Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
September 13, 2017
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – September 13, 2017

DATE: September 4, 2017

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

Enclosed are the following items related to the September 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/Medicaid Opioid Utilization Comparison – Appendix B

Action Item – Vote to Prior Authorize Radicava™ (Edaravone) – Appendix C

Action Item – Vote to Prior Authorize Eucrisa™ (Crisaborole 2% Ointment), Dupixent® (Dupilumab Injection), & Prudoxin™ and Zonalon® (Doxepin 5% Cream) – Appendix D

Action Item – Vote to Prior Authorize Vimizim® (Elosulfase Alfa) – Appendix E

Action Item – Vote to Prior Authorize Rayaldee® (Calcifediol), Parsabiv™ (Etelcalcetide), Zemplar® (Paricalcitol Capsules), and Hectorol® (Doxercalciferol Capsules) – Appendix F

Action Item – Vote to Prior Authorize Marplan® (Isocarboxazid) and Desyrel® (Trazodone 300mg Tablets) – Appendix G

Action Item – Vote to Prior Authorize Choline Fenofibrate Delayed-Release (Trilipix®) 135mg Capsules and Fenofibrate Micronized (Lofibra®) 200mg Capsules – Appendix H

Action Item – Vote to Prior Authorize Arymo™ ER (Morphine Sulfate Extended-Release), Troxyca® ER (Oxycodone/Naltrexone Extended-Release), Vantrela™ ER (Hydrocodone Extended-Release), Oxaydo® (Oxycodone), and RoxyBond™ (Oxycodone) – Appendix I

Action Item – Vote to Prior Authorize Brineura™ (Cerliponase Alfa) – Appendix J

Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Kisqali® (Ribociclib), Kisqali® Femara® Co-Pack (Ribociclib/Letrozole), and Nerlynx™ (Neratinib) – Appendix K

Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] and Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated] – Appendix L

Action Item – Annual Review of Growth Hormone – Appendix M

Annual Review of Synagis® (Palivizumab) – Appendix N

30-Day Notice to Prior Authorize Endari™ (L-Glutamine) – Appendix O

Action Item – Annual Review of Insomnia Medications – Appendix P

30-Day Notice to Prior Authorize Fabrazyme® (Agalsidase Beta) – Appendix Q

Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Zypitamag™ (Pitavastatin Magnesium) and Nikita™ (Pitavastatin Sodium) – Appendix R

Annual Review of Alzheimer's Disease Medications and 30-Day Notice to Prior Authorize Namenda XR® (Memantine Extended-Release Capsules) – Appendix S

Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – Appendix T

Industry News and Updates – Appendix U

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – September 13, 2017 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. 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. July 12, 2017 DUR Minutes – Vote
B. July 12, 2017 DUR Recommendations Memorandum
C. Correspondence

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

4. Update on Medication Coverage Authorization Unit/Medicaid Opioid Utilization Comparison – See Appendix B

A. Medication Coverage Activity for July 2017
B. Pharmacy Help Desk Activity for July 2017
C. Medication Coverage Activity for August 2017
D. Pharmacy Help Desk Activity for August 2017
E. Medicaid Opioid Utilization Comparison

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

5. Action Item – Vote to Prior Authorize Radicava™ (Edaravone) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Eucrisa™ (Crisaborole 2% Ointment), Dupixent® (Dupilumab Injection), & Prudoxin™ and Zonalon® (Doxepin 5% Cream) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Vimizim® (Elosulfase Alfa) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Rayaldee® (Calcifediol), Parsabiv™ (Etelcalcetide), Zemplar® (Paricalcitol Capsules), and Hectorol® (Doxercalciferol Capsules) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Marplan® (Isocarboxazid) and Desyrel® (Trazodone 300mg Tablets) – See Appendix G

A. Introduction
B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Choline Fenofibrate Delayed-Release (Trilipix®) 135mg Capsules and Fenofibrate Micronized (Lofibra®) 200mg Capsules – See Appendix H

A. Cost Comparison
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Arymo™ ER (Morphine Sulfate Extended-Release), Troxyca® ER (Oxycodone/Naltrexone Extended-Release), Vantrela™ ER (Hydrocodone Extended-Release), Oxaydo® (Oxycodone), and RoxyBond™ (Oxycodone) – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

12. Action Item – Vote to Prior Authorize Brineura™ (Cerliponase Alfa) – See Appendix J

A. Introduction
B. College of Pharmacy Recommendations

Items to be presented by Dr. Schmidt, Dr. Borders, Dr. Medina, Dr. Muchmore, Chairman:

13. Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Kisqali® (Ribociclib), Kisqali® Femara® Co-Pack (Ribociclib/Letrozole), and Nerlynx™ (Neratinib) – See Appendix K

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Breast Cancer Medications
D. Prior Authorization of Breast Cancer Medications
E. Market News and Updates
F. Product Summaries
G. Recommendations
H. Utilization Details of Breast Cancer Medications

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

14. Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] and Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated] – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Factor Replacement Products
C. Prior Authorization of Factor Replacement Products
D. Mark News and Updates
E. Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] Product Summary
F. Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated] Product Summary
G. Recommendations
H. Utilization Details of Factor Replacement Products

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

15. Action Item – Annual Review of Growth Hormone – See Appendix M

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

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

16. Annual Review of Synagis® (Palivizumab) – See Appendix N

A. Current Prior Authorization Criteria
B. Utilization of Synagis® (Palivizumab)
C. Prior Authorization of Synagis® (Palivizumab)
D. Season Comparison
E. Market News and Updates
F. College of Pharmacy Recommendations

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

17. 30-Day Notice to Prior Authorize Endari™ (L-Glutamine) – See Appendix O

A. Introduction
B. Market News and Updates
C. Endari™ (L-Glutamine) Product Summary
D. College of Pharmacy Recommendations

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

18. Action Item – Annual Review of Insomnia Medications – See Appendix P

A. Current Prior Authorization Criteria
B. Utilization of Insomnia Medications
C. Prior Authorization of Insomnia Medications
D. Market News and Updates
E. Non-24-Hour Sleep-Wake Rhythm Disorder
F. College of Pharmacy Recommendations
G. Utilization Details of Insomnia Medications

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

19. 30-Day Notice to Prior Authorize Fabrazyme® (Agalsidase Beta) – See Appendix Q

A. Introduction
B. Utilization of Fabrazyme® (Agalsidase Beta)
C. Market News and Updates
D. Fabrazyme® (Agalsidase Beta) Product Summary
E. Coverage Information
F. College of Pharmacy Recommendations

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

20. Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Zypitamag™ (Pitavastatin Magnesium) and Nikita™ (Pitavastatin Sodium) – See Appendix R

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

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

21. Annual Review of Alzheimer's Disease Medications and 30-Day Notice to Prior Authorize Namenda XR® (Memantine Extended-Release Capsules) – See Appendix S

A. Current Prior Authorization Criteria
B. Utilization of Alzheimer's Disease Medications
C. Prior Authorization of Alzheimer's Disease Medications
D. Market News and Updates
E. Namenda XR® (Memantine Extended-Release Capsules) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Alzheimer's Disease Medications

Non-Presentation; Questions Only:

22. Annual Review of Anticoagulants and Platelet Aggregation Inhibitors – See Appendix T

A. Current Prior Authorization Criteria
B. Utilization of Anticoagulants and Platelet Aggregation Inhibitors
C. Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors
D. Market News and Updates
E. College of Pharmacy Recommendations
F. Utilization Details of Anticoagulants
G. Utilization Details of Platelet Aggregation Inhibitors

Non-Presentation; Questions Only:

23. Industry News and Updates – See Appendix U

A. Introduction
B. News and Updates

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

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

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

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

October meeting rescheduled to October 4, 2017 at 4PM

A. Topical Corticosteroid Medications
B. Targeted Immunomodulator Agents
C. Allergy Immunotherapies
D. Skin Cancer Medications
E. Malignant Hematology Medications
F. Constipation and Diarrhea Medications
G. Bladder Control Medications
H. Hereditary Angioedema Medications
I. Anti-Ulcer Medications
J. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

**Future business subject to change.*

26. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JULY 12, 2017

BOARD MEMBERS:	PRESENT	ABSENT
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Anetta Harrell, Pharm.D.	x	
Ashley Huddleston, Pharm.D., BCOP		x
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, Pharm.D.		x
James Osborne, Pharm.D.	x	
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
Bruna Varalli-Claypool, MHS, PA-C	x	
Eric Winegardner, D.Ph.		x

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
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): Not applicable		

