, harms, and costs of medications.

- **August 2017:** The American College of Rheumatology (ACR) published guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis (GIOP). The guideline recommendations for adults and special patient populations include:
  - Strong recommendations (all age groups):
    - Calcium and vitamin D intake should be optimized and lifestyle modifications should be implemented (e.g., weight-bearing and strength-building exercise, smoking cessation, limiting alcohol intake).
    - Men and women (not of childbearing potential) at moderate-to-high fracture risk should be treated with oral bisphosphonates, intravenous (IV) bisphosphonates, teriparatide, or denosumab. Raloxifene is recommended for postmenopausal women for whom none of the other medications are appropriate.
  - Conditional recommendations (special populations):
    - Adult women of childbearing potential at moderate-to-high risk who are not planning a pregnancy during osteoporosis treatment should be treated with oral bisphosphonates.
    - Solid organ transplant patients who are continuing glucocorticoid treatment and have a glomerular filtration rate (GFR) >30mL/min/1.73m^2 should be treated according to the recommendations for their age group.
    - For children 4 to 17 years of age, calcium and vitamin D intake should be optimized, and oral bisphosphonates should be added if the child has sustained an osteoporotic fracture and is continuing glucocorticoids at ≥0.1mg/kg for ≥3 months.
    - Patients who are treated with very high-dose glucocorticoids (≥30mg of prednisone and a cumulative dose of >5g in a year) and are age 30 or older should be treated with oral bisphosphonates.
  - Special considerations:
    - Those who fail treatment, have a fracture after 18 months of oral bisphosphonates, or have a significant BMD loss of more than 10% in a year should be treated with teriparatide, denosumab, or IV bisphosphonates.

- Patients who have completed oral bisphosphonate treatment but remain at high fracture risk should continue an active treatment.
- Patients who have discontinued glucocorticoid treatment should stop osteoporosis treatment if reassessment shows they are now at low risk, or should complete the treatment if they are at moderate-to-high risk for fracture.

News:

- **September 2017:** The administration of Tymlos™ (abaloparatide) for 18 months followed by alendronate for 2 years was associated with dramatic reductions in fracture risk among postmenopausal women, according to the ACTIVE trial. More than 1,100 women completed the placebo-controlled phase of the trial and enrolled in the extension phase of the study. Of those initially randomized to abaloparatide followed by alendronate, 0.9% had a new vertebral fracture during the subsequent 2 years compared with 5.6% of those who had initially been given placebo before receiving alendronate. This represented an 84% relative risk reduction ($p<0.0001$) with sequential therapy.
- **November 2017:** A study presented at the ACR annual meeting reported that analysis of more than 150,000 female Medicare beneficiaries identified through records as "highly adherent, long-term bisphosphonate users" showed that those stopping treatment for more than 2 years were 40% more like to develop hip fractures after adjustment for potential confounders, compared with otherwise similar women who stayed on the medications**.** It was noted that avoiding drug holidays may increase risks associated with bisphosphonates such as osteonecrosis of the jaw. Quantitative risks and benefits of drug stoppage have not been established, nor have the optimal holiday duration or the factors that may go into estimating it.
- **December 2017:** A systematic review and meta-analysis published in *The Journal of the American Medical Association* (*JAMA)* found the use of supplements that included calcium, vitamin D, or both was not associated with a significant difference in the risk of hip fractures compared with placebo or no treatment. The meta-analysis included 33 randomized clinical trials that included 51,145 community-dwelling adults older than 50 years of age. Hip fracture was defined as the primary outcome. Secondary outcomes were nonvertebral fracture, vertebral fracture, and total fracture. No significant associations were found between calcium, vitamin D, or combined calcium and vitamin D supplements and the incidence of nonvertebral, vertebral, or total fractures.
- **January 2018:** *The Lancet* published the results of the Screening for Osteoporosis in Older Women for the Prevention of Fracture (SCOOP) trial which recruited 12,483 women 70 to 85 years of age from 100 general practices. Each participant's 10-year probability of sustaining either a hip or another major osteoporotic fracture was determined by the fracture risk assessment tool (FRAX). Based on this score, women were deemed to be "low risk" or "high risk." The primary endpoint was the proportion of participants who had at least one osteoporosis-related fracture over the 5-year follow-up. After a follow-up of 5 years, rates of any osteoporosis-related fracture were similar at 12.9% in women randomly assigned to the screening group compared with

those who received usual care. On the other hand, at the end of 5 years, there was a 28% relative risk reduction in hip fracture among women who had been screened compared with the usual care group at 2.6% vs 3.5%, respectively (p=0.002).

Pipeline:

- **Evenity™ (romosozumab):** Romosozumab is an investigational humanized monoclonal antibody that inhibits sclerosin, giving it a unique mechanism of action. It rapidly increases bone formation and reduces bone resorption simultaneously, increases BMD, and reduces the risk of fracture. In July 2017 a complete response letter was issued to Amgen and its partner UCB by the FDA, rejecting romosozumab due to increased risk of cardiovascular adverse events. In the FRAME trial, romosozumab reduced the rate of vertebral fractures by 73% compared with placebo. The FDA has requested data from all three trials for romosozumab to further evaluate the risk-benefit profile.

Tymlos™ (Abaloparatide) Product Summary[13]

Indication(s): Tymlos™ (abaloparatide) is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

- Limitation of Use: Because of the unknown relevance of the rodent osteosarcoma findings to humans, cumulative use of abaloparatide and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

Dosing:

- Tymlos™ is supplied as a pre-assembled single-patient-use disposable pen. Each disposable pen contains a glass cartridge that contains 3,120mcg of abaloparatide in 1.56mL (2,000mcg/mL) of sterilized, clear, colorless fluid. Each pen provides a 30-day supply for once daily injections of 80mcg abaloparatide in 40mcL.
- The recommended dosage of abaloparatide is 80mcg subcutaneously (SQ) once daily into the periumbilical region of the abdomen.
- Supplemental calcium and vitamin D is recommended if dietary intake is inadequate.
- The site of the injection should be rotated every day and the injection should be administered at approximately the same time every day.
- The first several doses should be administered while seated or lying down if necessary, in case symptoms of orthostatic hypotension occur.

Mechanism of Action: Abaloparatide is a PTHrP (1-34) analog which acts as an agonist at the PTH1 receptor (PTH1R). This results in activation of the cAMP signaling pathway in target cells. In rats and monkeys, abaloparatide had an anabolic effect on bone, demonstrated by increases in BMD and bone mineral content (BMC) that correlated with increases in bone strength at vertebral and/or non-vertebral sites.

Boxed Warning: Risk of Osteosarcoma

- Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma, a malignant bone tumor, in male and female rats. It is unknown whether abaloparatide will cause osteosarcoma in humans.
- Use of abaloparatide is not recommended in patients at increased risk for osteosarcoma.
- Cumulative use of abaloparatide and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

Contraindication(s): None.

Warnings and Precautions:

- Risk of Osteosarcoma: Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma in male and female rats after SQ administration at exposures 4 to 28 times the human exposure at the clinical dose of 80mcg. It is unknown whether it will cause osteosarcoma in humans. Abaloparatide is not recommended in patients at increased risk of osteosarcoma including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, open epiphyses, bone metastases or skeletal malignancies, hereditary disorders predisposing to osteosarcoma, or prior external beam or implant radiation therapy involving the skeleton.
- Orthostatic Hypotension: Orthostatic hypotension may occur with abaloparatide, typically within 4 hours of injection. Associated symptoms may include dizziness, palpitations, tachycardia, or nausea.
- Hypercalcemia: Abaloparatide may cause hypercalcemia. It is not recommended in patients with preexisting hypercalcemia or in patients who have an underlying hypercalcemic disorder, such as primary hyperparathyroidism, because of the possibility of exacerbating hypercalcemia.
- Hypercalciuria and Urolithiasis: Abaloparatide may cause hypercalciuria. It is unknown whether abaloparatide may exacerbate urolithiasis in patients with active or a history of urolithiasis. If active urolithiasis or pre-existing hypercalciuria is suspected, measurement of urinary calcium excretion is recommended.

Adverse Reactions: Common adverse reactions reported in ≥2% of abaloparatide-treated postmenopausal women with osteoporosis include the following:

- Hypercalciuria
- Dizziness
- Nausea
- Headache
- Palpitations
- Fatigue
- Abdominal pain
- Vertigo

Use in Specific Populations:

- Pregnancy: Abaloparatide is not indicated for use in females of reproductive potential. There are no human data with abaloparatide use in pregnant women to inform any drug associated risks. Animal reproduction studies with abaloparatide have not been conducted.

- Lactation: Abaloparatide is not indicated for use in females of reproductive potential. There is no information on the presence of abaloparatide in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of abaloparatide have not been established in pediatric patients. Abaloparatide is not recommended for use in pediatric patients with open epiphyses or hereditary disorders predisposing to osteosarcoma because of an increased baseline risk of osteosarcoma.
- Geriatric Use: Of the total number of patients in the postmenopausal osteoporosis clinical studies of abaloparatide, 82% were age 65 years and older, and 19% were age 75 years and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.
- Renal Impairment: No dosage adjustment is required for patients with mild, moderate, or severe renal impairment. Patients with severe renal impairment may have increased abaloparatide exposure that may increase the risk of adverse reactions. Therefore, it is recommended to monitor these patients for adverse reactions.

Efficacy: The efficacy of abaloparatide for the treatment of postmenopausal osteoporosis was evaluated in an 18-month, randomized, multicenter, double-blind, placebo-controlled clinical trial in postmenopausal women 49 to 86 years of age (mean age of 69) who were randomized to receive abaloparatide 80mcg (N = 824) or placebo (N = 821) given SQ once daily. At baseline, 24% of patients had at least one prevalent vertebral fracture and 48% had at least one prior nonvertebral fracture. Patients took daily supplemental calcium (500 to 1000mg) and vitamin D (400 to 800 IU). The efficacy study was extended as an open-label study where patients were no longer receiving abaloparatide or placebo but were maintained in their original randomized treatment group and received 70mg alendronate weekly, with calcium and vitamin D supplements for 6 months.

- Effect on New Vertebral Fractures: The primary endpoint was the incidence of new vertebral fractures in patients treated with abaloparatide compared to placebo. Abaloparatide resulted in a significant reduction in the incidence of new vertebral fractures compared to placebo at 18 months ($p<0.0001$). The absolute risk reduction in new vertebral fractures was 3.6% at 18 months and the relative risk reduction was 86% for abaloparatide compared to placebo. The incidence of new vertebral fractures at 25 months was 0.6% in patients treated with abaloparatide then alendronate, compared to 4.4% in patients treated with placebo then alendronate ($p<0.0001$).
- Effect on Nonvertebral Fractures: Abaloparatide resulted in a significant reduction in the incidence of nonvertebral fractures at the end of the 18 months of treatment plus one month follow-up where no drug was administered (2.7% for abaloparatide-treated patients compared to 4.7% for placebo-treated patients). The cumulative incidence of nonvertebral fractures at 25 months was 2.7% for patients treated with abaloparatide then alendronate, compared to 5.6% in patients treated with placebo then alendronate.
- Effect on BMD: Treatment with abaloparatide for 18 months resulted in significant increases in BMD compared to placebo at the lumbar spine, total hip, and femoral neck, each with $p<0.0001$. Similar findings were seen with the 25-month study.

Cost Comparison:

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Tymlos™ (abaloparatide) injection	**$1,041.67**	**$1,625.01**	**$19,500.12**
Forteo® (teriparatide) injection	$1,204.89	$2,891.74	$34,700.88
Prolia® (denosumab) injection	$1,089.62	$181.60*	$2,179.24
zoledronic acid intravenous solution	$3.00	$25.00+	$300.00

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.
*Prolia® (denosumab) dosed every six months; therefore, cost per 30 days based on cost per year.
+Zoledronic acid dosed yearly; therefore, cost per 30 days based on cost per year.

Recommendations

The College of Pharmacy recommends the placement of Tymlos™ (abaloparatide) into the Special Prior Authorization (PA) Tier of the Osteoporosis Product Based Prior Authorization (PBPA) category with the following criteria:

Tymlos™ (Abaloparatide) Approval Criteria:

1. A diagnosis of postmenopausal osteoporosis confirmed by the following:
    a. History of vertebral fracture(s) or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years; or
    b. A Bone Mineral Density test (T-score at or below -2.5) within the last month in the spine, femoral neck, total hip, or 33% radius; or
    c. Those with a T-score between -1.0 and -2.5 in the spine, femoral neck, total hip, or 33% radius, if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3%; and
2. One of the following [if a 12-month bisphosphonate trial is inappropriate for the member, the member must have trial of Prolia® or a selective estrogen receptor modulator (SERM) or a patient-specific, clinically significant reason why Prolia® or a SERM is not appropriate]:
    a. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D; or
    b. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or
    c. A 12-month trial of a SERM, unless contraindicated, intolerant, or allergic, that did not yield adequate results; and
3. A patient-specific, clinically significant reason why the member cannot use Forteo® (teriparatide) must be provided; and
4. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
5. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy; and
6. A quantity limit of one pen per 30 days will apply.

The College of Pharmacy also recommends the following criteria updates based on the new FDA approved indication for Xgeva® (denosumab) and net cost after rebates for Forteo® (teriparatide):

Xgeva® (Denosumab) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors; or
    b. Treatment of adults and skeletally mature adolescents with giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity; or
        i. Prescriber must document that tumor is unresectable or that surgical resection is likely to result in severe morbidity.
    c. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.
        ii. Member must have albumin-corrected calcium of greater than 12.5mg/dL (3.1mmol/L) despite treatment with intravenous bisphosphonate therapy in the last 30 days prior to initiation of Xgeva® therapy.

Forteo® (Teriparatide) Approval Criteria:

1. ~~A Bone Mineral Density test (T-score at or below -2.5) within the last month; and~~
2. A diagnosis of one of the following:
    a. Treatment of postmenopausal women with osteoporosis at high risk for fracture; or
    b. To increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture; or
    c. Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture; or
    d. Treatment of non-healing fracture; and ~~or Prolia®~~.
3. ~~One of the following (if a 12-month bisphosphonate trial is inappropriate for the member, the member must have trial of Prolia® or a patient-specific, clinically significant reason why Prolia® is not appropriate):~~
4. A minimum 12-month trial with a bisphosphonate plus adequate calcium and vitamin D or a patient-specific, clinically significant reason the member cannot use a bisphosphonate; and
    ~~a. A 12-month trial of Prolia® (denosumab), unless contraindicated, intolerant, or allergic, that did not yield adequate results; or~~
5. The diagnosis of non-healing fracture may be approved for 6 months; and
6. Treatment duration including other parathyroid hormone analogs has not exceeded a total of 24 months during the patient's lifetime; and
7. Approval will be for a maximum of 2 years of parathyroid hormone analog therapy.

Finally, the College of Pharmacy recommends moving ibandronate tablets (Boniva®) from Tier-2 to Tier-1 based on national average drug acquisition cost (NADAC).

Osteoporosis Medications		
Tier-1	**Tier-2**	**Special PA**
alendronate tabs (Fosamax®)	alendronate + vitamin D tabs (Fosamax® + D)	**abaloparatide inj (Tymlos™)**
calcium + vitamin D*	risedronate tabs (Actonel®)	alendronate effervescent tabs (Binosto®)
ibandronate tabs (Boniva®)		alendronate soln (Fosamax®)
zoledronic acid inj (Reclast®)		alendronate 40mg tabs (Fosamax®)
		denosumab inj (Prolia®)
		ibandronate inj (Boniva® IV)
		risedronate 30mg tabs (Actonel®)
		risedronate DR tabs (Atelvia®)
		teriparatide inj (Forteo®)

*Must be used in combination with a bisphosphonate to count as a Tier-1 trial.
tabs = tablets; inj = injection; soln = solution; DR = delayed-release
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Utilization Details of Osteoporosis Medications: Fiscal Year 2017

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
ALENDRONATE PRODUCTS					
ALENDRONATE TAB 70MG	2,430	481	$16,239.29	$0.24	$6.68
ALENDRONATE TAB 35MG	285	57	$2,109.86	$0.26	$7.40
ALENDRONATE TAB 10MG	107	24	$1,047.77	$0.33	$9.79
ALENDRONATE TAB 5MG	35	5	$318.16	$0.31	$9.09
SUBTOTAL	**2,857**	**567**	**$19,715.08**	**$0.24**	**$6.90**
ZOLEDRONIC ACID PRODUCTS$^{\Delta}$					
ZOLEDRONIC INJ 5MG/100ML	1	1	$73.61	$0.20	$73.61
SUBTOTAL	**1**	**1**	**$73.61**	**$0.20**	**$73.61**
TIER-1 SUBTOTAL	**2,858**	**568**	**$19,788.69**	**$0.24**	**$6.92**
TIER-2 PRODUCTS					
IBANDRONATE PRODUCTS					
IBANDRONATE TAB 150MG	83	21	$3,825.85	$0.75	$46.09
SUBTOTAL	**83**	**21**	**$3,825.85**	**$0.75**	**$46.09**
RISEDRONATE PRODUCTS					
RISEDRONATE TAB 35MG	47	6	$2,977.74	$2.26	$63.36
RISEDRONATE TAB 150MG	19	3	$2,002.75	$3.51	$105.41
RISEDRONATE TAB 5MG	11	1	$1,160.69	$3.70	$105.52
SUBTOTAL	**77**	**10**	**$6,141.18**	**$2.79**	**$79.76**
ALENDRONATE PRODUCTS					
FOSAMAX + D TAB 70MG-5600IU	1	1	$168.40	$6.01	$168.40
SUBTOTAL	**1**	**1**	**$168.40**	**$6.01**	**$168.40**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-2 SUBTOTAL	**161**	**32**	**$10,135.43**	**$1.38**	**$62.95**
SPECIAL PA PRODUCTS					
TERIPARATIDE PRODUCTS					
FORTEO SOL 600MCG/2.4ML	87	17	$235,859.69	$95.96	$2,711.03
SUBTOTAL	**87**	**17**	**$235,859.69**	**$95.96**	**$2,711.03**
DENOSUMAB PRODUCTS					
PROLIA SOL 60MG/ML	36	26	$36,216.23	$5.71	$1,006.01
SUBTOTAL	**36**	**26**	**$36,216.23**	**$5.71**	**$1,006.01**
ALENDRONATE PRODUCTS					
ALENDRONATE SOL 70MG/75ML	13	2	$1,247.37	$3.41	$95.95
ALENDRONATE TAB 40MG	9	2	$1,045.15	$2.77	$116.13
SUBTOTAL	**22**	**4**	**$2,292.52**	**$3.09**	**$104.21**
RISEDRONATE PRODUCTS					
RISEDRONATE TAB 30MG	1	1	$1,572.68	$52.42	$1,572.68
SUBTOTAL	**1**	**1**	**$1,572.68**	**$52.42**	**$1,572.68**
SPECIAL PA SUBTOTAL	**146**	**48**	**$275,941.12**	**$28.83**	**$1,890.01**
TOTAL	**3,165**	**632***	**$305,865.24**	**$3.11**	**$96.64**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Δ Zoledronic acid IV solution was moved from Tier-2 to Tier-1 by OHCA on October 9, 2017. The utilization above occurred during fiscal year 2017, but is shown under the Tier-1 products to reflect the current tier placement.

Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
XGEVA J0897	268	57	$513,738.28	$1,916.93
PROLIA J0897	35	29	$23,195.01	$662.71
ZOLEDRONIC ACID J3489	5	5	$353.05	$70.61
RECLAST J3489	1	1	$67.05	$67.05
TOTAL	**309**	**92***	**$537,353.39**	**$1,739.01**

*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: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 12/2017. Last accessed 01/24/2018.
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Appendix J

Fiscal Year 2017 Annual Review of Antiviral Medications and 30-Day Notice to Prior Authorize Prevymis™ (Letermovir Tablets and Injection)

Oklahoma Health Care Authority
February 2018

Current Prior Authorization Criteria

RibaPak® (Ribavirin Dose Pack), Rebetol® (Ribavirin Solution), and Ribasphere® (Ribavirin 400mg and 600mg Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the 200mg tablets or 200mg capsules in place of the unique dosage formulations.

Sitavig® (Acyclovir Buccal Tablets), Xerese® (Acyclovir/Hydrocortisone Cream), and Denavir® (Penciclovir Cream) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets.

Zovirax® (Acyclovir Ointment) Approval Criteria:

1. An FDA approved indication of management of initial genital herpes or in limited non-life-threatening mucocutaneous herpes simplex virus (HSV) infections in immunocompromised patients; and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets.

Zovirax® (Acyclovir Suspension) Approval Criteria:

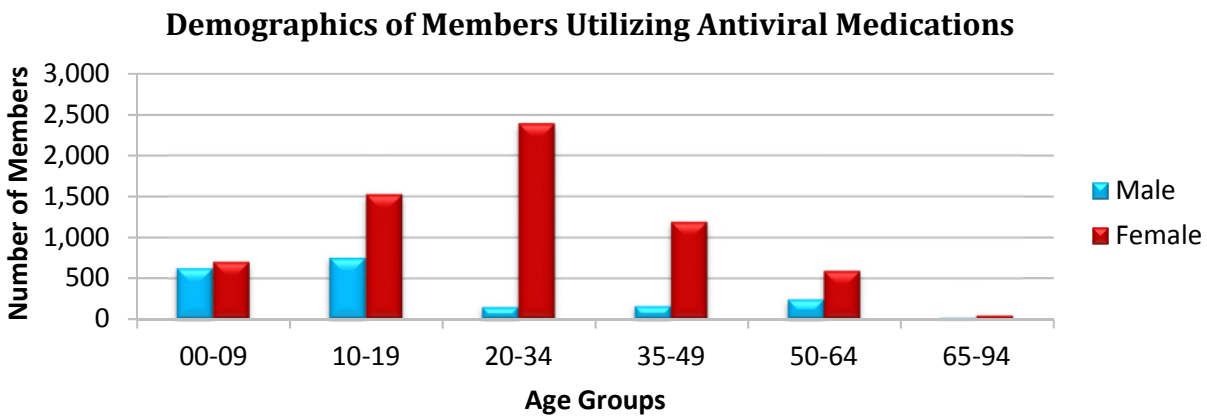
1. An age restriction of seven years and younger will apply. Members older than seven years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

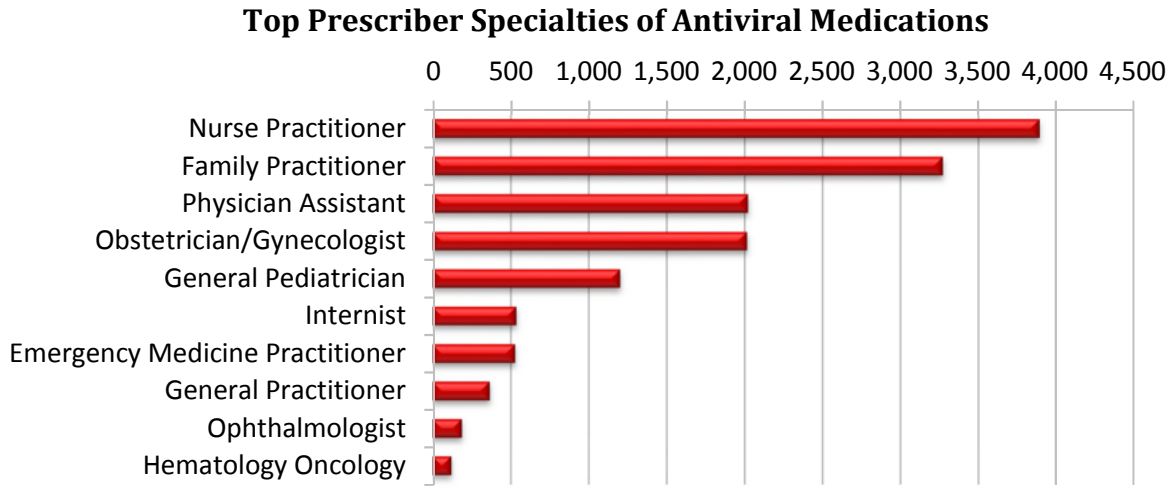
Utilization of Antiviral Medications: Fiscal Year 2017

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	8,420	15,224	$1,233,481.51	$81.02	$4.44	777,913	278,064
2017	8,346	15,207	$1,014,003.71	$66.68	$3.67	768,016	276,092
% Change	**-0.90%**	**-0.10%**	**-17.80%**	**-17.70%**	**-17.30%**	**-1.30%**	**-0.70%**
Change	**-74**	**-17**	**-$219,477.80**	**-$14.34**	**-$0.77**	**-9,897**	**-1,972**

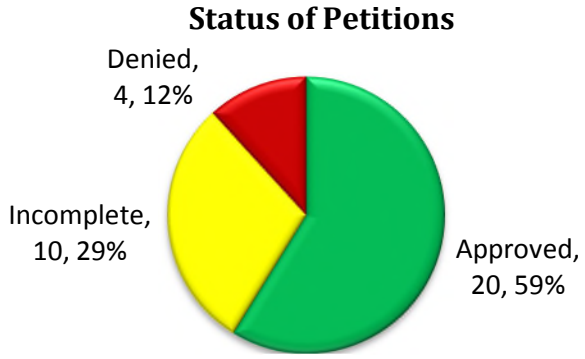
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Antiviral Medications

There were 34 prior authorization requests submitted for antiviral medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017. Please note, the prior authorization criteria for Zovirax® (acyclovir ointment), Xerese® (acyclovir/hydrocortisone cream), and Denavir® (penciclovir cream) and the age restriction for Zovirax® (acyclovir suspension) did not go into effect until November 13, 2017.



Market News and Updates[1,2,3]

Anticipated Patent Expiration(s):

- Denavir® (penciclovir cream): June 2020
- Xerese® (acyclovir/hydrocortisone cream): November 2022
- Prevymis™ (letermovir injection and tablets): May 2024
- Sitavig® (acyclovir buccal tablets): June 2030

New U.S. Food and Drug Administration (FDA) Approval(s):

- **November 2017:** The FDA approved Prevymis™ (letermovir), a once-daily oral tablet or injection for intravenous (IV) infusion, for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogenic hematopoietic stem cell transplant (HSCT). Letermovir has been granted Orphan Drug designation for the prevention of CMV disease in at-risk populations.

Pipeline:

- **Maribavir:** Maribavir, a benzimidazole riboside, is currently in Phase 3 development for patients with CMV infection undergoing HSCT or solid organ transplant who are resistant or refractory to drugs currently used to treat these infections. Results of a Phase 2 trial, which included 120 patients ages 12 years and older with CMV infection resistant or refractory to (val)ganciclovir or foscarnet, showed 67% of patients treated with varying doses of maribavir (400mg to 1,200mg twice daily) for up to 24 weeks had no detectable levels of the virus in their blood plasma within six weeks of starting treatment.

Cytomegalovirus Prevention in Hematopoietic Stem Cell Transplant Recipients[4,5,6,7,8]

CMV, human herpesvirus 5, is a common virus that infects people of all ages. In the United States, over half of adults by age 40 have been infected with CMV, and once infected, the virus stays in the body for life and can reactivate. Most people with healthy immune systems that are infected with CMV show no signs or symptoms. For people who are immunocompromised, CMV can result in serious, even life-threatening, complications including blindness, pneumonitis, diarrhea, bleeding ulcers in the esophagus or intestines, inflammation of the brain, and seizures. CMV infection in hematopoietic stem cell transplant (HSCT) recipients is associated with high morbidity and mortality. The risk of reactivation is significant in HSCT recipients who are CMV-seropositive, especially for those that are given grafts from CMV-seronegative donors due to the lack of donor-transferred CMV-specific immunity during host reactivation of endogenous latent CMV. Based on data from large studies, the rate of CMV recurrence after allogenic HSCT in CMV-seropositive patients is approximately 30% to 80%, with a median value of 37%, compared to the rate of those that are CMV-seronegative being approximately 0% to 12%.

Current guidelines recommend HSCT recipients at risk for post-transplant CMV disease (i.e., CMV-seropositive HSCT recipients, and all CMV-seronegative recipients with a CMV-seropositive donor) should be placed on a CMV disease prevention program from the time of engraftment until at least 100 days after HSCT. A prophylaxis strategy against early CMV

disease (less than 100 days after HSCT) for at-risk allogenic HSCT recipients involves administering prophylaxis throughout the period from engraftment to 100 days after HSCT. Ganciclovir is currently the standard of care treatment recommended by guidelines for CMV prophylaxis in at-risk HSCT recipients. Other additional treatment options available include high dose acyclovir and valacyclovir.

Prevymis™ (Letermovir) Product Summary[9]

Indication(s): Prevymis™ (letermovir) is a CMV DNA terminase complex inhibitor indicated for prophylaxis of CMV infection and disease in adult CMV-seropositive recipients (R+) of an allogeneic HSCT.

Dosing:

- Prevymis™ is supplied as 240mg and 480mg oral tablets or 240mg/12mL and 480mg/24mL single-dose vials for IV injection.
  - Tablet Formulation: Tablets should be swallowed whole and can be taken with or without food. Tablets should be stored in the original container until used.
  - Injection Formulation: Injections should be diluted in 250mL of compatible diluent and administered IV via a peripheral catheter or central venous line at a constant rate over 1 hour. Letemovir should not be administered as an IV bolus injection. Letemovir injection should be used only in patients unable to take oral therapy. Patients should switch to oral letemovir as soon as they are able to take oral medications. The injection formulation should be stored in original cartons to protect from light exposure.
  - Letemovir tablet and injection formulations may be used interchangeably; no dosage adjustment is needed when switching formulations.
- The recommended dosage of letermovir is 480mg administered orally or IV once daily.
  - Letermovir should be initiated between day 0 and day 28 post-transplantation and continued through day 100 post-transplant.
  - If letermovir is co-administered with cyclosporine, the dosage of letermovir should be decreased to 240mg once daily.

Mechanism of Action: Letermovir inhibits the CMV DNA terminase complex, which is required for viral DNA processing and packaging.

Contraindication(s):

- Letermovir is contraindicated in patients receiving pimozide or ergot alkaloids.
  - Concomitant administration of letermovir and pimozide may result in increased concentrations of pimozide due to inhibition of CYP3A4 by letermovir, which may lead to QT prolongation and torsades de pointes.
  - Concomitant administration of letermovir and ergot alkaloids may result in increased concentrations of ergot alkaloids due to inhibition of CYP3A4 by letermovir, which may lead to ergotism.
- Letermovir is contraindicated in patients receiving pitavastatin or simvastatin when co-administered with cyclosporine. Concomitant administration of letermovir in

combination with cyclosporine may result in significantly increased pitavastatin or simvastatin concentrations, which may lead to myopathy or rhabdomyolysis.

Warnings and Precaution(s):

- Risk of Adverse Reactions or Reduced Therapeutic Effect Due to Drug Interactions: The concomitant use of letermovir and certain drugs may result in potentially significant drug interactions, some of which may lead to adverse reactions or reduced therapeutic effects of letermovir or the concomitant drug.

Adverse Reactions:

- The most commonly reported adverse events occurring in at least 10% of subjects receiving letermovir in clinical trials were nausea, diarrhea, vomiting, peripheral edema, cough, headache, fatigue, and abdominal pain.
- The cardiac adverse event rate was higher in subjects receiving letermovir (13%) compared to placebo (6%). The most common cardiac adverse events were tachycardia (4% of letermovir subjects vs 2% of placebo subjects) and atrial fibrillation (3% of letermovir subjects vs 1% of placebo subjects).

Use in Specific Populations:

- Pregnancy: There is no adequate human data available to establish whether letermovir poses a risk to pregnancy outcomes.
- Lactation: It is not known whether letermovir is present in human breast milk, affects human milk production, or has effects on the breastfed child.
- Females and Males of Reproductive Potential: There are no data available on the effect of letermovir on human fertility.
- Pediatric Use: The safety and efficacy of letermovir in patients 18 years of age and younger have not been established.
- Geriatric Use: Safety and efficacy were similar across older and younger subjects using letermovir. No adjustment of letermovir is required based on age.
- Renal Impairment: No dosage adjustment is required for patients with creatinine clearance (CrCl) greater than 10mL/min. The safety and efficacy of letermovir in patients with end-stage renal disease (CrCl less than 10mL/min), including patients on dialysis, has not been established.
- Hepatic Impairment: No dosage adjustment is required for patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Letermovir is not recommended for patients with severe (Child-Pugh Class C) hepatic impairment.

Efficacy: The efficacy of letermovir prophylaxis therapy for CMV infection or disease in CMV-seropositive [R+] HSCT recipients at high risk for CMV reactivation was assessed in a multicenter, double-blind, placebo-controlled Phase 3 trial. Subjects were randomized to receive either letermovir 480mg once daily (adjusted to 240mg once daily if co-administered with cyclosporine) or placebo. The study drug was initiated after HSCT (at any time from day 0 to day 28 post-transplant) and continued through week 14 post-transplant. The primary efficacy endpoint was the incidence of clinically significant CMV infection through week 24 post-transplant (prophylaxis failure). Clinically significant CMV infection was defined as the

occurrence of either CMV end-organ damage, or initiation of anti-CMV pre-emptive therapy (PET) based on documented CMV viremia and the clinical condition of the subject. The Non-Complete = Failure approach was used, where subjects who discontinued from the trial prior to week 24 post-transplant or had a missing outcome at week 24 post-transplant were counted as failures. The results showed the proportion of subjects who failed prophylaxis was 35% in the letermovir group versus 61% in the placebo group. The cumulative rate of clinically significant CMV infection at week 24 was 18.9% in the letermovir group versus 44.3% in the placebo group. A Kaplan-Meier event rate for all-cause mortality in the letermovir group was 12% versus 17% in the placebo group at week 24 post-transplant, and 24% versus 28%, respectively, at week 48 post-transplant.

Cost:

Medication	Cost Per Dose	Cost per 28 Days of Therapy	Cost per 100 Days of Therapy
Prevymis™ (letermovir tablets)	**$195.00**	**$5,460.00**	**$19,500.00**
Prevymis™ (letermovir injection)	**$270.00**	**$7,560.00**	**$27,000.00**

Costs do not reflect rebated prices or net costs. Costs based on Wholesale Acquisition Costs (WAC).

Recommendations

The College of Pharmacy recommends the prior authorization of Prevymis™ (letermovir tablets and injection) with the following criteria:

Prevymis™ (Letermovir Tablets and Injection) Approval Criteria:

1. An FDA approved indication of prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogenic hematopoietic stem cell transplant (HSCT); and
2. Member must be CMV R+; and
3. Member must have received a HSCT within the last 28 days; and
4. Members taking concomitant cyclosporine will only be approved for the 240mg dose; and
5. Members must not be taking the following medications:
    a. Pimozide; or
    b. Ergot alkaloids (e.g., ergotamine, dihydroergotamine); or
    c. Rifampin; or
    d. Atorvastatin, lovastatin, pitavastatin, simvastatin, or repaglinide when co-administered with cyclosporine; and
6. Prevymis™ must be prescribed by an oncology, hematology, infectious disease, or transplant specialist or advanced care practitioner with a supervising physician who is an oncology, hematology, infectious disease, or transplant specialist; and
7. Prescriber must verify the member will be monitored for CMV reactivation while on therapy; and
8. Approvals will be for the duration of 100 days post-transplant.
    a. For Prevymis™ vials, authorization will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and

b. Approval length for vial formulation will be based on duration of need.

9. A quantity limit of one tablet or vial per day will apply.

The College of Pharmacy also recommends the following changes to current antiviral product prior authorization criteria based on low net cost of acyclovir cream.

Sitavig® (Acyclovir Buccal Tablets), Xerese® (Acyclovir/Hydrocortisone Cream), and Denavir® (Penciclovir Cream) Approval Criteria:

1. An FDA approved diagnosis of recurrent herpes labialis (cold sores); and
2. A patient-specific, clinically significant reason why the member cannot use oral acyclovir, famciclovir, or valacyclovir tablets; and
3. A patient-specific, clinically significant reason why the member cannot use acyclovir cream.