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	
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:		
Melanie Brenner, Opko Health	Dan Doyle, Trividia	Brian Maves, Pfizer
Aaron Zimmermen, Teva	Rachel Gragg, Teva	Linzy Hendrickson, Indivior
Kent Douglas, NAE	Chad Farris, Neurocrine	Toby Thompson, Pfizer
Ron Cain, Pfizer	Audrey Rattan, Alkermes	Charlie Collins, Genzyme
David Gibson, Regeneron	Lee Marks, Orexo	Jim Chapman, AbbVie
James Gaustad, Purdue	Scott Black, DSI	Lerryn Trzcinski, DSI
Jason Ophus, Pfizer	Mary Stewart Crane, J&J	Mark Herlehy, Lundbeck
John Schillo, Lundbeck	Kari Suttee, Novartis	Matt Forney, Merck
Lee Hennigan, Novartis	Deron Grothe, Teva	Kristin Pareja, Otsuka
Terry McCurren, Otsuka	Gwendolyn Caldwell, PhRMA	Michael Dutro, Pfizer
Heather Dehlin, Pfizer	Cherian Karunapuzha, OUHSC	Rose Mullen, Alkermes
Clarence L. Wiley, Dermatology	Kathryn Munoz, Sanofi-Genzyme	Jeremy Jones, OSU-CHS

PRESENT FOR PUBLIC COMMENT:	
Melanie Brenner	Opko Health
Heather Dehlin	Pfizer
Cherian Karunapuzha, MD	OUHSC
Rose Mullen	Alkermes
Clarence L. Wiley, MD	Beauty Thru Health Dermatology
Kathryn Munoz	Sanofi-Genzyme
Jeremy Jones, DO	OSU-CHS

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: CHERIAN KARUNAPUZHA, MD
2B: AGENDA ITEM NO. 13 SPEAKER: HEATHER DEHLIN
2C: AGENDA ITEM NO. 13 SPEAKER: CLARENCE WILEY, MD
2D: AGENDA ITEM NO. 13 SPEAKER: KATHRYN MUNOZ
2E: AGENDA ITEM NO. 13 SPEAKER: JEREMY JONES, DO
2F: AGENDA ITEM NO. 15 SPEAKER: MELANIE BRENNER
2G: AGENDA ITEM NO. 16 SPEAKER: ROSE MULLEN

ACTION: NONE REQUIRED

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

3A: JUNE 14, 2017 DUR MINUTES – VOTE
3B: JUNE 14, 2017 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Cothran
Dr. Preslar moved to approve; seconded by Dr. Harrell

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/SOONERCARE OPIOID INITIATIVE UPDATE**

4A: MEDICATION COVERAGE ACTIVITY FOR JUNE 2017
4B: PHARMACY HELP DESK ACTIVITY FOR JUNE 2017
4C: SOONERCARE OPIOID INITIATIVE UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE AUSTEDO™ (DEUTETRABENAZINE) AND XENAZINE® (TETRABENAZINE)

5A: INTRODUCTION

5B: XENAZINE® (TETRABENAZINE) OFF-LABEL USES

5C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO UPDATE THE INHALED TOBRAMYCIN PRODUCTS, PULMOZYME® (DORNASE ALFA), AND CAYSTON® (AZTREONAM) PRIOR AUTHORIZATION CRITERIA

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE INGREZZA™ (VALBENAZINE)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO UPDATE THE ATYPICAL ANTIPSYCHOTIC PRIOR AUTHORIZATION CRITERIA AND TIER CHART

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

8C: RECOMMENDED PRIOR AUTHORIZATION CRITERIA

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE CARAC® (FLUOROURACIL 0.5% CREAM), GONITRO™ (NITROGLYCERIN SUBLINGUAL POWDER), SOLTAMOX® (TAMOXIFEN CITRATE ORAL SOLUTION), TAYTULLA™ (NORETHINDRONE ACETATE/ETHINYL ESTRADIOL CAPSULES & FERROUS FUMARATE CAPSULES), TIROSINT®-SOL (LEVOTHYROXINE SODIUM ORAL SOLUTION), XATMEP™ (METHOTREXATE ORAL SOLUTION), ZOVIRAX® (ACYCLOVIR OINTMENT AND SUSPENSION), XERESE® (ACYCLOVIR/HYDROCORTISONE CREAM), & DENAVIR® (PENCICLOVIR CREAM)

9A: INTRODUCTION

9B: 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. 10: VOTE TO PRIOR AUTHORIZE ACZONE® (DAPSONE GEL) AND TAZORAC® (TAZAROTENE CREAM AND GEL)

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nichols

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE VYVANSE® (LISDEXAMFETAMINE CHEWABLE TABLETS) AND UPDATE THE ADHD PRIOR AUTHORIZATION CRITERIA AND TIER CHART

11A: INTRODUCTION
11B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
Ms. Varalli-Claypool moved to approve; seconded by Dr. Harrell
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: 30-DAY NOTICE TO PRIOR AUTHORIZE RADICAVA™ (EDARAVONE)
12A: INTRODUCTION
12B: MARKET NEWS AND UPDATES
12C: RADICAVA™ (EDARAVONE) PRODUCT SUMMARY
12D: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF ATOPIC DERMATITIS (AD) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE EUCRISA™ (CRISABOROLE 2% OINTMENT), DUPIXENT® (DUPILUMAB INJECTION), & PRUDOXIN™ AND ZONALON® (DOXEPIN 5% CREAM)
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF AD MEDICATIONS
13C: PRIOR AUTHORIZATION OF AD MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: EUCRISA™ (CRISABOROLE 2% OINTMENT) PRODUCT SUMMARY
13F: DUPIXENT® (DUPILUMAB INJECTION) PRODUCT SUMMARY
13G: PRUDOXIN™ AND ZONALON® (DOXEPIN 5% CREAM) PRODUCT SUMMARY
13H: COLLEGE OF PHARMACY RECOMMENDATIONS
13I: UTILIZATION DETAILS OF AD MEDICATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: 30-DAY NOTICE TO PRIOR AUTHORIZE VIMIZIM® (ELOSULFASE ALFA)
14A: INTRODUCTION
14B: VIMIZIM® (ELOSULFASE ALFA) PRODUCT SUMMARY
14C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF NATPARA® (PARATHYROID HORMONE INJECTION) AND 30-DAY NOTICE TO PRIOR AUTHORIZE RAYALDEE® (CALCIFEDIOL), PARSABIV™ (ETELCALCETIDE), ZEMPLAR® (PARICALCITOL CAPSULES), AND HECTOROL® (DOXERCALCIFEROL CAPSULES)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF PARATHYROID MEDICATIONS
15C: PRIOR AUTHORIZATION OF NATPARA®, CALCIMIMETICS, AND VITAMIN D ANALOGS
15D: MARKET NEWS AND UPDATES
15E: PRODUCT SUMMARIES
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF CALCIMIMETICS AND VITAMIN D ANALOGS
15H: UTILIZATION DETAILS OF NATPARA® (PARATHYROID HORMONE INJECTION)
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF OPIOID ANALGESICS AND OPIOID MEDICATION ASSISTED TREATMENT (MAT) MEDICATIONS & 30-DAY NOTICE TO PRIOR AUTHORIZE ARYMO™ ER (MORPHINE SULFATE EXTENDED-RELEASE), TROXYCA® ER (OXYCODONE/NALTREXONE EXTENDED-

RELEASE), VANTRELA™ ER (HYDROCODONE EXTENDED-RELEASE), OXAYDO® (OXYCODONE), AND ROXYBOND™ (OXYCODONE)

16A: CURRENT PRIOR AUTHORIZATION CRITERIA
16B: UTILIZATION OF OPIOID ANALGESICS AND MAT MEDICATIONS
16C: PRIOR AUTHORIZATION OF OPIOID ANALGESICS & MAT MEDICATIONS
16D: MARKET NEWS AND UPDATES
16E: PRODUCT SUMMARIES
16F: COLLEGE OF PHARMACY RECOMMENDATIONS
16G: UTILIZATION DETAILS OF OPIOID ANALGESICS
16H: UTILIZATION DETAILS OF MAT MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: 30-DAY NOTICE TO PRIOR AUTHORIZE BRINEURA™ (CERLIPONASE ALFA)

17A: INTRODUCTION
17B: MARKET NEWS AND UPDATES
17C: BRINEURA™ (CERLIPONASE ALFA) PRODUCT SUMMARY
17D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF ANTIDEPRESSANTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MARPLAN® (ISOCARBOXAZID) AND DESYREL® (TRAZODONE 300MG TABLETS)

18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF ANTIDEPRESSANTS
18C: PRIOR AUTHORIZATION OF ANTIDEPRESSANTS
18D: MARKET NEWS AND UPDATES
18E: MARPLAN® (ISOCARBOXAZID) PRODUCT SUMMARY
18F: COST COMPARISON
18G: COLLEGE OF PHARMACY RECOMMENDATIONS
18H: UTILIZATION DETAILS OF ANTIDEPRESSANTS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: ANNUAL REVIEW OF FIBRIC ACID DERIVATIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE CHOLINE FENOFIBRATE DELAYED-RELEASE (TRILIPIX®) 135MG CAPSULES AND FENOFIBRATE MICRONIZED (LOFIBRA®) 200MG CAPSULES