Utilization Details of Antiviral Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ACYCLOVIR PRODUCTS					
ACYCLOVIR TAB 400MG	3,932	2,086	$44,468.53	1.88	$11.31
ACYCLOVIR TAB 800MG	1,538	1,103	$21,790.45	1.39	$14.17
ACYCLOVIR SUS 200MG/5ML	1,351	1,056	$172,037.54	1.28	$127.34
ACYCLOVIR OIN 5%	949	803	$285,491.55	1.18	$300.83
ACYCLOVIR CAP 200MG	941	556	$9,950.87	1.69	$10.57
ZOVIRAX CRE 5%	367	295	$277,922.81	1.24	$757.28
ACYCLOVIR NA INJ 50MG/ML	9	3	$306.10	3	$34.01
SUBTOTAL	**9,087**	**5,491**	**$811,967.85**	**1.65**	**$89.35**
ACYCLOVIR/HYDROCORTISONE PRODUCTS					
XERESE CRE 5-1%	7	7	$7,742.61	1	$1,106.09
SUBTOTAL	**7**	**7**	**$7,742.61**	**1**	**$1,106.09**
FAMCICLOVIR PRODUCTS					
FAMCICLOVIR TAB 500MG	239	148	$7,766.88	1.61	$32.50
FAMCICLOVIR TAB 250MG	69	30	$2,488.39	2.3	$36.06
FAMCICLOVIR TAB 125MG	15	2	$585.88	7.5	$39.06
SUBTOTAL	**323**	**180**	**$10,841.15**	**1.79**	**$33.56**
PENCICLOVIR PRODUCTS					
DENAVIR CRE 1%	66	56	$49,205.02	1.18	$745.53
SUBTOTAL	**66**	**56**	**$49,205.02**	**1.18**	**$745.53**
RIBAVIRIN PRODUCTS					
RIBAVIRIN TAB 200MG	107	44	$10,766.74	2.43	$100.62
RIBASPHERE TAB 200MG	33	14	$4,006.68	2.36	$121.41
RIBAVIRIN CAP 200MG	12	8	$1,823.91	1.5	$151.99
MODERIBA TAB 200MG	4	2	$509.88	2	$127.47
SUBTOTAL	**156**	**65**	**$17,107.21**	**2.4**	**$109.66**
VALACYCLOVIR PRODUCTS					
VALACYCLOVIR TAB 500MG	2,831	1,430	$54,616.45	1.98	$19.29
VALACYCLOVIR TAB 1GM	2,737	1,702	$62,523.42	1.61	$22.84
SUBTOTAL	**5,568**	**2,981**	**$117,139.87**	**1.87**	**$21.04**
TOTAL	**15,207**	**8,346***	**$1,014,003.71**	**1.82**	**$66.68**

*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. Last revised 12/2017. Last accessed 01/29/2018.

[2] Merck & Co., Inc. Merck Receives FDA Approval of Prevymis™ (letermovir) for Prevention of Cytomegalovirus (CMV) Infection and Disease in Adult Allogenic Stem Cell Transplant Patients. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20171109005397/en/Merck-Receives-FDA-Approval-PREVYMIS%e2%84%a2-letermovir-Prevention. Issued 11/09/2017. Last accessed 12/13/2017.

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[9] Prevymis™ Prescribing Information. Merck & Co., Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209939Orig1s000,209940Orig1s000lbl.pdf. Last revised 11/2017. Last accessed 12/13/2017.

Appendix K

Fiscal Year 2017 Annual Review of Glaucoma Medications and 30-Day Notice to Prior Authorize Rhopressa® (Netarsudil Ophthalmic Solution) and Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution)

Oklahoma Health Care Authority
February 2018

Current Prior Authorization Criteria

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Indicates available oral medications.
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.

Glaucoma Medications Tier-2 Approval Criteria:

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

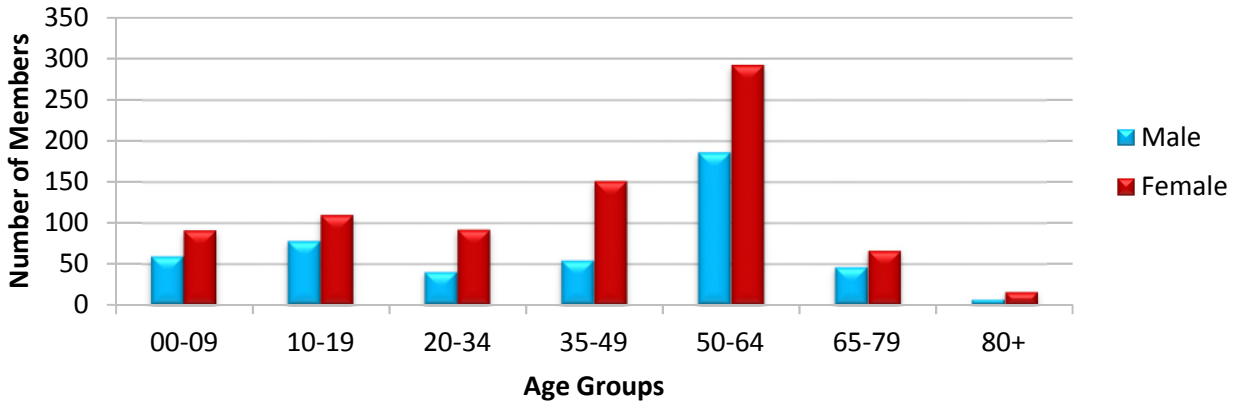
Utilization of Glaucoma Medications: Fiscal Year 2017

Comparison of Fiscal Years

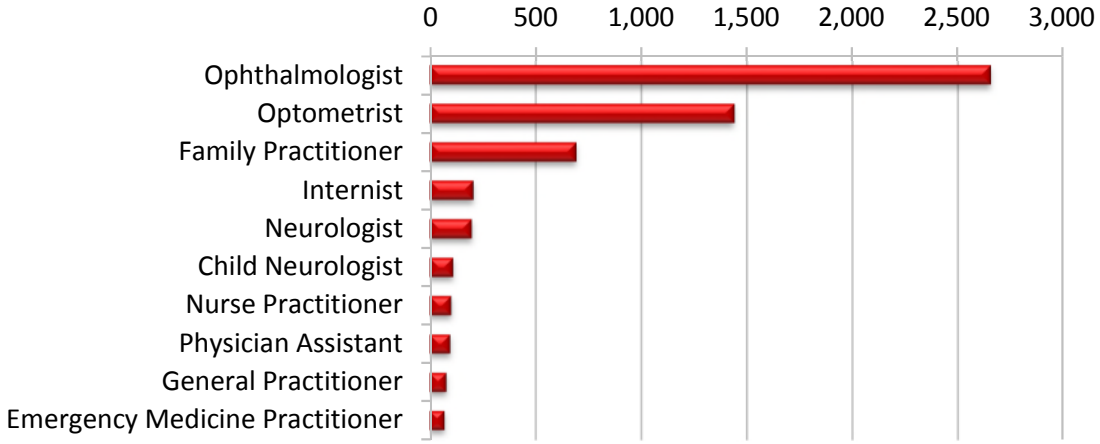
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	1,300	6,278	$559,624.47	$89.14	$2.76	88,359	202,926
2017	1,287	6,081	$549,769.68	$90.41	$2.68	99,473	205,253
% Change	**-1.00%**	**-3.10%**	**-1.80%**	**1.40%**	**-2.90%**	**12.60%**	**1.10%**
Change	**-13**	**-197**	**-$9,854.79**	**$1.27**	**-$0.08**	**11,114**	**2,327**

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

Demographics of Members Utilizing Glaucoma Medications



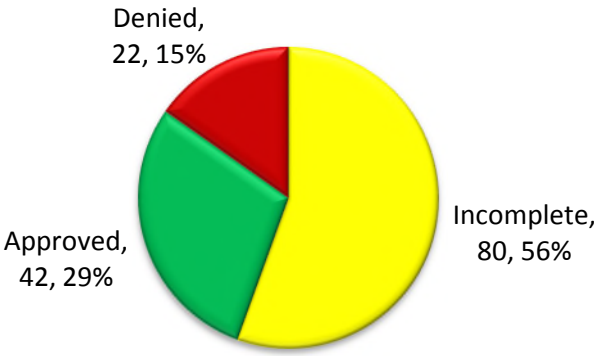
Top Prescriber Specialties of Glaucoma Medications by Number of Claims



Prior Authorization of Glaucoma Medications

There were 144 prior authorization requests submitted for glaucoma medications during fiscal year 2017. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Istalol® (timolol maleate): November 2018
- Zioptan™ (tafluprost): December 2022
- Combigan® (brimonidine/timolol): January 2023
- Alphagan-P® (brimonidine tartrate): March 2024
- Vyzulta™ (latanoprostene bunod): October 2025
- Lumigan® (bimatoprost): June 2027
- Travatan-Z® (travoprost): October 2029
- Simbrinza® (brinzolamide/brimonidine): October 2030
- Rhopressa® (netarsudil): November 2030

U.S. Food and Drug Administration (FDA) Approval(s):

- **November 2017:** The FDA approved Vyzulta™ (latanoprostene bunod ophthalmic solution) for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension (HTN).
- **December 2017:** The FDA approved Rhopressa® (netarsudil ophthalmic solution) for the lowering of elevated IOP in patients with open-angle glaucoma or ocular HTN.

Pipeline Update(s):

- **Roclatan™ (netarsudil/latanoprost):** Roclatan™ is a combination product of netarsudil, which inhibits both Rho kinase (ROCK) and norepinephrine transporter (NET), and latanoprost, a prostaglandin analog. Aerie Pharmaceuticals, Inc. plans to submit a New Drug Application (NDA) to the FDA for Roclatan™ in the first half of 2018.

Rhopressa® (Netarsudil Ophthalmic Solution) Product Summary[5,6]

Indication(s): Rhopressa® (netarsudil ophthalmic solution) is a Rho kinase inhibitor indicated for the reduction of elevated IOP in patients with open-angle glaucoma or ocular HTN.

Dosing:

- Rhopressa® is supplied as a 0.2mg/mL ophthalmic solution in a 2.5mL dropper bottle.
  - Netarsudil should be refrigerated until opened. After opening, netarsudil may be kept at 2°C to 25°C (36°F to 77°F) for up to six weeks.
- The recommended dosage is one drop in the affected eye(s) once daily in the evening.
  - If one dose is missed, treatment should continue with the next dose in the evening. Twice daily dosing is not well tolerated and is not recommended.
  - If netarsudil is to be used concomitantly with other topical ophthalmic drug products, each drug product should be administered at least five minutes apart.

Mechanism of Action: Netarsudil is a Rho kinase inhibitor, which is thought to reduce IOP by increasing the outflow of aqueous humor through the trabecular meshwork route.

Contraindication(s): None.

Warnings and Precautions:

- Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients, who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.
- Use with Contact Lens: Contact lenses should be removed prior to the administration of netarsudil. Contact lenses may be reinserted 15 minutes after administration.

Adverse Reactions: The most common ocular adverse reaction during clinical trials was conjunctival hyperemia, which was reported in 53% of patients. Other common ocular adverse reactions reported in approximately 20% of patients included corneal verticillata, instillation site pain, and conjunctival hemorrhage. Instillation site erythema, corneal staining, blurred

vision, increased lacrimation, erythema of eyelid, and reduced visual acuity were reported in 5% to 10% of patients.

Use in Specific Populations:

- Pregnancy: There are no available data on netarsudil use in pregnant women to inform any drug associated risk; however, systemic exposure to netarsudil from ocular administration is low.
- Lactation: There are no available data on the presence of netarsudil in human milk, the effects on the breastfed infant, or the effects of milk production, however, systemic exposure to netarsudil from ocular administration is low.
- Pediatric Patients: The safety and effectiveness of netarsudil in pediatric patients younger than 18 years of age have not been established.
- Geriatric Patients: No overall differences in safety and effectiveness have been observed between elderly and other adult patients.

Efficacy: The efficacy of netarsudil was evaluated in three randomized, double-masked, non-inferiority Phase 3 trials in patients with open-angle glaucoma or ocular HTN. The first two studies enrolled subjects with baseline IOP lower than 27mmHg and the third enrolled subjects with IOP lower than 30mmHg. Patients were randomized into two treatment groups: netarsudil 0.02% (placebo in both eyes in morning and netarsudil in both eyes in evening) or timolol 0.5% in both eyes twice daily. The primary efficacy outcome was mean IOP at three time points (8:00am, 10:00am, and 4:00pm) at week 2, week 6, and month 3 visits. During the study periods of all three trials, IOP was measured at baseline and on day 15, 43, and 90. The three studies demonstrated up to 5mmHg reductions in IOP for subjects treated with netarsudil 0.02% once daily in the evening. For patients with baseline IOP <25mmHg, the IOP reductions with netarsudil were similar to those with timolol 0.5% dosed twice daily. For patients with baseline IOP ≥25mmHg, netarsudil resulted in smaller mean IOP reductions at the morning time points on days 43 and 90 than those in the timolol 0.5% arm.

Cost/Launch Information: Rhopressa® (netarsudil ophthalmic solution) cost and launch information are not available at this time.

Vyzulta™ (Latanoprostene Bunod Ophthalmic Solution) Product Summary[7,8,9]

Indication: Vyzulta™ (latanoprostene bunod) is a prostaglandin analog ophthalmic solution indicated for the reduction of IOP in patients with open-angle glaucoma or ocular HTN.

Dosing:

- Vyzulta™ is supplied as a 0.24mg/mL ophthalmic solution in a 5mL dropper bottle.
  - Unopened bottles of latanoprostene bunod should be refrigerated (2° to 8°C).
  - Once opened, latanoprostene bunod may be stored at room temperature for eight weeks.
- The recommended dosage of latanoprostene bunod is one drop in the conjunctival sac of the affected eye(s) once daily in the evening.

Mechanism of Action: Latanoprostene bunod is thought to lower IOP by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes.

Contraindication(s): None.

Warnings and Precautions:

- Pigmentation: Latanoprostene bunod may cause changes to pigmented tissues. The most frequently reported changes with prostaglandin analogs have been increased pigmentation of the iris and periorbital tissue.
- Eyelash Changes: Latanoprostene bunod may gradually change eyelashes and vellus hair in the treated eye, including increased length, thickness, and number of lashes or hairs. Eyelash changes are usually reversible upon discontinuation of treatment.
- Intraocular Inflammation: Latanoprostene bunod should be used with caution in patients with a history of intraocular inflammation and should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition.
- Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Latanoprostene bunod should be used with caution in aphakic patients, in pseudophakic patients with torn posterior lens capsule, and in patients with known risk factors for macular edema.
- Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients, who, in most cases, had a concurrent corneal disease or a disruption of ocular epithelial surface.
- Use with Contact Lens: Contact lenses should be removed prior to the administration of latanoprostene bunod because this product contains benzalkonium chloride. Contact lenses may be reinserted 15 minutes after administration.

Adverse Reactions: The most common ocular adverse reactions observed in patients treated with latanoprostene bunod included conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%).

Use in Specific Populations:

- Pregnancy: There are no available human data for the use of latanoprostene bunod during pregnancy to inform any drug-associated risks.
- Lactation: There are no data on the presence of latanoprostene bunod in human milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Patients: Use in pediatric patients 16 years of age and younger is not recommended because of potential safety concerns related to increased pigment following long-term chronic use.
- Geriatric Patients: No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.

Efficacy: The efficacy of latanoprostene bunod was demonstrated in two randomized, double-masked, parallel-group Phase 3 trials. Subjects were randomized to receive either latanoprostene bunod 0.024% (LBN) one drop in study eye(s) once daily in the evening or timolol maleate 0.5% one drop in study eye(s) twice daily for a period of three months. The primary efficacy endpoint was the IOP in the subject's study eye(s) measured at 8am, 12pm, and 4pm at each post-baseline visit (week 2, week 6, and month 3). The key secondary efficacy endpoints were the proportion of subjects with IOP ≤18mmHg consistently at all nine time

points in the first 3 months and the proportion of subjects with IOP reduction ≥25% from baseline consistently across all nine time points.

- Study 1 Results: A total of 387 subjects completed the study (LBN 0.024%, n=264; timolol 0.5%, n=123). At all nine time points, the mean IOP in the study eye(s) was significantly lower in the LBN 0.024% group than the timolol 0.5% group. At all nine time points, the percentage of subjects with mean IOP ≤18mmHg and the percentage with IOP reduction ≥25% were significantly higher in the LBN 0.024% group versus the timolol 0.5% group.
- Study 2 Results: A total of 387 subjects completed the study (LBN 0.024%, n=259; timolol 0.5%, n=128). The mean IOP reduction with LBN was found non-inferior to timolol. Of the LBN 0.024% and timolol 0.5% treated subjects, respectively, 31.0% and 18.5% had their IOP reduced ≥25% from baseline (p=0.007) and 17.7% and 11.1% had their IOP reduced to ≤18mmHg over all the time points in the study (p=0.84).

Cost Comparison:

Medication	Cost Per mL	Cost Per 30 Days
Vyzulta™ (latanoprostene bunod 0.024%)	**$72.00**	**$360.00**
Travatan-Z® (travoprost 0.004%)	$62.93	$314.66
latanoprost 0.005%	$1.99	$4.98

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 following changes to the Glaucoma Product Based Prior Authoriation (PBPA) category:

1. The creation of a Special Prior Authorization (PA) category to account for very high net cost products.
    a. Placement of brimonidine (Alphagan-P® 0.15%), dorzolamide/timolol (Cosopt® PF), timolol maleate (Timoptic Ocudose®, Timoptic-XE®), netarsudil ophthalmic solution (Rhopressa®), and latanoprostene bunod ophthalmic solution (Vyzulta™) into Special PA category of the Glaucoma PBPA category based on net cost.
2. Move echothiophate iodide (Phospholine Iodide®) from Tier-2 to Tier-1 based on low net cost.
3. Move pilocarpine (Isopto® Carpine®, Pilopine HS®) from Tier-1 to Tier-2 based on net cost. Current Tier-2 criteria will apply.