19A: CURRENT PRIOR AUTHORIZATION CRITERIA
19B: UTILIZATION OF FIBRIC ACID DERIVATIVE MEDICATIONS
19C: PRIOR AUTHORIZATION OF FIBRIC ACID DERIVATIVE MEDICATIONS
19D: MARKET NEWS AND UPDATES
19E: COST COMPARISON
19F: COLLEGE OF PHARMACY RECOMMENDATIONS
19G: UTILIZATION DETAILS OF FIBRIC ACID DERIVATIVE MEDICATIONS

Materials included in agenda packet; presented by Dr. Nichols

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: ANNUAL REVIEW OF FIBROMYALGIA MEDICATIONS

20A: CURRENT PRIOR AUTHORIZATION CRITERIA
20B: UTILIZATION OF FIBROMYALGIA MEDICATIONS
20C: PRIOR AUTHORIZATION OF FIBROMYALGIA MEDICATIONS
20D: MARKET NEWS AND UPDATES
20E: COLLEGE OF PHARMACY RECOMMENDATIONS

20F: UTILIZATION DETAILS OF FIBROMYALGIA MEDICATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: ANNUAL REVIEW OF OCALIVA® (OBETICHOLIC ACID)
21A: INTRODUCTION
21B: CURRENT PRIOR AUTHORIZATION CRITERIA
21C: UTILIZATION OF OCALIVA® (OBETICHOLIC ACID)
21D: PRIOR AUTHORIZATION OF OCALIVA® (OBETICHOLIC ACID)
21E: MARKET NEWS AND UPDATES
21F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 22: INDUSTRY NEWS AND UPDATES
22A: INTRODUCTION
22B: NEWS AND UPDATES
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 23: 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. 24: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
No meeting scheduled for August 2017.
24A: SYNAGIS® (PALIVIZUMAB)
24B: GROWTH HORMONE
24C: FABRAZYME® (AGALSIDASE BETA)
24D: ALLERGY IMMUNOTHERAPIES
24E: BREAST CANCER
24F: HEMOPHILIA MEDICATIONS
24G: INSOMNIA MEDICATIONS
24H: ALZHEIMER'S MEDICATIONS
24I: ANTICOAGULANTS & PLATELET AGGREGATION INHIBITORS
Future business subject to change.
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 25: ADJOURNMENT
The meeting was adjourned at 5:55pm

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

Memorandum

Date: July 13, 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 July 12, 2017

Recommendation 1: Opioid Initiative Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Austedo™ (Deutetrabenazine) and Xenazine® (Tetrabenazine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Xenazine® (tetrabenazine) and Austedo™ (deutetrabenazine) with the following criteria:

Xenazine® (Tetrabenazine) Approval Criteria:

1. Authorization of generic tetrabenazine (in place of brand Xenazine®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
2. A diagnosis of one of the following:
   a. Chorea associated with Huntington's disease; or
   b. Tardive dyskinesia; or
   c. Tourette syndrome; and

3. Xenazine® must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Xenazine® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter-2 (VMAT2) inhibitor (e.g., deutetrabenazine, valbenazine) concurrently with Xenazine®; and
9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Xenazine® [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. Patients who require doses of tetrabenazine greater than 50mg per day must be tested and genotyped to determine if they are poor metabolizers (PMs), intermediate metabolizers (IMs), or extensive metabolizers (EMs) by their ability to express the drug metabolizing enzyme, CYP2D6. The following dose limits will apply based on patient metabolizer status:
    a. Extensive and Intermediate CYP2D6 Metabolizers: 100mg divided daily; or
    b. Poor CYP2D6 Metabolizers: 50mg divided daily; and
11. The daily dose of Xenazine® must not exceed 50mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion); and
12. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea, tardive dyskinesia, or Tourette syndrome have decreased and the member is not showing worsening signs of depression.