Tier-1 products are covered with no prior authorization necessary.

Glaucoma Medications Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. The member must attempt at least three Tier-1 trials of a minimum of four weeks duration each within the last 120 days. Tier-1 trials may be from any pharmacologic class; or

3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365 day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Glaucoma Special Prior Authorization Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason why a special formulation is needed over a Tier-1 or Tier-2 product; or
3. Approvals may be granted if there is a documented adverse effect, drug interaction, or contraindication to all Tier-1 and Tier-2 medications; or
4. Approvals may be granted if there is a unique FDA approved indication not covered by all Tier-1 and Tier-2 medications; and
5. The member must have had a comprehensive, dilated eye exam within the last 365 day period as recommended by the National Institute of Health; and
6. Approvals will be for the duration of one year.

Proposed changes can be seen in red in the following Tier chart:

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
Alpha-2 Adrenergic Agonists		
brimonidine 0.2% (Alphagan® 0.2%)	apraclonidine (Iopidine®)	**brimonidine (Alphagan-P® 0.15%)**
brinzolamide/brimonidine (Simbrinza®)	brimonidine (Alphagan-P® 0.1%)	
	brimonidine/timolol (Combigan®)	
Beta-Blockers		
carteolol (Ocupress® 1%)	betaxolol (Betoptic® 0.5%, Betoptic-S®)	**dorzolamide/timolol (Cosopt® PF)**
dorzolamide/timolol (Cosopt®)	brimonidine/timolol (Combigan®)	**timolol maleate (Timoptic Ocudose®, Timoptic-XE®)**
levobunolol (Betagan®)	timolol (Betimol®)	
metipranolol (OptiPranolol®)		
timolol maleate (Istalol®, Timoptic®)		
Carbonic Anhydrase Inhibitors		
acetazolamide (Diamox®)+		**dorzolamide/timolol (Cosopt® PF)**
brinzolamide (Azopt®)		

Glaucoma Medications*		
Tier-1	**Tier-2**	**Special PA**
brinzolamide/brimonidine (Simbrinza®)		
dorzolamide (Trusopt®)		
dorzolamide/timolol (Cosopt®)		
methazolamide (Neptazane®)+		
Cholinergic Agonists/Cholinesterase Inhibitors		
echothiophate iodide (Phospholine Iodide®)	carbachol (Miostat®)	
	pilocarpine (Isopto® Carpine®, Pilopine HS®)	
Prostaglandin Analogs		
latanoprost (Xalatan®)	bimatoprost (Lumigan®)	**latanoprostene bunod (Vyzulta™)**
travoprost 0.004% (Travatan-Z®)	tafluprost (Zioptan™)	
	travoprost 0.004% (Travatan®)	
Rho Kinase Inhibitors		
		netarsudil (Rhopressa®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Indicates available oral medications.
Please note: Combination products are included in both applicable pharmaceutical classes; therefore, combination products are listed twice in the tier chart.

Utilization Details of Glaucoma Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TIER-1 UTILIZATION					
ALPHA-2 ADRENERGIC AGONIST PRODUCTS					
SIMBRINZA SUS 1-0.2%	275	69	$37,222.04	3.99	$135.35
BRIMONIDINE SOL 0.2% OP	263	97	$3,452.22	2.71	$13.13
SUBTOTAL	**538**	**165**	**$40,674.26**	**3.26**	**$75.60**
BETA-BLOCKER PRODUCTS					
DORZOL/TIMOL SOL 22.3-6.8	486	140	$8,221.99	3.47	$16.92
TIMOLOL MAL SOL 0.5% OP	461	189	$4,718.30	2.44	$10.23
TIMOLOL MAL SOL 0.25% OP	73	39	$612.86	1.87	$8.40
LEVOBUNOLOL SOL 0.5% OP	10	4	$119.33	2.5	$11.93
ISTALOL SOL 0.5% OP	1	1	$149.76	1	$149.76
SUBTOTAL	**1,031**	**356**	**$13,822.24**	**2.9**	**$13.41**
CARBONIC ANHYDRASE INHIBITOR PRODUCTS					
ACETAZOLAMID TAB 250MG	489	135	$65,386.41	3.62	$133.71
ACETAZOLAMID CAP 500MG ER	295	92	$38,817.52	3.21	$131.58
DORZOLAMIDE SOL 2% OP	161	53	$2,789.37	3.04	$17.33
ACETAZOLAMID TAB 125MG	71	26	$11,277.05	2.73	$158.83

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
AZOPT SUS 1% OP	66	24	$18,260.36	2.75	$276.67
SUBTOTAL	**1,082**	**303**	**$136,530.71**	**3.57**	**$126.18**
CHOLINERGIC AGONIST/CHOLINESTERASE INHIBITOR PRODUCTS					
PILOCARPINE SOL 1% OP	19	11	$1,141.80	1.73	$60.09
PILOCARPINE SOL 4% OP	8	2	$684.00	4	$85.50
ISOPTO CARP SOL 4% OP	2	1	$183.78	2	$91.89
PILOCARPINE SOL 2% OP	2	2	$166.51	1	$83.26
ISOPTO CARP SOL 1% OP	2	1	$137.28	2	$68.64
SUBTOTAL	**33**	**16**	**$2,313.37**	**2.06**	**$70.10**
PROSTAGLANDIN ANALOG PRODUCTS					
LATANOPROST SOL 0.005%	1,744	439	$20,116.99	3.97	$11.53
TRAVATAN Z DRO 0.004%	915	250	$201,220.64	3.66	$219.91
SUBTOTAL	**2,659**	**668**	**$221,337.63**	**3.98**	**$83.24**
TIER-1 SUBTOTAL	**5,343**	**1,192**	**$414,678.21**	**4.48**	**$77.61**
TIER-2 UTILIZATION					
ALPHA-2 ADRENERGIC AGONIST PRODUCTS					
BRIMONIDINE SOL 0.15%	97	17	$16,225.07	5.71	$167.27
ALPHAGAN P SOL 0.1%+	89	27	$18,590.94	3.3	$208.89
ALPHAGAN P SOL 0.15%+	10	1	$2,801.07	10	$280.11
SUBTOTAL	**196**	**43**	**$37,617.08**	**4.56**	**$191.92**
BETA-BLOCKER PRODUCTS					
COMBIGAN SOL 0.2/0.5%+	238	66	$48,343.46	3.61	$203.12
TIMOLOL GEL SOL 0.5% OP	149	65	$15,182.20	2.29	$101.89
TIMOLOL GEL SOL 0.25% OP	7	4	$697.00	1.75	$99.57
BETAXOLOL SOL 0.5% OP	1	1	$53.25	1	$53.25
SUBTOTAL	**395**	**136**	**$64,275.91**	**2.9**	**$162.72**
CHOLINERGIC AGONIST/CHOLINESTERASE INHIBITOR PRODUCTS					
PHOSPHOLINE SOL 0.125% OP	2	2	$198.44	1	$99.22
SUBTOTAL	**2**	**2**	**$198.44**	**1**	**$99.22**
PROSTAGLANDIN ANALOG PRODUCTS					
LUMIGAN SOL 0.01%	142	28	$32,753.04	5.07	$230.66
TRAVOPROST DRO 0.004%	3	2	$247.00	1.5	$82.33
SUBTOTAL	**145**	**29**	**$33,000.04**	**5**	**$227.59**
TIER-2 SUBTOTAL	**738**	**198**	**$135,091.47**	**3.73**	**$183.05**
TOTAL	**6,081**	**1,287***	**$549,769.68**	**4.72**	**$90.41**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

+Moved to Tier-2 from Tier-1 on 01/01/2018 due to no longer participating in supplemental rebates. The utilization above occurred during fiscal year 2017, but is shown under the Tier-2 products to reflect the current tier placement.

[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 12/2017. Last accessed 01/30/2017.

[2] Han DH. Vyzulta Approved to Treat Patients with Open-Angle Glaucoma, Ocular HTN. *MPR*. Available online at: http://www.empr.com/news/vyzulta-latanoprost-nitric-oxide-glaucoma-intraocular-pressure/article/705048/?DCMP=EMC-MPR_DailyDose_20171103&cpn=&hmSubId=0TmDkQDez9w1&hmEmail=epKwVN5dM4mI9OkG5crxKw22KX5GqEAd5W22CZjZ2mg1&NID=1912253915&c_id=&dl=0&spMailingID=18413447&spUserID=Mzc0NTA3MDg2NjQwS0&spJobID=1140247027&spReportId=MTE0MDI0NzAyNwS2. Issued 11/03/2017. Last accessed 02/05/2018.

[3] Aerie Pharmaceuticals, Inc. Aerie Pharmaceuticals Announces U.S. FDA Approval of Rhopressa™ (netarsudil ophthalmic solution) 0.02% for the Lowering of Elevated Intraocular Pressure in Patients with Open-Angle Glaucoma or Ocular Hypertension. *Business Wire*. Available online at: https://www.businesswire.com/news/home/20171218006125/en/Aerie-Pharmaceuticals-Announces-U.S.-FDA-Approval-Rhopressa%C2%AE. Issued 12/18/2017. Last accessed 02/05/2018.

[4] Aerie Pharmaceuticals, Inc. Aerie Pharmaceuticals Reports Postive Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005% Phase 3 12-month Topline Safety Results. *Business Wire*. Available online at: http://www.businesswire.com/news/home/20170719006087/en/Aerie-Pharmaceuticals-Reports-Positive-Roclatan%E2%84%A2-netarsudillatanoprost-ophthalmic. Issued 07/19/2017. Last accessed 02/05/2018.

[5] Rhopressa® Prescribing Information. Aerie Pharmaceuticals, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208254lbl.pdf. Last revised 12/2017. Last accessed 02/05/2018.

[6] Serle JB, Katz LJ, McLaurin E, et al. Two Phase 3 Clinical Trials Comparing the Safety and Efficacy of Netarsudil to Timolol in Patients With Elevated Intraocular Pressure: Rho Kinase Elevated IOP Treatment Trial 1 and 2 (ROCKET-1 and ROCKET-2). *Am J Ophthalmol* 2017; 186; 116-27.

[7] Vyzulta™ Prescribing Information. Bausch + Lomb Inc. Available online at: http://www.bausch.com/Portals/69/-/m/BL/United%20States/USFiles/Package%20Inserts/Pharma/vyzulta-prescribing-information.pdf. Last revised 11/2017. Last accessed 02/05/2018.

[8] Weinreb RN, Sforzolini BS, Vittitow J, et al. Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension: The APOLLO Study. *Ophthalmology* 2016; 123(5): 965-73.

[9] Medeiros FA, Martin KR, Peace J, et al. Comparison of Latanoprostene Bunod 0.024% and Timolol Maleate 0.5% in Open-Angle Glaucoma or Ocular Hypertension: The LUNAR Study. *Am J Ophthalmol* 2016; 168: 250-9.

Appendix L

Fiscal Year 2017 Annual Review of Parkinson's Disease (PD) Medications and 30-Day Notice to Prior Authorize Xadago® (Safinamide) and Gocovri™ (Amantadine Extended-Release)

Oklahoma Health Care Authority
February 2018

Current Prior Authorization Criteria

Requip XL® [Ropinirole Extended-Release (ER)] & Mirapex ER® (Pramipexole ER) Approval Criteria:

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

Neupro® (Rotigotine Transdermal System) Approval Criteria:

1. For the diagnosis of Parkinson's disease (PD) the following criteria apply:
    a. An FDA approved indication for the treatment of signs and symptoms of PD; 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 (RLS) the following criteria apply:
    a. An FDA approved indication of RLS; 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 (PD); 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 PD 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 (ER) Capsules] Approval Criteria

1. An FDA approved diagnosis of Parkinson's disease (PD), 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 ER tablets) must be provided.

Nuplazid® (Pimavanserin) Approval Criteria:

1. An FDA approved diagnosis of hallucinations and delusions associated with Parkinson's disease (PD) psychosis; and
2. Member must have concomitant diagnosis of PD; and
3. Nuplazid® will not be approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD 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 of PD Medications: Fiscal Year 2017

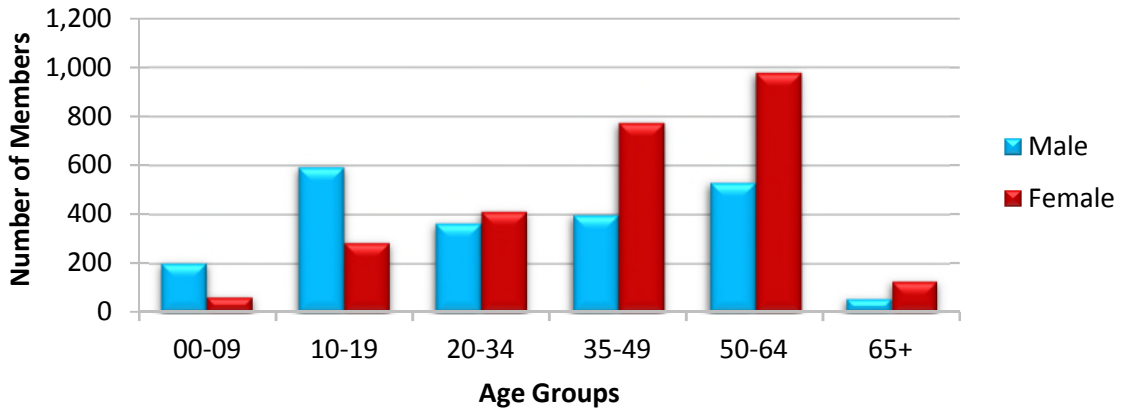
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	4,796	25,064	$750,853.35	$29.96	$0.94	1,656,281	801,357
2017	4,766	25,276	$840,907.99	$33.27	$1.04	1,648,108	806,457
% Change	**-0.60%**	**0.80%**	**12.00%**	**11.00%**	**10.60%**	**-0.50%**	**0.60%**
Change	**-30**	**212**	**$90,054.64**	**$3.31**	**$0.10**	**-8,173**	**5,100**

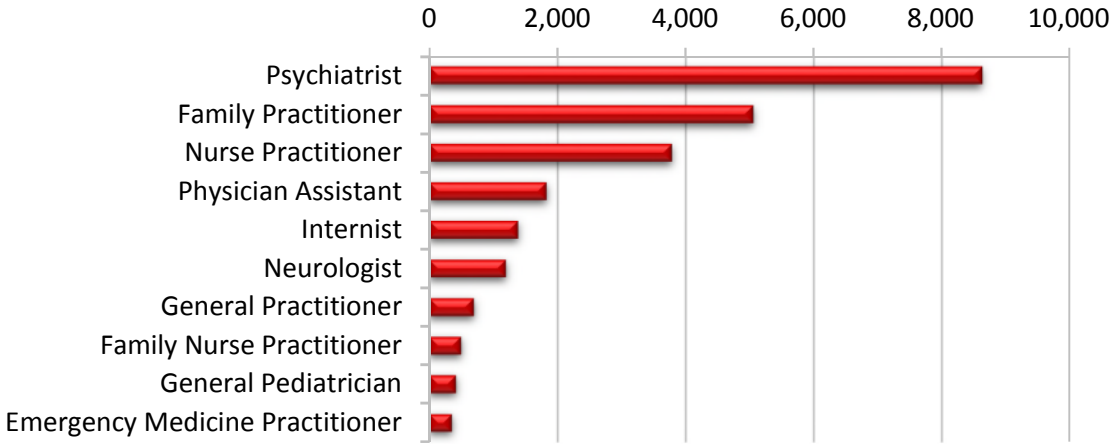
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- There were no paid medical claims for Duopa™ (carbidopa/levodopa enteral suspension) during fiscal year 2017.

Demographics of Members Utilizing PD Medications



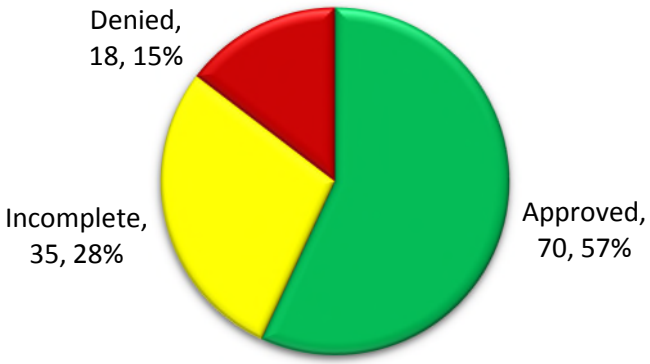
Top Prescriber Specialties of PD Medications by Number of Claims



Prior Authorization of PD Medications

There were 123 prior authorization requests submitted for PD medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.

Status of Petitions



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

Patent Expiration(s):

- Duopa™ (carbidopa/levodopa enteral suspension): There are no unexpired patents for Duopa™ however exclusivity expiration is anticipated in January 2022
- Azilect® (rasagiline tablets): August 2027
- Neupro® (rotigotine transdermal patches): September 2027
- Nuplazid® (pimavanserin tablets): June 2028
- Rytary™ [carbidopa/levodopa extended-release (ER) capsules]: December 2028
- Xadago® (safinamide tablets): December 2028
- Gocovri™ (amantadine ER capsules): December 2030

New U.S. Food and Drug Administration (FDA) Approval(s):

- **March 2017:** The FDA approved Xadago® (safinamide tablets), a monamine oxidase type B (MAO-B) inhibitor as adjunctive treatment for patients with PD who are currently taking levodopa/carbidopa and experiencing "off" episodes. An "off" episode is a time when a patient's medications are not working well, causing an increase in Parkinson's symptoms, such as tremor and difficulty walking.
- **August 2017:** The FDA approved Gocovri™ (amantadine ER capsules) for the treatment of dyskinesia in patients with PD receiving levodopa-based therapy, with or without concomitant dopaminergic medications.

News:

- **November 2017:** The American Academy of Neurology (AAN) requested public comment on a protocol for a proposed practice guideline project regarding the initiation of treatment for PD. The AAN plans to release a draft guideline for review and public comment in January 2019.
- **November 2017:** The Institute for Safe Medication Practices (ISMP) released a report detailing adverse events (AEs) associated with Nuplazid® (pimavanserin). ISMP found 2,236 AEs reported to the FDA Adverse Event Reporting System related to pimavanserin in 12 months. The most frequently reported AEs were divided into four groups: hallucinations (21.8%), drug ineffective (14.9%), confusion (11.5%), and death (10.9%). ISMP concluded that there was some evidence that AEs of hallucinations indicated that pimavanserin was potentially worsening psychosis or was ineffective in some patients.

Pipeline:

- **August 2016:** The FDA granted Fast Track designation for APL-130277, a sublingual film containing apomorphine, for the treatment of "off" episodes in patients with PD. Apomorphine was previously approved to treat acute, intermittent "off" episodes for advanced PD patients, but is currently only approved as a subcutaneous injection.
- **June 2017:** Acorda Therapeutics announced positive results from a Phase 3 trial of an inhaled formulation of levodopa (Inbrija™). At 12 weeks, Inbrija™ had significantly greater changes in Uniform Parkinson's Disease Rating Scale (UPDRS) Part III scores 30 minutes post dose compared to placebo (-9.83 vs. -5.91, p=0.009). As an inhaled formulation, Inbrija™ is able to bypass liver metabolism allowing for a faster onset of action and potential for on-demand use in patients experiencing "off" periods. In late August 2017, Acorda received a refusal to file letter from the FDA regarding its New Drug Application (NDA) for Inbrija™. The FDA determined that the NDA submitted in June 2017 was not sufficiently complete to permit a substantive review citing manufacturing issues. The company plans to seek a meeting with the FDA to respond to the issues.
- **November 2017:** Acorda Therapeutics announced that it will discontinue development of tozadenant, an investigational PD therapy, after Phase 3 studies revealed a serious risk of agranulocytosis.

Xadago® (Safinamide) Product Summary[10]

Indication(s): Xadago® (safinamide) is an MAO-B inhibitor indicated as adjunctive treatment to levodopa/carbidopa in patients with PD experiencing "off" episodes.

- Limitation of Use: Safinamide has not been shown to be effective as monotherapy for the treatment of PD.

Dosing:

- Xadago® is available as 50mg and 100mg oral tablets.
- The recommended starting dose of safinamide is 50mg by mouth once daily (at the same time of day). After two weeks, the dosage may be increased to 100mg once daily based on need and tolerability. Daily doses exceeding 100mg have not been shown to provide additional benefit and may increase the risk of adverse effects.
- The maximum recommended dose in patients with moderate hepatic impairment (Child-Pugh B) is 50mg once daily. Safinamide is contraindicated in patients with severe hepatic impairment (Child-Pugh C).
- Safinamide can be taken with or without food.

Mechanism of Action: Safinamide is a MAO-B inhibitor. Inhibition of MAO-B activity, by blocking the catabolism of dopamine, is thought to result in an increase in dopamine levels and a subsequent increase of dopaminergic activity in the brain.

Contraindication(s):

- Concomitant use of other drugs in the MAO inhibitor (MAOI) class or other drugs that are potent inhibitors of MAO, including linezolid.
- Concomitant use of opioid drugs (e.g., meperidine, methadone, propoxyphene, tramadol); serotonin-norepinephrine reuptake inhibitors (SNRIs); tricyclic, tetracyclic, or triazolopyridine antidepressants; cyclobenzaprine; methylphenidate; amphetamine; or St. John's wort.

Warnings and Precautions:

- Hypertension (HTN): Safinamide may cause HTN or exacerbate existing HTN. In clinical trials, the incidence of HTN was 7% for safinamide 50mg, 5% for safinamide 100mg, and 4% for placebo. Patients should be monitored for new onset HTN or HTN that is not adequately controlled after starting safinamide.
- Serotonin Syndrome: The development of a potentially life-threatening serotonin syndrome has been reported in patients on concomitant treatment with MAOIs, SNRIs, tricyclic antidepressants, tetracyclic antidepressants, triazolopyridine antidepressants, cyclobenzaprine, opioid drugs, methylphenidate, and amphetamine. Concomitant use of safinamide with these drugs is contraindicated.
- Falling Asleep During Activities of Daily Living (ADL): Patients treated with dopaminergic medications have reported falling asleep while engaged in ADL, including the operation of motor vehicles. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event.
- Dyskinesia: Safinamide may cause dyskinesia or exacerbate pre-existing dyskinesia. In clinical trials, the incidence of dyskinesia was 21% for safinamide 50mg, 18% for

safinamide 100mg, and 9% for placebo. There was a greater incidence of dyskinesia causing study discontinuation in PD patients treated with safinamide 50mg or 100mg (1%), compared to placebo (0%).

- Hallucinations/Psychotic Behavior: Patients with a major psychotic disorder should ordinarily not be treated with safinamide because of the risk of exacerbating the psychosis with an increase in central dopaminergic tone.
- Impulse Control/Compulsive Behaviors: Patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking safinamide. In some cases, these urges were reported to have stopped when the dose was reduced or the medication was discontinued.
- Withdrawal-Emergent Hyperprexia and Confusion: A symptom complex resembling neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in drugs that increase central dopaminergic tone.
- Retinal Pathology: Retinal degeneration and loss of photoreceptor cells were observed in rats administered safinamide in toxicity studies. Patients should be periodically monitored for visual changes.

Drug Interactions:

- MAOIs: Safinamide is contraindicated for use with other drugs in the MAOI class or other drugs that are potent inhibitors of monoamine oxidase (e.g., linezolid). Co-administration may lead to HTN crisis. At least 14 days should elapse between discontinuation of safinamide and treatment with other MAOIs.
- Opioid Drugs: Serious reactions have been precipitated with concomitant use of safinamide with opioid drugs (e.g., meperidine, methadone, propoxyphene, tramadol). Concomitant use of these drugs is contraindicated, and at least 14 days should elapse between discontinuation of safinamide and initiation of treatment with these drugs.
- Serotonergic Drugs: Concomitant use of safinamide with SNRIs; triazolopyridine, tricyclic or tetracyclic antidepressants; cyclobenzaprine; or St. John's wort is contraindicated. At least 14 days should elapse between discontinuation of safinamide and initiation of treatment with these drugs.
- Dextromethorphan: The combination of MAOIs and dextromethorphan has been reported to cause episodes of psychosis or bizarre behavior and is therefore contraindicated.
- Sympathomimetic Medications: Severe hypertensive reactions have followed the administration of sympathomimetics and nonselective MAOIs. Concomitant use of safinamide with methylphenidate, amphetamine, and their derivatives is contraindicated.
- Tyramine: MAO in the gastrointestinal (GI) tract and liver provides protection from exogenous amines (e.g., tyramine). Aged, fermented, cured, smoked, and pickled foods containing large amounts of exogenous amines (e.g., aged cheese, pickled herring) may cause release of norepinephrine resulting in a rise in blood pressure (tyramine reaction).

Patients should avoid foods containing a large amount of tyramine while taking safinamide.

- Substrates of Breast Cancer Resistance Protein (BCRP): Safinamide may inhibit GI BCRP. Inhibition of BCRP could increase plasma concentrations of BCRP substrates (e.g., methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, rosuvastatin, sulfasalazine, topotecan). Patients should be monitored for adverse effects of BCRP substrates if safinamide is used concomitantly.
- Dopaminergic Antagonists: Dopamine antagonists (e.g., antipsychotics, metoclopramide) may decrease the effectiveness of safinamide and exacerbate the symptoms of PD.

Adverse Reactions: The most common adverse reactions (≥2% and greater than placebo) reported during safinamide clinical trials were dyskinesia, fall, nausea, and insomnia.

Efficacy: The safety and effectiveness of safinamide were evaluated in two double-blind, placebo-controlled, 24-week studies conducted in PD patients experiencing "off" time during treatment with carbidopa/levodopa. In both studies, the primary measure of effectiveness was the change from baseline in total daily "on" time without troublesome dyskinesia, based on diaries completed by patients. Secondary endpoints included "off" time during the diary period and reduction in UPDRS Part III (motor examination).

- Study 1 (N=645): Safinamide 50mg/day and 100mg/day significantly increased "on" time compared to placebo [least squares difference (LSD) vs placebo: 50mg: 0.50 (0.03, 0.96, p=0.0356) and 100mg: 0.53 (0.07, 1.00, p=0.0238)]. The increase in "on" time without troublesome dyskinesia was accompanied by a similar significant reduction in "off" time and a reduction in UPDRS III scores (assessed during "on" time). Improvement in "on" time occurred without an increase in troublesome dyskinesia.
- Study 2 (N=549): Safinamide 100mg/day significantly increased "on" time compared to placebo [LSD vs placebo: 0.99 (0.58, 1.39, p<0.001)]. The observed increase in "on" time without troublesome dyskinesia was accompanied by a reduction in "off" time of similar magnitude and a reduction in UPDRS III score (assessed during "on" time).

Cost:

Medication	Cost Per Tablet	Cost Per Month	Cost Per Year
Xadago® (safinamide) 50mg & 100mg tablets	**$24.34**	**$730.20**	**$8,762.40**
selegiline 5mg tablets	$1.21	$72.60	$871.20
rasagiline 0.5mg tablets	$11.35	$340.50*	$4,086.00

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.
*Dosing based on adjunctive therapy in patients taking concomitant levodopa.

Gocovri™ [Amantadine Extended-Release (ER)] Product Summary[11,12]

Indication(s): Gocovri™ (amantadine ER) is indicated for the treatment of dyskinesia in patients with PD receiving levodopa-based therapy, with or without concomitant dopaminergic medications.

Dosing:

- Gocovri™ is available as 68.5mg and 137mg ER oral capsules.
- The recommended starting dose of amantadine ER is 137mg by mouth once daily at bedtime. After one week, the dosage should be increased to 274mg (two 137mg capsules) once daily at bedtime.
- No dosage adjustment is recommended in mild renal impairment [creatinine clearance (CrCl) 60 to 80mL/min/1.73m^2). Patients with moderate renal impairment (CrCl 30 to 59mL/min/1.73m^2) should initiate with a dose of 68.5mg and not exceed 137mg. Patients with severe renal impairment (CrCl 15 to 29mL/min/1.73m^2) should not exceed a dose of 68.5mg. Amantadine ER is not recommended in patients with end-stage renal disease (ESRD, CrCl<15mL/min/1.73m^2).
- Amantadine ER should be swallowed whole. If needed, amantadine ER can be administered by opening and sprinkling the entire contents of the capsule on a teaspoonful of soft food and swallowed immediately.
- Amantadine ER can be taken with or without food.
- Concomitant use of amantadine ER with alcohol is not recommended.

Mechanism of Action: The mechanism by which amantadine exerts efficacy in the treatment of dyskinesia in patients with PD is unknown. Amantadine is a weak uncompetitive antagonist of the N-methyl-D-aspartate (NMDA) receptor. Amantadine has not been shown to possess direct anticholinergic activity; however, it exhibits anticholinergic-like side effects such as dry mouth, urinary retention, and constipation in humans. Amantadine may have direct and indirect effects on dopamine neurons; it exerts dopaminergic-like side effects such as hallucinations and dizziness in humans.

Contraindication(s):

- Amantadine ER is contraindicated in patients with ESRD (CrCl<15mL/min/1.73m^2).

Warnings and Precautions:

- <u>Falling Asleep During ADL:</u> Patients treated for PD have reported falling asleep while engaged in ADL, including the operation of motor vehicles. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event.
- <u>Suicidality and Depression:</u> In clinical trials, suicidal ideation or suicide attempt was reported in 2% of amantadine ER-treated patients and 0% of placebo-treated patients. Depression or depressed mood was reported in 6% of amantadine ER-treated patients and 1% of placebo-treated patients. Patient should be monitored for depression, including suicidal ideation or behavior. Prescribers should consider whether the benefits outweigh the risks of treatment with amantadine ER in patients with a history of suicidality or depression.
- <u>Hallucinations/Psychotic Behavior:</u> Patients with a major psychotic disorder should ordinarily not be treated with amantadine ER because of the risk of exacerbating psychosis. In clinical trials, the incidence of patients who experienced visual hallucination, auditory hallucination, delusions, illusions, or paranoia was 25% in amantadine ER-treated patients and 3% in placebo-treated patients. Hallucinations

caused discontinuation of treatment in 8% of amantadine ER-treated patients and 0% of placebo-treated patients.

- Dizziness and Orthostatic Hypotension: In controlled clinical trials, 29% of amantadine ER-treated patients and 2% of placebo-treated patients experienced dizziness, syncope, orthostatic hypotension, presyncope, postural dizziness, or hypotension.
- Withdrawal-Emergent Hyperprexia and Confusion: A symptom complex resembling neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in drugs that increase central dopaminergic tone. Abrupt discontinuation of amantadine ER may cause an increase in the symptoms of PD or cause delirium, agitation, delusions, hallucinations, paranoid reaction, stupor, anxiety, depression, or slurred speech. It is recommended to avoid sudden discontinuation of amantadine ER.
- Impulse Control/Compulsive Behaviors: Patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking amantadine ER. In some cases, these urges were reported to have stopped when the dose was reduced or the medication was discontinued.

Drug Interactions:

- Other Anticholinergic Drugs: Products with anticholinergic properties may potentiate the anticholinergic-like side effects of amantadine. The dose of anticholinergic drugs or of amantadine ER should be reduced if atropine-like effects appear when these drugs are used concurrently.
- Drugs Affecting Urinary pH: The pH of urine has been reported to influence the excretion rate of amantadine. Urine pH is altered by diet, drugs (e.g., carbonic anhydrase inhibitors, sodium bicarbonate), and the clinical state of the patient (e.g., renal tubular acidosis, severe infections of the urinary tract). Since the excretion rate of amantadine increases rapidly when the urine is acidic, the administration of urine acidifying drugs may increase the elimination of the drug from the body. Alterations of urine pH towards the alkaline condition may lead to an accumulation of the drug with a possible increase in adverse reactions. It is recommended to monitor patients for efficacy or adverse reactions under conditions that alter the urine pH to more acidic or alkaline, respectively.
- Live Attenuated Influenza Vaccines: Because of its antiviral properties, amantadine may interfere with the efficacy of live attenuated influenza vaccines. Therefore, live vaccines are not recommended during treatment with amantadine ER. Inactivated influenza vaccines may be used.
- Alcohol: Concomitant use with alcohol is not recommended, as it may increase the potential for central nervous system (CNS) effects such as dizziness, confusion, lightheadedness, and orthostatic hypotension, and may result in dose-dumping.

Adverse Reactions: The most common adverse reactions (≥10% and greater than placebo) reported during amantadine ER clinical trials were hallucinations, dizziness, dry mouth, peripheral edema, constipation, falls, and orthostatic hypotension.

Efficacy: The safety and effectiveness of amantadine ER for the treatment of dyskinesia in PD patients were evaluated in two double-blind, placebo-controlled studies. In both studies, the primary measure of effectiveness was the change from baseline in Unified Dyskinesia Rating Scale (UDysRS). UDysRS evaluates involuntary movements via a historical questionnaire regarding experiences of ADL and an objective assessment performed by a healthcare professional. Secondary endpoints included patient diary reported changes in "on" time without troublesome dyskinesia and "off" time.

- Study 1 (N=121): A significant decrease in mean UDysRS total score (reduction in dyskinesia) was observed at week 12 in amantadine ER-treated patients compared to placebo (treatment difference: -7.9, p=0.0009).
- Study 2 (N=75): A significant decrease in mean UDysRS total score (reduction in dyskinesia) was observed at week 12 in amantadine ER-treated patients compared to placebo (treatment difference: -14.4, p<0.0001).
- In both studies, there was a significant increase in "on" time without troublesome dyskinesia, and a significant decrease in "off" time between baseline and week 12 in patients treated with amantadine ER, compared with placebo.

Cost:

Medication	Cost Per Unit*	Cost Per Month	Cost Per Year
Gocovri™ (amantadine ER) 68.5mg & 137mg capsule	**$39.58**	**$2,374.80**	**$28,497.60**
amantadine 100mg capsule	$0.76	$45.60*	$547.20
amantadine 100mg tablet	$1.29	$77.40*	$928.80
amantadine 50mg/5mL oral syrup	$0.03	$18.00*	$216.00

Unit = capsule, tablet, or mL
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.
*Dosing based on adjunctive therapy in patients taking concomitant levodopa.

Recommendations

The College of Pharmacy recommends the prior authorization of Xadago® (safinamide) and Gocovri™ (amantadine ER) with the following criteria:

Xadago® (Safinamide) Approval Criteria:

1. An FDA approved diagnosis of adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes; and
2. Member must be taking levodopa/carbidopa in combination with safinamide. Safinamide has not been shown to be effective as monotherapy for the treatment of PD; and
3. Member must not have severe hepatic impairment; and
4. Member must not be taking any of the following medications concomitantly with safinamide:
    a. Monoamine oxidase inhibitors (MAOIs); or
    b. Linezolid; or
    c. Opioid analgesics (including tramadol); or

d. Selective norepinephrine reuptake inhibitors (SNRIs); or
e. Tri- or tetra-cyclic or triazolopyridine antidepressants; or
f. St. John's wort; or
g. Cyclobenzaprine; or
h. Methylphenidate and its derivatives; or
i. Amphetamine and its derivatives; or
j. Dextromethorphan; and

5. Prescriber must verify member has been counseled on avoiding foods that contain a large amount of tyramine while taking safinamide; and
6. A quantity limit of one tablet daily will apply.

Gocovri™ [Amantadine Extended-Release (ER)] Approval Criteria:

1. An FDA approved indication for the treatment of dyskinesia in patients with Parkinson's disease (PD) receiving levodopa-based therapy; and
2. Member must use Gocovri™ concomitantly with levodopa therapy; and
3. Member must not have end-stage renal disease (ESRD, CrCl <15mL/min/1.73m^2); and
4. A patient-specific, clinically significant reason why amantadine immediate-release products cannot be used must be provided; and
5. A quantity limit of one 68.5mg capsule or two 137mg capsules per day will apply.