Austedo™ (Deutetrabenazine) Approval Criteria:

1. An FDA approved diagnosis of chorea associated with Huntington's disease; and
2. Austedo™ must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
3. A previous trial of Xenazine® (tetrabenazine) or a patient-specific, clinically significant reason why the member cannot use brand Xenazine® (tetrabenazine); and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Austedo™ therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and

8. Member must not use another vesicular monoamine transporter-2 (VMAT2) inhibitor (e.g., tetrabenazine, valbenazine) concurrently with Austedo™; and
9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Austedo™ [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. The daily dose of Austedo™ must not exceed 36mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) or if they are a known poor CYP2D6 metabolizer; and
11. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea have decreased and the member is not showing worsening signs of depression.

Recommendation 3: Vote to Update the Inhaled Tobramycin Products, Pulmozyme® (Dornase Alfa), and Cayston® (Aztreonam) Prior Authorization Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes noted in red to the inhaled tobramycin product prior authorization criteria:

Inhaled Tobramycin Products (Bethkis®, Tobi®, Tobi® Podhaler™, and Kitabis™ Pak), Pulmozyme® (Dornase Alfa), & Cayston® (Aztreonam) Approval Criteria:

1. Use of inhaled tobramycin products, Pulmozyme® (dornase alfa), and Cayston® (aztreonam) is reserved for members who have a diagnosis of cystic fibrosis.
    a. Authorization of Bethkis®, Tobi® Podhaler™, and Kitabis™ Pak requires a trial of tobramycin nebulized solution or a patient-specific, clinically significant reason why tobramycin nebulized solution is not appropriate for the member.
    b. Tobramycin nebulized solution, dornase alfa, and aztreonam inhalation will not require a prior authorization and claims will pay at the point of sale if member has a reported diagnosis of cystic fibrosis within the past 12 months of claims history.
    c. If the member does not have a reported diagnosis, a manual prior authorization will be required for coverage consideration.
2. Use of inhaled tobramycin products and Cayston® (aztreonam) is restricted to 28 days of therapy per every 56 days to ensure cycles of 28 days on therapy followed by 28 days off therapy.
    a. Use outside of this recommended regimen may be considered for coverage via a manual prior authorization submission with a patient-specific, clinically significant reason why the member would need treatment outside of the FDA approved dosing.
    b. Pharmacies should process the prescription claim with a 56 day supply.

Recommendation 4: Vote to Prior Authorize Ingrezza™ (Valbenazine)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ingrezza™ (valbenazine) with the following criteria:

Ingrezza™ (Valbenazine) Approval Criteria:

1. An FDA approved diagnosis of tardive dyskinesia meeting the following DSM-5 criteria:
   a. Involuntary athetoid or choreiform movements; and
   b. History of treatment with dopamine receptor blocking agent (DRBA); and
   c. Symptom duration lasting longer than 4 to 8 weeks; and
2. Member must be 18 years of age or older; and
3. Ingrezza™ must be prescribed by a neurologist or psychiatrist, or a mid-level practitioner with a supervising physician that is a neurologist or psychiatrist; and
4. Member must not be at significant risk for suicidal or violent behavior and must not have unstable psychiatric symptoms; and
5. The daily dose of Ingrezza™ must not exceed 40mg per day if the member is taking strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, clarithromycin); and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs); and
7. Member must not be taking other vesicular monoamine transporter 2 (VMAT2) inhibitors (e.g., tetrabenazine, deutetrabenazine); and
8. Female members must not be pregnant or breastfeeding; and
9. Prescriber must document a baseline evaluation using the Abnormal Involuntary Movement Scale (AIMS); and
10. A quantity limit of two 40mg capsules or a total dose of 80mg per day will apply; and
11. Approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by an improvement from baseline in the AIMS total score (a negative change in score indicates improvement).

Recommendation 5: Vote to Update the Atypical Antipsychotic Prior Authorization Criteria and Tier Chart

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Atypical Antipsychotic Product Based Prior Authorization (PBPA) category:

1. In addition to the Tier-3 criteria requirements for consideration of Symbyax® (olanzapine/fluoxetine), approval would require a patient-specific, clinically significant reason why the member could not use olanzapine and fluoxetine as individual components, both of which are available without prior authorization.
2. The movement of Seroquel® XR (quetiapine extended-release [ER]) to Tier-1 of the Atypical Antipsychotics PBPA Tier chart once the cost is comparable to other Tier-1 generic medications.

3. A trial of Seroquel® XR (*pending Tier-1 move*) will be required for approval of Latuda® (lurasidone) for a diagnosis of bipolar depression.
4. For atypical antipsychotic Tier-2 approval consideration, a trial of any Tier-1 medication at least 14 days in duration, titrated to recommended dose that did not yield adequate response or resulted in intolerable effects will be required in place of a required aripiprazole trial.
5. In addition to the current Tier-3 criteria, a trial of any Tier-1 medication at least 14 days in duration, titrated to recommended dose that did not yield adequate response or resulted in intolerable effects will be required in place of a required aripiprazole trial.