Utilization Details of PD Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
AMANTADINE PRODUCTS						
AMANTADINE CAP 100MG	3,746	621	$282,693.09	6.03	$2.53	$75.47
AMANTADINE TAB 100MG	1,343	467	$167,765.38	2.88	$4.13	$124.92
AMANTADINE SYP 50MG/5ML	230	54	$3,613.18	4.26	$0.55	$15.71
AMANTADINE POW HCL	6	2	$276.37	3	$1.54	$46.06
SUBTOTAL	**5,325**	**1,026**	**$454,348.02**	**5.19**	**$2.85**	**$85.32**
BENZTROPINE PRODUCTS						
BENZTROPINE TAB 1MG	5,176	1,053	$59,055.34	4.92	$0.37	$11.41
BENZTROPINE TAB 2MG	2,278	448	$28,180.51	5.08	$0.40	$12.37
BENZTROPINE TAB 0.5MG	1,692	339	$19,272.36	4.99	$0.38	$11.39
SUBTOTAL	**9,146**	**1,663**	**$106,508.21**	**5.5**	**$0.38**	**$11.65**
ROPINIROLE PRODUCTS						
ROPINIROLE TAB 1MG	1,486	406	$15,348.61	3.66	$0.28	$10.33
ROPINIROLE TAB 0.5MG	1,214	365	$13,206.98	3.33	$0.31	$10.88
ROPINIROLE TAB 2MG	866	220	$9,495.33	3.94	$0.28	$10.96
ROPINIROLE TAB 0.25MG	610	218	$6,832.40	2.8	$0.34	$11.20
ROPINIROLE TAB 4MG	247	57	$2,749.72	4.33	$0.26	$11.13
ROPINIROLE TAB 3MG	223	57	$2,811.24	3.91	$0.33	$12.61
ROPINIROLE TAB 5MG	70	19	$1,152.67	3.68	$0.46	$16.47
SUBTOTAL	**4,716**	**1,147**	**$51,596.95**	**4.11**	**$0.30**	**$10.94**
TRIHEXYPHENIDYL PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
TRIHEXYPHEN TAB 2MG	1,352	317	$10,941.28	4.26	$0.27	$8.09
TRIHEXYPHEN TAB 5MG	1,332	245	$15,909.72	5.44	$0.39	$11.94
TRIHEXYPHEN ELX 0.4MG/ML	111	20	$2,923.66	5.55	$0.91	$26.34
SUBTOTAL	**2,795**	**543**	**$29,774.66**	**5.15**	**$0.35**	**$10.65**
CARBIDOPA/LEVODOPA PRODUCTS						
CARB/LEVO TAB 25-100MG	730	145	$11,516.41	5.03	$0.52	$15.78
CARB/LEVO TAB 25-250MG	223	37	$5,989.64	6.03	$0.91	$26.86
CARB/LEVO TAB 10-100MG	196	43	$3,197.37	4.56	$0.48	$16.31
CARB/LEVO ER TAB 50-200MG	140	23	$5,041.37	6.09	$1.09	$36.01
CARB/LEVO ER TAB 25-100MG	73	17	$2,315.26	4.29	$1.00	$31.72
CARB/LEVO TAB 10-100MG	12	2	$572.63	6	$1.38	$47.72
RYTARY CAP 195MG	6	1	$3,613.02	6	$20.07	$602.17
RYTARY CAP 245MG	3	1	$2,229.55	3	$24.77	$743.18
CARB/LEVO TAB 25-100MG	3	2	$334.41	1.5	$3.45	$111.47
CARB/LEVO TAB 25-250MG	1	1	$92.93	1	$3.10	$92.93
SUBTOTAL	**1,387**	**251**	**$34,902.59**	**5.53**	**$0.81**	**$25.16**
CARBIDOPA/LEVODOPA/ENTACAPONE PRODUCTS						
CARB/LEVO/ENTACA TAB 12.5/50/200	17	3	$3,519.68	5.67	$7.18	$207.04
CARB/LEVO/ENTACA TAB 37.5/150/200	13	2	$2,254.29	6.5	$5.78	$173.41
CARB/LEVO/ENTACA TAB 25/100/200	9	3	$2,223.75	3	$8.24	$247.08
CARB/LEVO/ENTACA TAB 50/200/200	6	2	$1,125.70	3	$6.25	$187.62
SUBTOTAL	**45**	**7**	**$9,123.42**	**6.43**	**$6.86**	**$202.74**
CARBIDOPA PRODUCTS						
CARBIDOPA TAB 25MG	1	1	$486.78	1	$16.23	$486.78
SUBTOTAL	**1**	**1**	**$486.78**	**1**	**$16.23**	**$486.78**
PRAMIPEXOLE PRODUCTS						
PRAMIPEXOLE TAB 0.25MG	401	119	$3,718.57	3.37	$0.26	$9.27
PRAMIPEXOLE TAB 0.125MG	373	118	$3,419.01	3.16	$0.27	$9.17
PRAMIPEXOLE TAB 0.5MG	349	99	$3,202.82	3.53	$0.24	$9.18
PRAMIPEXOLE TAB 1MG	241	68	$2,600.94	3.54	$0.27	$10.79
PRAMIPEXOLE TAB 1.5MG	64	17	$579.14	3.76	$0.22	$9.05
PRAMIPEXOLE TAB 0.75MG	18	6	$197.85	3	$0.38	$10.99
SUBTOTAL	**1,446**	**369**	**$13,718.33**	**3.92**	**$0.26**	**$9.49**
BROMOCRIPTINE PRODUCTS						
BROMOCRIPTIN TAB 2.5MG	260	68	$37,828.74	3.82	$4.76	$145.50
BROMOCRIPTIN CAP 5MG	47	11	$16,950.81	4.27	$12.06	$360.66
SUBTOTAL	**307**	**74**	**$54,779.55**	**4.15**	**$5.86**	**$178.44**
ENTACAPONE PRODUCTS						
ENTACAPONE TAB 200MG	26	4	$9,421.50	6.5	$12.53	$362.37
SUBTOTAL	**26**	**4**	**$9,421.50**	**6.5**	**$12.53**	**$362.37**
RASAGILINE PRODUCTS						
AZILECT TAB 1MG	24	7	$12,911.48	3.43	$18.13	$537.98
RASAGILINE TAB 1MG	19	5	$7,014.25	3.8	$12.31	$369.17

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
SUBTOTAL	**43**	**9**	**$19,925.73**	**4.78**	**$15.54**	**$463.39**
ROTIGOTINE PRODUCTS						
NEUPRO DIS 8MG/24HR	6	2	$3,570.12	3	$19.83	$595.02
NEUPRO DIS 4MG/24HR	6	1	$3,555.11	6	$19.75	$592.52
NEUPRO DIS 2MG/24HR	2	1	$1,202.04	2	$20.03	$601.02
SUBTOTAL	**14**	**4**	**$8,327.27**	**3.5**	**$19.83**	**$594.81**
SELEGILINE PRODUCTS						
SELEGILINE CAP 5MG	1	1	$98.01	1	$3.27	$98.01
SUBTOTAL	**1**	**1**	**$98.01**	**1**	**$3.27**	**$98.01**
PIMAVANSERIN PRODUCTS						
NUPLAZID TAB 17MG	24	9	$47,896.97	2.67	$68.72	$1,995.71
SUBTOTAL	**24**	**9**	**$47,896.97**	**2.67**	**$68.72**	**$1,995.71**
TOTAL	**25,276**	**4,766***	**$840,907.99**	**5.3**	**$1.04**	**$33.27**

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

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Appendix M

30-Day Notice to Prior Authorize Mepsevii™ (Vestronidase Alfa-vjbk)

Oklahoma Health Care Authority
February 2018

Introduction[1,2,3]

Sly syndrome, also known as mucopolysaccharidosis VII or MPS VII, is a rare disorder caused by mutations in the gene encoding beta-glucuronidase (GUSB). The enzyme deficiency causes accumulation of heparan sulfate, dermatan sulfate, chondroitin-4-sulfate, and chondroitin-6-sulfate. Sly syndrome is inherited in an autosomal recessive pattern. The exact incidence of Sly syndrome is unknown; however, it is estimated to occur in 1 in 250,000 newborns. Sly syndrome is one of the rarest forms of MPS.

Clinical presentation of Sly syndrome is variable. Clinical features and complications of Sly syndrome may be similar to MPS I, with significant soft tissue and skeletal abnormalities. The most severe cases are characterized by hydrops fetalis and may account for a large proportion of patients that are unrecognized because they do not survive to be diagnosed. Other individuals with MPS VII may begin to show symptoms in early childhood. The features of MPS VII include macrocephaly, hydrocephalus, macroglossia, and distinctive-looking facial features that are described as "coarse". Individuals affected with MPS VII frequently develop hepatosplenomegaly, heart valve abnormalities, and umbilical or inguinal hernias. Patients may have developmental delay, but in some people with this condition, intelligence is unaffected. The life expectancy of MPS VII depends on the severity of symptoms with some affected individuals not surviving infancy while others may live into adolescence or adulthood. Life expectancy is reduced as a result of frequent upper respiratory tract infections, neurodegenerative complications, and abnormalities of the gastrointestinal tract.

The U.S. Food and Drug Administration (FDA) approved Mepsevii™ (vestronidase alfa-vjbk), an enzyme replacement therapy (ERT), in November 2017 for the treatment of Sly syndrome. Mepsevii™ is the first and only FDA-approved ERT for Sly syndrome. Other treatment options for Sly syndrome are supportive and symptomatic.

Mepsevii™ (Vestronidase Alfa-vjbk) Product Summary[4]

Indication(s): Mepsevii™ (vestronidase alfa-vjbk) is a recombinant human lysosomal beta glucuronidase indicated in adult and pediatric patients for the treatment of mucopolysaccharidosis VII (MPS VII, Sly syndrome).

- Limitations of use: The effect of Mepsevii™ on the central nervous system manifestations of MPS VII has not been determined.

Dosing:

- Mepsevii™ is available as a carton containing one 10mg/5mL single-dose vial.

- The recommended dosage of vestronidase alfa-vjbk is 4mg/kg administered every two weeks as an intravenous (IV) infusion. It is recommended to administer the infusion over approximately 4 hours.
- Premedication with a non-sedating antihistamine with or without an anti-pyretic is recommended 30 to 60 minutes prior to the start of the infusion.

Boxed Warning: Anaphylaxis

- Anaphylaxis has occurred with vestronidase alfa-vjbk administration, as early as the first dose. Therefore, appropriate medical support should be readily available when vestronidase alfa-vjbk is administered. Patients should be closely observed during and for 60 minutes after the vestronidase alfa-vjbk infusion. The infusion should be immediately discontinued if the patient experiences anaphylaxis.

Mechanism of Action: MPS VII is a lysosomal disorder characterized by the deficiency of human beta-glucuronidase (GUS) that results in glycosaminoglycan (GAG) accumulation in cells throughout the body leading to multisystem tissue and organ damage. Vestronidase alfa-vjbk is a recombinant form of human GUS and is intended to provide exogenous GUS enzyme for uptake into cellular lysosomes. Mannose-6-phosphate (M6P) residues on the oligosaccharide chains allow binding of the enzyme to cell surface receptors, leading to cellular uptake of the enzyme, targeting to lysosomes, and subsequent catabolism of accumulated GAGs in affected tissues.

Contraindication(s): None.

Warnings and Precautions:

- Anaphylaxis: In the clinical program, anaphylaxis to vestronidase alfa-vjbk was reported in 2 of 20 patients. These reactions occurred during infusion of vestronidase alfa-vjbk and were observed as early as the first dose for one patient. Manifestations included respiratory distress, cyanosis, decreased oxygen saturation, and hypotension. The two patients with anaphylaxis to vestronidase alfa-vjbk during the clinical trials had one occurrence each and tolerated subsequent infusions of vestronidase alfa-vjbk, without recurrence.

Adverse Reactions: The most common adverse reactions (occurring in one or more patients) are infusion site extravasation, diarrhea, rash, anaphylaxis, infusion site swelling, peripheral swelling, and pruritus.

Use in Specific Populations:

- Pregnancy: There are no available data on vestronidase alfa-vjbk use in pregnant women to determine a drug-associated risk of adverse developmental outcomes. In animal reproductive studies, vestronidase alfa-vjbk administered IV to pregnant rats and rabbits during the period of organogenesis showed no maternal toxicity or adverse developmental outcomes at doses causing maternal serum exposures up to 1.6 and 10 times the exposure at the recommended human dose, respectively for rats and rabbits.

- Lactation: There are no data on the presence of vestronidase alfa-vjbk in either human or animal milk, the effects on the breastfed infant, or the effects on milk production.
- Pediatric Use: The safety and effectiveness of vestronidase alfa-vjbk have been established in pediatric patients younger than 18 years of age.
- Geriatric Use: Clinical trials of vestronidase alfa-vjbk did not include any patients 65 years of age or older. It is not known whether elderly patients respond differently from younger patients.

Efficacy: The clinical program for vestronidase alfa-vjbk included 23 patients with MPS VII, 17 of whom were evaluable for efficacy, 20 for safety, and 23 for immunogenicity. The patients ranged in age from 5 months to 25 years and 16 patients were younger than 18 years of age. Patients were enrolled in clinical trials and expanded access protocols. Patients received treatment at doses up to 4mg/kg once every two weeks for up to 164 weeks.

- Studies 301 and 202: Study 301 was a randomized start trial of vestronidase alfa-vjbk 4mg/kg every two weeks in patients with MPS VII. Twelve patients were randomized to one of four placebo durations before crossing over to active treatment. Patients either received vestronidase alfa-vjbk immediately for a duration of 48 weeks, placebo for 8 weeks then vestronidase alfa-vjbk for 40 weeks, placebo for 16 weeks then vestronidase alfa-vjbk for 32 weeks, or placebo for 24 weeks then vestronidase alfa-vjbk for 24 weeks. Patients enrolled in Study 301 were eligible to roll over to Study 202, an open-label extension trial in which patients received additional doses of vestronidase alfa-vjbk at 4mg/kg every two weeks for up to 124 weeks. Motor function, forced vital capacity, and visual acuity were assessed in Study 301 after 24 weeks of vestronidase alfa-vjbk treatment and measured against pre-specified minimal important differences. The extremely small population of patients with MPS VII globally necessitated the enrollment of all patients able to participate resulting in a highly heterogeneous group. Due to the extent of disease, age, or level of cognition, clinical endpoints were not assessable in some patients. In 10 of 12 patients, repeated assessments of the six minute walk test (6MWT) were feasible. Of the three patients who improved on their 6MWT, two also were noted to have improvement in balance and gross motor proficiency as assessed by the Bruininks-Oseretsky Test Motor Proficiency. The mean difference in 6MWT distance between vestronidase alfa-vjbk and placebo are presented in the following table.

Duration of Vestronidase Alfa-vjbk Treatment	LS Mean 6MWT (Meters) (± Standard Error)*	Number and Treatment Assignment of Patients Included in Analysis**
8 weeks	-11 (± 24)	5 placebo period; 8 vestronidase alfa-vjbk period
16 weeks	13 (± 32)	5 placebo period; 8 vestronidase alfa-vjbk period
24 weeks	18 (± 33)	5 placebo period; 8 vestronidase alfa-vjbk period

*ANCOVA analysis of change from baseline in least squares (LS) mean between placebo and vestronidase alfa-vjbk for different periods, after adjusting for study cohort, age, and baseline 6MWT distance. Patients who used assistive devices were imputed as zeros in the analysis.

**Based upon a randomized start trial design and patient ability to complete testing. Due to no placebo period for the three patients who received 48 weeks of vestronidase alfa-vjbk in the first cohort of the randomized start design, more data were available for analyses during the treatment period (n=8) than during the placebo period (n=5). Data from eight participants were available at each time point; however, due to missing observations, the eight participants were not the same across all time points.

- Study 201: Study 201 was a single-arm, open-label, dose exploration trial completed outside the United States. Three MPS VII patients were enrolled, ranging in age from 5 to 25 years. After 120 weeks of treatment with vestronidase alfa-vjbk, one patient demonstrated a 21% improvement over baseline in forced vital capacity on pulmonary function testing in addition to a 105 meter improvement in the 6MWT. Two other patients with baseline hepatosplenomegaly had reduction in liver volume (24% and 53%) and spleen volume (28% and 47%) after 36 weeks of vestronidase alfa-vjbk treatment.
- Expanded access to vestronidase alfa-vjbk treatment was provided to a pediatric patient who required continuous ventilatory support at the start of treatment and after 164 weeks of vestronidase alfa-vjbk treatment was able to tolerate 9 hours daily off ventilator support.

Cost: The wholesale acquisition cost (WAC) of Mepsevii™ (vestronidase alfa-vjbk) is $2,115.00 per 10mg/5mL single-use vial for IV infusion.

Patient Weight	Dosing Regimen	Vials Per Infusion	Cost Per Infusion	Cost Per Year
10kg	40mg Q2W	4	$8,460.00	$219,960.00
20kg	80mg Q2W	8	$16,920.00	$439,920.00
55kg	220mg Q2W	22	$46,530.00	$1,209,780.00

Q2W = every 2 weeks
Costs based on WAC and do not reflect rebated prices or net costs. Cost per year based on 26 infusions.

Recommendations

The College of Pharmacy recommends the prior authorization of Mepsevii™ (vestronidase alfa-vjbk) with the following criteria:

Mepsevii™ (Vestronidase Alfa-vjbk) Approval Criteria:

1. An FDA approved diagnosis of Sly syndrome (mucopolysaccharidosis type VII; MPS VII) confirmed by:
    a. Enzyme assay demonstrating a deficiency of beta-glucuronidase (GUSB) activity; or
    b. Genetic testing to confirm diagnosis of MPS VII; and
2. Mepsevii™ must be administered by a healthcare professional prepared to manage anaphylaxis; and
3. Initial approvals will be for the duration of twelve months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.
4. 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.