Atypical Antipsychotics*		
Tier-1	**Tier-2**	**Tier-3**
aripiprazole (Abilify®)¥	aripiprazole (Abilify Maintena®)	brexpiprazole (Rexulti®)
clozapine (Clozaril®)◊	aripiprazole lauroxil (Aristada®)	cariprazine (Vraylar™)
olanzapine (Zyprexa®)	asenapine (Saphris®)	clozapine (Fazaclo®)
quetiapine (Seroquel®)		clozapine oral suspension (Versacloz™)
quetiapine ER (Seroquel XR®)**	**lurasidone (Latuda®)±**	iloperidone (Fanapt®)
risperidone (Risperdal®)	paliperidone (Invega® Sustenna®)	**olanzapine/fluoxetine (Symbyax®)α**
risperidone (Risperdal Consta®)	paliperidone (Invega® Trinza™)∞	paliperidone (Invega®)
ziprasidone (Geodon®)		

Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
ER = extended-release
*Mandatory generic plan applies
◊Does not count toward a Tier-1 trial
∞In addition to tier trials, use of Invega® Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.
¥Aripiprazole (Abilify®) orally disintegrating tablets (ODT) are considered a special formulation and will require a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation. Aripiprazole oral solution for members older than seven years of age requires a patient-specific, clinically significant reason why the oral tablet formulation cannot be used. Aripiprazole oral solution will not require prior authorization for ages five to seven years of age. Prior authorization requests for members younger than five years of age are reviewed by an OHCA-contracted child psychiatrist.
**Seroquel® XR (quetiapine ER) move to Tier-1 dependent on generic cost.
± Latuda® (lurasidone) requires a trial of Seroquel® XR (quetiapine ER) (*pending Tier-1 move*) for a diagnosis of bipolar depression.
α In addition to the Tier-3 criteria requirements, approval requires a patient-specific, clinically significant reason why the member cannot use olanzapine and fluoxetine as individual components.

Tier-1 products are available without prior authorization for ages five years and older. Prior authorization requests for members younger than five years of age are reviewed by an Oklahoma Health Care Authority (OHCA)-contracted child psychiatrist.

Atypical Antipsychotic Tier-2 Approval Criteria:

1. A trial of a Tier-1 medication at least 14 days in duration, titrated to recommended dose that did not yield adequate response or resulted intolerable adverse effects.
   a. Clozapine does not count towards a Tier-1 trial.

Atypical Antipsychotic Tier-3 Approval Criteria:

1. A trial of a Tier-1 medication at least 14 days in duration, titrated to recommended dose that did not yield adequate response or resulted intolerable adverse effects; and

a. Clozapine does not count towards a Tier-1 trial; and
2. Trials of all oral Tier-2 medications, at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; or
3. A manual prior authorization may be submitted for consideration of a Tier-3 medication when the member has had at least four trials of Tier-1 and Tier-2 products (two trials must be from Tier-1) that did not yield an adequate response or resulted in intolerable adverse effects; and
4. Use of Versacloz™ (clozapine oral suspension) and Fazaclo® (clozapine orally disintegrating tablet) requires a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

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

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

Recommendation 6: Vote to Prior Authorize Carac® (Fluorouracil 0.5% Cream), GoNitro™ (Nitroglycerin Sublingual Powder), Soltamox® (Tamoxifen Citrate Oral Solution), Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules), Tirosint®-SOL (Levothyroxine Sodium Oral Solution), Xatmep™ (Methotrexate Oral Solution), Zovirax® (Acyclovir Ointment and Suspension), Xerese® (Acyclovir/Hydrocortisone Cream), & Denavir® (Penciclovir Cream)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Carac® (fluorouracil 0.5% cream), GoNitro™ (nitroglycerin sublingual powder), Soltamox® (tamoxifen citrate oral solution), Taytulla™ (norethindrone acetate/ethinyl estradiol capsules & ferrous fumarate capsules), Tirosint®-SOL (levothyroxine sodium oral solution), Xatmep™ (methotrexate oral solution), Zovirax® (acyclovir ointment and suspension), Xerese® (acyclovir/hydrocortisone cream), and Denavir® (penciclovir cream) with the following criteria:

Carac® (Fluorouracil 0.5% Cream) Approval Criteria:

1. An FDA approved diagnosis of multiple actinic or solar keratoses of the face and anterior scalp in adults; and
2. Carac® must be prescribed by a dermatologist or an advanced care practitioner with a supervising physician who is a dermatologist; and
3. A patient-specific, clinically significant reason why the member cannot use fluorouracil 5% cream, fluorouracil 5% solution, or fluorouracil 2% solution.