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Appendix N

Fiscal Year 2017 Annual Review of Anti-Migraine Medications and 30-Day Notice to Prior Authorize Ergomar® (Ergotamine Sublingual Tablets)

Oklahoma Health Care Authority
February 2018

Current Prior Authorization Criteria

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/naproxen (Treximet®)

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

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 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 components 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 or dihydroergotamine injection (D.H.E. 45®).

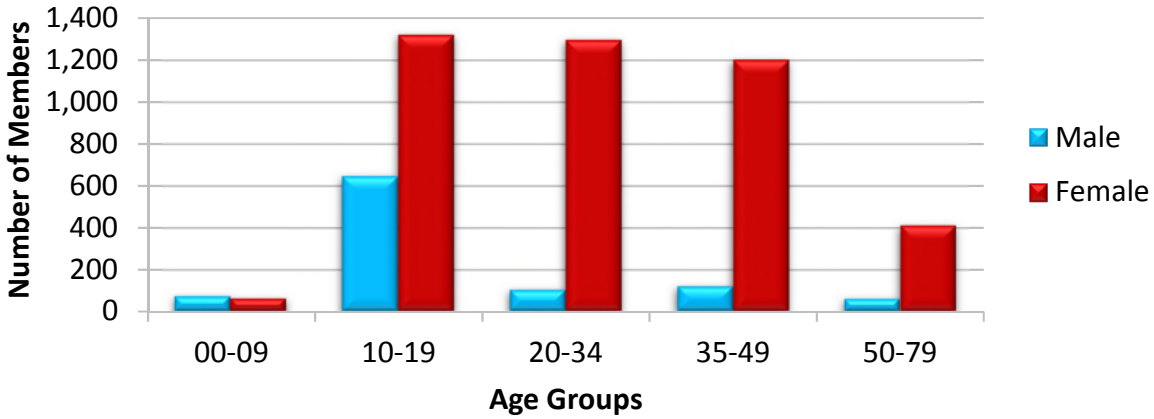
Utilization of Anti-Migraine Medications: Fiscal Year 2017

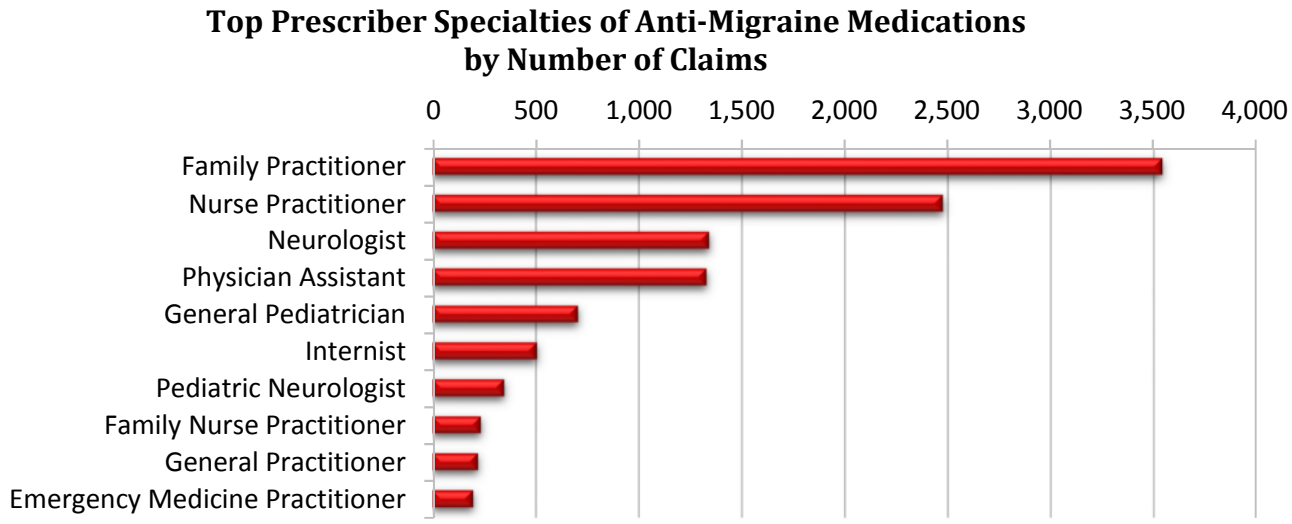
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	5,382	11,516	$418,545.64	$36.34	$2.25	122,720	186,170
2017	5,281	11,503	$263,993.38	$22.95	$1.45	123,586	182,232
% Change	**-1.90%**	**-0.10%**	**-36.90%**	**-36.80%**	**-35.60%**	**0.70%**	**-2.10%**
Change	**-101**	**-13**	**-$154,552.26**	**-$13.39**	**-$0.80**	**866**	**-3,938**

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

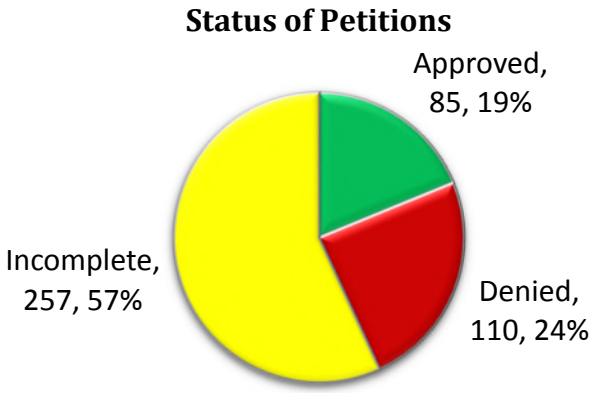
Demographics of Members Utilizing Anti-Migraine Medications





Prior Authorization of Anti-Migraine Medications

There were 452 prior authorization requests submitted for anti-migraine medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.



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

Anticipated Patent Expiration(s):

- Zomig® (zolmitriptan nasal spray): May 2021
- Treximet® (sumatriptan/naproxen tablets): April 2026
- Sumavel® DosePro® 6mg/0.5mL (sumatriptan needle-free injection): November 2026
- Onzetra® Xsail® (sumatriptan nasal powder): December 2030

Generic Availability:

- **July 2017:** Generic versions of Relpax® (eletriptan) were launched.

News:

- **June 2016:** Teva Pharmaceuticals announced it was voluntarily discontinuing the marketing and distribution of Zecuity® (sumatriptan transdermal system) based on post-

marketing reports of burning and scarring at the patch application site. Teva also launched a recall of the medication from pharmacies. The discontinuation followed an alert from the U.S. Food and Drug Administration (FDA) that cited "severe redness, pain, skin discoloration, blistering, and cracked skin."

Pipeline:

- **Erenumab:** In January 2018, Amgen announced positive results from the Phase 3b LIBERTY study assessing the efficacy and safety of Aimovig™ (erenumab) 140mg. The study included patients with episodic migraine who had experienced two to four previous preventive treatment failures, due to lack of efficacy or intolerable side effects. The study met is primary endpoint, with significantly more patients in the erenumab-treated group experiencing a 50% reduction from baseline in their monthly migraine days as compared to placebo. Erenumab is the only investigational fully human monoclonal antibody designed to block the calcitonin gene-related peptide (CGRP) receptor. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date for erenumab of May 17, 2018.
- **Galcanezumab:** A Phase 2b dosing trial of galcanezumab suggests that subcutaneous (SC) injections of the investigational CGRP antibody is especially effective at 120mg for the prevention of episodic migraine. In December 2017, the study findings were published online in *JAMA Neurology*. The study included more than 400 patients and showed that those who self-administered a once-monthly injection of galcanezumab 120mg or 300mg had significantly greater overall change from baseline to three months in migraine headache days (MHDs) compared to those receiving placebo. However, only the 120mg dose met the primary objective of "posterior probability of greater improvement (Bayesian analysis) in MHDs" than the specified threshold of 95% for mean change versus placebo. Common treatment related adverse events for the galcanezumab group versus the placebo group included injection site pain, upper respiratory tract infection, and nasopharyngitis. According to a press release from Eli Lilly and Co., the FDA has accepted a Biologics License Application (BLA) to review galcanezumab.
- **Fremanezumab:** Teva Pharmaceuticals announced in October 2017 the submission of a BLA to the FDA for fremanezumab, an anti-CGRP monoclonal antibody for the preventive treatment of migraine. The BLA includes data from the HALO clinical trial program, which enrolled more than 2,000 patients with episodic migraine (EM) and chronic migraine (CM), evaluating both monthly and quarterly dose regimens of fremanezumab.
- **Eptinezumab:** Alder BioPharmaceuticals announced that eptinezumab, an investigational monoclonal antibody for migraine prevention that targets CGRP, met the primary endpoint in its Phase 3 PROMISE 2 clinical trial. Following a single eptinezumab infusion, subjects had an 8.2 monthly migraine day reduction from baseline compared to 5.6 days for placebo ($p<0.0001$). The company plans to submit a BLA in the second half of 2018.
- **Lasmiditan:** Eli Lilly and Company announced in August 2017 that lasmiditan, an investigational, oral, first-in-class molecule for the acute treatment of migraine, met its

primary endpoint in a second Phase 3 study, SPARTAN. A greater percentage of patients treated with lasmiditan were migraine pain-free compared to placebo at two hours after the first dose. The results were statistically significant across all three study doses (50mg, 100mg, and 200mg). These findings were consistent with the first Phase 3 study evaluating the safety and efficacy of lasmiditan for the acute treatment of migraine. In this study, lasmiditan met both the primary and key secondary endpoints with statistical significance.

Ergomar® (Ergotamine Sublingual Tablets) Product Summary[10]

Indication(s): Ergomar® (ergotamine tartrate) is indicated as therapy to abort or prevent vascular headache (e.g., migraine, migraine variants, so-called "histaminic cephalalgia").

Dosing:

- Ergomar® is available as sublingual tablets containing 2mg of ergotamine tartrate. They are supplied in unit-dose cartons of 20 tablets.
- At the first sign of an attack or to relieve symptoms after onset of an attack, the recommended dosage is to place one 2mg tablet under the tongue. It is recommended that dosage start at the first sign of an attack as early administration gives maximum effectiveness. Another tablet should be taken at half hour intervals thereafter, if necessary, but dosage must not exceed three tablets in any 24-hour period. The total weekly dosage should not exceed five tablets (10mg) in any one week.
- Ergomar® should not be used for chronic daily administration.

Boxed Warning: Serious and/or Life-Threatening Peripheral Ischemia

- Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of ergotamine tartrate with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 inhibition elevates the serum levels of ergotamine tartrate, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Concomitant use of these medications is contraindicated.

Mechanism of Action: Ergotamine is an alpha-adrenergic blocking agent with a direct stimulating effect on the smooth muscle of peripheral and cranial blood vessels and produces depression of central vasomotor centers. The compound also has the properties of serotonin antagonism. In comparison to hydrogenated ergotamine, the adrenergic blocking actions are less pronounced and vasoconstrictive actions are greater.

Contraindication(s):

- Coadministration of ergotamine with potent CYP 3A4 inhibitors (ritonavir, nelfinavir, indinavir, erythromycin, clarithromycin, and troleandomycin) has been associated with acute ergot toxicity (ergotism) characterized by vasospasm and ischemia of the extremities, with some cases requiring amputation. There have been rare reports of cerebral ischemia in patients on protease inhibitor therapy when ergotamine was coadministered, at least one resulting in death. Due to the increased risk of ergotism and other serious vasospastic adverse events, ergotamine use is contraindicated with

these medications and other potent CYP 3A4 inhibitors (e.g., ketoconazole, itraconazole).

- Ergotamine sublingual tablets may cause fetal harm when administered to pregnant women. Ergotamine sublingual tablets are contraindicated in women who are or may become pregnant. If the medication is used during pregnancy or if the patient becomes pregnant while taking this medication, the patient should be apprised of the potential hazard to the fetus.
- Peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, and sepsis.
- Hypersensitivity to any of the components.

Warnings and Precautions:

- CYP 3A4 Inhibitors: Coadministration of ergotamine with potent CYP 3A4 inhibitors has been associated with serious adverse reactions and these medications should not be given concomitantly with ergotamine. These reactions have not been reported with less potent CYP 3A4 inhibitors; however, there is a potential risk for serious toxicity including vasospasm when these medications are used with ergotamine. Examples of less potent CYP 3A4 inhibitors include: saquinavir, grapefruit juice, metronidazole, clotrimazole, fluconazole, fluoxetine, and nefazodone. This list is not exhaustive and the prescriber should consider the effects on CYP 3A4 of other agents being considered for concomitant use with ergotamine.
- Fibrotic Complications: There have been a few reports of patients on ergotamine and caffeine therapy developing retroperitoneal and/or pleuropulmonary fibrosis. There have also been rare reports of fibrotic thickening of the aortic, mitral, tricuspid, and/or pulmonary valves with long-term continuous use of ergotamine with caffeine. Ergomar® should not be used for chronic daily administration.
- General: Although signs and symptoms of ergotism rarely develop even after long-term intermittent use of the medication, care should be exercised to remain within the recommended dosage limits. Ergotism is manifested by intense arterial vasoconstriction, producing signs and symptoms of peripheral vascular ischemia. Ergotamine induces vasoconstriction by a direct action on vascular smooth muscle. In chronic intoxication with ergot derivatives, headache, intermittent claudication, muscle pains, numbness, coldness, and pallor of the digits may occur. If the condition is allowed to progress untreated, gangrene may result. While most cases of ergotism associated with ergotamine treatment result from frank overdosage, some cases have involved apparent hypersensitivity. There are few reports of ergotism in patients who took doses within the recommended limits or for brief periods of time. In rare instances, patients, particularly those patients who have used the medication indiscriminately over long periods of time, may display withdrawal symptoms consisting of rebound headache upon discontinuation of the medication.

Adverse Reactions: The following adverse reactions have been reported with ergotamine: vasoconstrictive complications of a serious nature (i.e., ischemia, cyanosis, absence of pulse, cold extremities, gangrene, precordial distress and pain, EKG changes, and muscle pains),

transient tachycardia or bradycardia, hypertension, nausea, vomiting, paresthesias, numbness, weakness, vertigo, localized edema, itching, and fibrotic complications.

Use in Specific Populations:

- Pregnancy: Pregnancy Category X. There are no studies on the placental transfer or teratogenicity of Ergomar®. Ergotamine crosses the placenta in small amounts, although it does not appear to be embryotoxic in this quantity. However, prolonged vasoconstriction of the uterine vessels and/or increased myometrial tone leading to reduced myometrial and placental blood flow may have contributed to fetal growth retardation observed in animals. Ergomar® is contraindicated in pregnancy due to oxytocic effects of ergotamine.
- Lactation: Ergot medications are known to inhibit prolactin but there are no reports of decreased lactation with Ergomar®. Ergotamine is excreted in breast milk and may cause symptoms of vomiting, diarrhea, weak pulse, and unstable blood pressure in nursing infants.
- Pediatric Use: The safety and effectiveness of Ergomar® have not been established in pediatric patients.

Efficacy: Availability of efficacy data regarding Ergomar® is limited. No specific efficacy data is included in the Ergomar® prescribing information.

Cost:

Medication	Cost Per Tablet	Cost Per Month*
Ergomar® 2mg (ergotamine tartrate sublingual tablet)	**$56.35**	**$1,127.00**
Maxalt® 10mg (rizatriptan tablet)	$0.86	$10.32
Zomig-ZMT® 5mg (zolmitriptan sublingual tablet)	$6.72	$40.32

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 for Ergomar® based on cost of one carton containing 20 tablets. The maximum recommended total weekly dosage should not exceed five tablets in any one week. Cost per month for triptan products based on maximum monthly dose according to package labeling.

Recommendations

The College of Pharmacy recommends the following:

1. Moving Zomig® (zolmitriptan nasal spray) from Tier-3 to Tier-2 of the Anti-Migraine Medication Product Based Prior Authorization (PBPA) category based on net cost. Current Tier-2 criteria would apply.
2. Brand name Relpax® (eletriptan) will be preferred over the generic formulation. Approval of generic eletriptan would require a patient-specific, clinically significant reason the member cannot use the brand formulation.
3. The placement of Ergomar® (ergotamine sublingual tablets) into the Special Prior Authorization (PA) Tier of the Anti-Migraine Medication PBPA category with the following criteria:

a. **Ergomar® (Ergotamine Sublingual Tablets) Approval Criteria:**
   i. Use of Ergomar® (ergotamine sublingual tablets) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan medications; and
   ii. A quantity limit of 20 tablets per 28 days will apply.

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

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

Utilization Details of Anti-Migraine Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	%COST
TIER-1 PRODUCTS						
SUMATRIPTAN TAB 100MG	3,536	1,476	$50,699.82	$1.03	$14.34	19.20%
SUMATRIPTAN TAB 50MG	3,214	1,750	$46,387.01	$1.04	$14.43	17.57%
SUMATRIPTAN TAB 25MG	2,162	1,250	$34,380.79	$1.16	$15.90	13.02%
RIZATRIPTAN TAB 10MG	1,074	483	$21,071.48	$0.85	$19.62	7.98%
RIZATRIPTAN TAB 10MG ODT	644	311	$14,354.44	$0.98	$22.29	5.44%
RIZATRIPTAN TAB 5MG ODT	294	177	$6,176.31	$0.92	$21.01	2.34%
RIZATRIPTAN TAB 5MG	293	157	$5,791.14	$0.84	$19.76	2.19%
RELPAX TAB 40MG	82	39	$37,345.60	$32.85	$455.43	14.15%
RELPAX TAB 20MG	16	15	$7,629.29	$45.14	$476.83	2.89%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	%COST
TIER-1 SUBTOTAL	**11,315**	**5,658**	**$223,835.88**	**$1.26**	**$19.78**	**84.78%**
TIER-2 PRODUCTS						
NARATRIPTAN TAB 2.5MG	53	15	$2,059.60	$1.90	$38.86	0.78%
ZOLMITRIPTAN TAB 5MG	26	11	$1,409.58	$1.92	$54.21	0.53%
ZOLMITRIPTAN TAB 2.5MG	5	1	$270.58	$1.80	$54.12	0.10%
ZOLMITRIPTAN TAB 5MG	4	1	$223.58	$1.86	$55.90	0.08%
NARATRIPTAN TAB 1MG	3	1	$156.22	$7.44	$52.07	0.06%
ZOLMITRIPTAN TAB 2.5MG	1	1	$47.92	$1.60	$47.92	0.02%
TIER-2 SUBTOTAL	**92**	**30**	**$4,167.48**	**$1.95**	**$45.30**	**1.57%**
TIER-3 PRODUCTS						
ZOMIG SPR 5MG	11	5	$3,759.69	$11.39	$341.79	1.42%
ZOMIG SPR 2.5MG	2	1	$758.88	$12.65	$379.44	0.29%
ALMOTRIP MAL TAB 12.5MG	1	1	$301.84	$60.37	$301.84	0.11%
FROVATRIPTAN TAB 2.5MG	1	1	$512.99	$102.60	$512.99	0.19%
TIER-3 SUBTOTAL	**15**	**8**	**$5,333.40**	**$13.33**	**$355.56**	**2.01%**
SPECIAL PA PRODUCTS						
SUMATRIPTAN INJ 6MG/0.5	35	4	$17,733.13	$22.85	$506.66	6.72%
SUMATRIPTAN INJ 6MG/0.5	16	3	$2,056.47	$8.10	$128.53	0.78%
SUMATRIPTAN SPR 20MG/ACT	12	1	$3,496.03	$10.37	$291.34	1.32%
SUMATRIPTAN INJ 6MG/0.5	11	1	$4,565.49	$26.24	$415.04	1.73%
SUMATRIPTAN SPR 5MG/ACT	7	3	$2,805.50	$21.25	$400.79	1.06%
SPECIAL PA SUBTOTAL	**81**	**12**	**$30,656.62**	**$18.32**	**$378.48**	**11.61%**
TOTAL	**11,503**	**5,281***	**$263,993.38**	**$1.45**	**$22.95**	**100%**

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

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Appendix O

Industry News and Updates

Oklahoma Health Care Authority
February 2018

Introduction

The following report is an overview of recent issues, important literature, and select guideline updates impacting pharmacy and health care. Information that is expected to have a particular impact in the SoonerCare population has been included for review.

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

News:

- **Narrow-Spectrum Antibiotics:** Researchers reported in the *Journal of the American Medical Association* that broad-spectrum antibiotics were not associated with better clinical outcomes; however, their use was associated with higher rates of adverse events. In a retrospective, cohort analysis involving approximately 30,000 children treated for otitis media, acute sinusitis, or other respiratory infections, treatment with penicillin, amoxicillin, and other narrow-spectrum antibiotics were as effective as broad-spectrum antibiotics. Broad-spectrum antibiotics were associated with a slightly worse child quality of life on the Pediatric Quality of Life Inventory score [-1.4% score difference for full matched analysis; 95% confidence interval (CI) -2.4% to -0.4%]. The researchers stated the findings "support the use of narrow-spectrum antibiotics for most children with acute respiratory tract infections." They noted that the current recommendations for the choice of antibiotics in the treatment of acute respiratory tract infections in the pediatric setting are inconsistent. The American Academy of Pediatrics recommends penicillin or amoxicillin as first-line therapy for most children with acute otitis media and amoxicillin is also included as a first-line treatment for acute sinusitis. The Infectious Disease Society of America recommends the use of amoxicillin-clavulanate, a broad-spectrum antibiotic, for these pediatric patients.
- **Oral Microbiome:** Two case-control studies suggest that certain bacteria in the oral microbiome may be associated with esophageal and gastric cancer. In an analysis of gene sequencing data from oral microbiota embedded in oral wash samples taken from 122,000 participants in large cohort studies, a greater abundance of *Porphyromonas gingivalis* trended towards a higher risk of esophageal squamous cell carcinoma and higher levels of *Tenneralla forsythia* were associated with an increased risk of esophageal adenocarcinoma. A different study from the New York University (NYU) College of Dentistry and the NYU School of Medicine also found that an increase in certain oral pathogens along with decreased bacterial diversity in the mouth were associated with an increased risk of precancerous lesions of gastric cancer.
- **Cancer Statistics:** The latest report on cancer statistics was published in *CA: A Cancer Journal for Clinicians*. The most common cancer in men is prostate cancer and the most common cancer in women is breast cancer; however, prostate and breast cancer are not

the most common cause of cancer death. Prostate cancer accounts for 19% of cancers in men and breast cancer accounts for 30% of cancers in women, but the most common cause of cancer death in both sexes is lung cancer. Lung cancer accounts for one-quarter of cancer deaths in both sexes while breast cancer accounts for 14% of deaths in women and prostate cancer causes 9% of deaths in men. The cancer death rate dropped approximately 1.5% a year from 1991 to 2015, resulting in a total decrease of 26% or nearly 2.4 million fewer cancer deaths. The American Cancer Society predicts that in 2018 there will be 1,735,350 new cases of cancer and 609,640 deaths.

- **Opioid Cough Medications:** The U.S. Food and Drug Administration (FDA) announced it will require label changes to limit the use of prescription opioid cough and cold medications containing codeine or hydrocodone to adults 18 years of age and older. The FDA will also require additional safety information be added to the "boxed warning" on these medications highlighting the risks of misuse, abuse, addiction, overdose, death, and slowed or difficulty breathing. The FDA advises healthcare professionals to reassure caregivers that cough due to a cold or upper respiratory tract infection is self-limited and generally does not require treatment. In children for whom cough treatment is necessary, alternative medications are available, such as over-the-counter dextromethorphan or prescription benzonatate products.
- **Flu Vaccinations:** According to the Centers for Disease Control and Prevention (CDC) director Dr. Brenda Fitzgerald, of the 30 U.S. children who have died from the flu so far this season, around 85% had not been vaccinated. Dr. Fitzgerald urged Americans to get a flu shot during one of the most severe flu seasons seen in years. During this flu season, the dominant strain is influenza A (H3N2) and has been linked with severe disease and death in past seasons. Although it is estimated the vaccine is about 30% effective against H3N2 strain, studies have shown that it reduces severity and duration if people do become infected, according to Dr. Dan Jerigan, director of the influenza division of the CDC.

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Appendix P

U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates (additional information can be found at http://www.fda.gov/Drugs/default.htm)

FDA NEWS RELEASE

For Immediate Release: January 12th, 2018

FDA approves first treatment for breast cancer with a certain inherited genetic mutation

FDA approves first treatment for breast cancer with a certain inherited genetic mutation

The FDA expanded the approved use of Lynparza® (olaparib tablets) to include the treatment of patients with certain types of breast cancer that have spread (metastasized) and whose tumors have a specific inherited (germline) genetic mutation, making it the first drug in its class (PARP inhibitor) approved to treat breast cancer, and it is the first time any drug has been approved to treat certain patients with metastatic breast cancer who have a "BRCA" gene mutation. Patients are selected for treatment with Lynparza® based on an FDA-approved genetic test, called the BRACAnalysis CDx.

Breast cancer is the most common form of cancer in the United States. The National Cancer Institute at the National Institutes of Health estimates approximately 252,710 women will be diagnosed with breast cancer this year, and 40,610 will die of the disease. Approximately 20 to 25% of patients with hereditary breast cancers and 5 to 10% of patients with any type of breast cancer have a BRCA mutation. BRCA genes are involved with repairing damaged DNA and normally work to prevent tumor development. However, mutations of these genes may lead to certain cancers, including breast cancers.

Lynparza® is a PARP (poly ADP-ribose polymerase) inhibitor that blocks an enzyme involved in repairing damaged DNA. By blocking this enzyme, DNA inside the cancerous cells with damaged BRCA genes may be less likely to be repaired, leading to cell death and possibly a slow-down or stoppage of tumor growth.

Lynparza® was first approved by the FDA in 2014 to treat certain patients with ovarian cancer and is now indicated for the treatment of patients with germline breast cancer susceptibility gene (BRCA) mutated, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer, who have been previously treated with chemotherapy. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior hormonal (endocrine) therapy or be considered inappropriate for endocrine treatment.

The FDA also expanded the approval of the BRACAnalysis CDx, an approved companion diagnostic to Lynparza®, to include the detection of BRCA mutations in blood samples from patients with breast cancer.

The safety and efficacy of Lynparza® for the treatment of breast cancer was based on a randomized clinical trial of 302 patients with HER2-negative metastatic breast cancer with a germline BRCA mutation. The trial measured the length of time the tumors did not have significant growth after treatment (progression-free survival). The median progression-free survival for patients taking Lynparza® was 7 months compared to 4.2 months for patients taking chemotherapy only.

Common side effects of Lynparza® include low levels of red blood cells (anemia), low levels of certain white blood cells (neutropenia, leukopenia), nausea, fatigue, vomiting, common cold (nasopharyngitis), respiratory tract infection, influenza, diarrhea, joint pain (arthralgia/myalgia), unusual taste sensation (dysgeusia), headache, indigestion (dyspepsia), decreased appetite, constipation, and inflammation and sores in the mouth (stomatitis).

Severe side effects of Lynparza® include development of certain blood or bone marrow cancers (myelodysplastic syndrome/acute myeloid leukemia) and inflammation in the lungs (pneumonitis). Lynparza® can cause harm to a developing fetus; women should be advised of the potential risk to the fetus and to use effective contraception. Women taking Lynparza® should not breastfeed as it could cause harm to a newborn baby.

This application was granted Priority Review, under which the FDA's goal is to take action on an application within six months where the agency determines that the drug, if approved, would significantly improve the safety or effectiveness of treating, diagnosing, or preventing a serious condition.

Lynparza® is also approved for the treatment of patients with BRCA-mutated, advanced ovarian cancer who have received three or more treatments of chemotherapy, and for the maintenance treatment of patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer whose tumors have completely or partially responded to chemotherapy.

The FDA granted the approval of Lynparza® to AstraZeneca Pharmaceuticals LP. The approval of the BRACAnalysis CDx was granted to Myriad Genetic Laboratories, Inc.

Safety Announcements

FDA Drug Safety Communication: FDA requires labeling changes for prescription opioid cough and cold medicines to limit their use to adults 18 years and older

[01/11/2018] The FDA is requiring safety labeling changes for prescription cough and cold medicines containing codeine or hydrocodone to limit the use of these products to adults 18 years and older because the risks of these medicines outweigh their benefits in children younger than 18. The FDA is also requiring the addition of safety information about the risks of misuse, abuse, addiction, overdose, death, and slowed or difficult breathing to the Boxed Warning, their most prominent warning, of the drug labels for prescription cough and cold medicines containing codeine or hydrocodone. The FDA is taking this action after conducting an extensive review and convening a panel of outside experts. Both of these determined the risks of slowed or difficult breathing, misuse, abuse, addiction, overdose, and death with these medicines outweigh their benefits in patients younger than 18.

Health care professionals should be aware that the FDA is changing the age range for which prescription opioid cough and cold medicines are indicated. These products will no longer be indicated for use in children, and their use in this age group is not recommended. Health care professionals should reassure parents that cough due to a cold or upper respiratory infection is self-limited and generally does not need to be treated. For those children in whom cough treatment is necessary, alternative medicines are available. These include over-the-counter (OTC) products such as dextromethorphan, as well as prescription benzonatate products.

Parents and caregivers should be aware that prescription opioid cough and cold medicines that include codeine or hydrocodone should not be used in children. Codeine and hydrocodone may carry serious risks when used in children. It is important for parents and caregivers to understand that a cough due to a common cold often does not need medicines for treatment. If a cough medicine is prescribed, they should ask their child's health care professional or a pharmacist if it contains an opioid such as codeine or hydrocodone. Patients should always read the labels on prescription bottles. If the medicine prescribed for their child contains an opioid, caregivers should talk to their child's health care professional about a different, non-opioid medicine, or if they have any questions or concerns.

Codeine and hydrocodone are available in combination with other medicines, such as antihistamines and decongestants, in prescription medicines to treat coughs and symptoms associated with allergies or the common cold. Other non-opioid prescription and OTC medicines are available to treat these symptoms.

Other *Boxed Warnings* and *Warnings and Precautions* will also be added to the label for prescription cough and cold medicines containing codeine or hydrocodone, to be consistent with the safety issues described in the labels of prescription opioid pain medicines. The FDA previously communicated about these safety issues for immediate-release opioid pain medicines and extended-release and long-acting opioid pain medicines.

Today's action is for opioid cough and cold medicines requiring a prescription. Some codeine cough medicines are available OTC in a few states, and the FDA is also considering regulatory action for these products. The FDA urges health care professionals and patients to report side effects involving opioid cough and cold medicines or other medicines to the FDA MedWatch program.

Safety Announcements

Baxter Expands Voluntary Nationwide Recall to Include Second Lot of Nexterone® Injection Due to Presence of Particulate Matter

[01/16/2018] Following the issuance of a voluntary recall dated November 10, 2017 of one lot of Nexterone® (amiodarone HCl) 150mg/100mL Premixed Injection, Baxter International Inc. announced it is expanding the recall to include a second lot (NC109123) of Nexterone® due to the potential presence of particulate matter. The affected lots were distributed between 07/21/2017 and 10/02/2017 in the United States to wholesalers/ distributors and healthcare facilities. The particulate matter may have entered the solution during the manufacturing process.

Intravenous administration of a solution containing sterile particulate matter may lead to adverse health consequences. The extent and severity of harm depends on the size, number and composition of the foreign material, and the patient's underlying medical condition. In the absence of in-line filtration, these particles may

cause local vein irritation, inflammatory reaction, aggravation of preexisting infections, allergic reactions, phlebitis, pulmonary emboli, pulmonary granulomas, immune system dysfunction, pulmonary dysfunction, pulmonary infarction, and systemic embolization. To date, there have been no reports of adverse events associated with this issue.
Nexterone® is a prescription antiarrhythmic agent indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy.
The particulate matter was identified by Baxter during a stability study, and was consistent with polyethylene, the primary constituent of the film and ports used to manufacture the bag in which Nexterone® is packaged. Anyone with an existing inventory of the recalled lots should stop use and distribution and quarantine the product immediately. Health care professionals should be informed of this recall. If anyone has further distributed the recalled product, they should notify any accounts or additional locations which may have received the recalled product. Further, entities that may have received the recalled product should be instructed that if they redistributed the product, they should notify their accounts, locations, or facilities of the recall to the hospital/retail user level. Recalled product should be returned to Baxter for credit by contacting Baxter Healthcare Center for Service at 888-229-0001, Monday through Friday, between 7 a.m. and 6 p.m. Central Time.
Customers with questions regarding this recall can contact Baxter Corporate Product Surveillance at 800-437-5176, Monday through Friday, between 8 a.m. and 5 p.m. Central Time. Customers should contact their physician or healthcare provider if they have experienced any problems that may be related to using this product.
Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program.

Safety Announcements

FDA Drug Safety Communication: FDA limits packaging for anti-diarrhea medicine Loperamide (Imodium®) to encourage safe use

This is an update to the FDA Drug Safety Communication: FDA warns about serious heart problems with high doses of the antidiarrheal medicine loperamide (Imodium®), including from abuse and misuse issued on June 7, 2016

[01/30/2018] To foster safe use of the over-the counter (OTC) anti-diarrhea drug loperamide, the FDA is working with manufacturers to use blister packs or other single dose packaging and to limit the number of doses in a package. The FDA continues to receive reports of serious heart problems and deaths with much higher than the recommended doses of loperamide, primarily among people who are intentionally misusing or abusing the product, despite the addition of a warning to the medicine label and a previous communication. Loperamide is a safe drug when used as directed.
Loperamide is FDA-approved to help control symptoms of diarrhea, including Travelers' Diarrhea. The maximum approved daily dose for adults is 8mg per day for OTC use and 16mg per day for prescription use. It is sold under the OTC brand name Imodium A-D®, as store brands, and as generics. Loperamide acts on opioid receptors in the gut to slow the movement in the intestines and decrease the number of bowel movements. It is safe at approved doses, but when much higher than recommended doses are taken, it can lead to serious problems, including severe heart rhythm problems and death.
Patients and consumers should only take the dose of loperamide directed by their health care professionals or according to the OTC Drug Facts label, as taking more than prescribed or listed on the label can cause severe heart rhythm problems or death. If patients are using OTC loperamide and their diarrhea lasts more than two days, they should stop taking the medicine and contact their health care professional. Patients should seek medical attention immediately by calling 911 if they experience any of the following, and tell health care professionals the person has been taking loperamide:

- Fainting
- Rapid heartbeat or irregular heart rhythm
- Unresponsiveness, meaning that the person can't wake up or the person doesn't answer or react normally

Health care professionals should be aware that using much higher than recommended doses of loperamide, either intentionally or unintentionally, can result in serious cardiac adverse events, including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest. In cases of abuse, individuals often use other drugs together with loperamide in attempts to increase its absorption and

penetration across the blood-brain barrier, inhibit loperamide metabolism, and enhance its euphoric effects. Some individuals are taking high doses of loperamide to treat symptoms of opioid withdrawal. If loperamide toxicity is suspected, the drug should be promptly discontinued and necessary therapy started. For some cases of abnormal heart rhythms in which drug treatment is ineffective, electrical pacing or cardioversion may be required. Also patients should be counseled to take loperamide only as prescribed or according to the OTC Drug Facts label, and advised that drug interactions with commonly used medicines may increase the risk of serious cardiac events.
The FDA previously issued a Drug Safety Communication about this safety concern and added warnings about serious heart problems to the drug label of prescription loperamide and to the Drug Facts label of OTC loperamide products. The FDA is continuing to evaluate this safety issue and will update the public when more information is available. The FDA urges patients, consumers, and health care professionals to report side effects involving loperamide or other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of February 6th, 2018):

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

Amino Acids	***Currently in Shortage***
Aminocaproic Acid Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Betaine Hydrochloride (Cystadane) for Oral Solution	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended Release Tablets	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Deferoxamine Mesylate for Injection, USP	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Folic Acid Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***

Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nitrous Oxide, Gas	***Currently in Shortage***
Pantoprazole (Protonix) Powder for Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***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***
Phosphate Injection Products	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Progesterone Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Sterile Water	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***