GoNitro™ (Nitroglycerin Sublingual Powder) Approval Criteria:

1. An FDA approved indication of acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease; and
2. A patient-specific, clinically significant reason why the member cannot use nitroglycerin sublingual tablets or nitroglycerin lingual spray.

Soltamox® (Tamoxifen Citrate 10mg/5mL Oral Solution) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. Treatment of metastatic breast cancer in women and men; or
    b. Adjuvant treatment of node-positive breast cancer in postmenopausal women and for the adjuvant treatment of axillary node-negative breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation; or
    c. The reduction in risk of invasive breast cancer in women with ductal carcinoma in situ (DCIS), following breast surgery and radiation; or
    d. To reduce the incidence of breast cancer in women at high risk for breast cancer; and
2. A patient-specific, clinically significant reason why the member cannot use tamoxifen tablets.

Taytulla™ (Norethindrone Acetate/Ethinyl Estradiol Capsules & Ferrous Fumarate Capsules) Approval Criteria:

1. An FDA approved indication to prevent pregnancy in women; and
2. A patient-specific, clinically significant reason why the member cannot use all other generic formulations of norethindrone acetate/ethinyl estradiol tablets with ferrous fumarate tablets.

Tirosint®-SOL (Levothyroxine Sodium Oral Solution) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Hypothyroidism: As replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism; or
    b. Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer; and
2. A patient-specific, clinically significant reason why the member cannot use all other formulations of levothyroxine sodium in the place of oral solution even when tablets are crushed.

Xatmep™ (Methotrexate 2.5mg/mL Oral Solution) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen; or
    b. Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy; and
2. A patient-specific, clinically significant reason why the oral tablets or generic injectable formulation cannot be used.

Zovirax® (Acyclovir 5% 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 200mg/5mL 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.

Sitavig® (Acyclovir Buccal Tablets), Xerese® (Acyclovir/Hydrocortisone 5%/1% Cream), and Denavir® (Penciclovir 1% 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.

Recommendation 7: Vote to Prior Authorize Aczone® (Dapsone Gel) and Tazorac® (Tazarotene Cream and Gel)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Aczone® (dapsone gel) and generic tazarotene cream and gel with the following criteria based, in part, on cost after rebates:

Aczone® (Dapsone Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris; and
2. Member must be 20 years of age or younger; and
3. A previous trial of benzoyl peroxide or a patient-specific, clinically significant reason why benzoyl peroxide is not appropriate for the member; and
4. A previous trial of a topical antibiotic, such as clindamycin or erythromycin, or a patient-specific, clinically significant reason why a topical antibiotic is not appropriate for the member.

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. Authorization of generic tazarotene (in place of brand Tazorac®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
4. For a diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and
5. A quantity limit of 60 grams per 30 days will apply.

Recommendation 8: Vote to Prior Authorize Vyvanse® (Lisdexamfetamine Chewable Tablets) and Update the ADHD Prior Authorization Criteria and Tier Chart

MOTION CARRIED by unanimous approval.

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

1. Place Vyvanse® (lisdexamfetamine chewable tablets) into Tier-1 based on net cost after rebates.
    a. Current Tier-1 criteria will apply.
    b. A quantity limit of 30 chewable tablets per 30 days will apply.
    c. Vyvanse® capsules and chewable tablets have currently provided a supplemental rebate to be placed in Tier-1; however, Vyvanse® capsules and chewable tablets will be moved to a higher tier based on net cost in comparison to other available products if the manufacturer chooses not to participate in supplemental rebates.
2. Move Aptensio XR™ (methylphenidate ER capsules), generic Metadate CD® (methylphenidate ER capsules), and generic Ritalin LA® (methylphenidate ER capsules) into Tier-1 based on net cost after rebates. Metadate CD® and Ritalin LA® will no longer be brand preferred.
    a. Current Tier-1 criteria will apply.
    b. Aptensio XR™ capsules have currently provided a supplemental rebate to be placed in Tier-1; however, Aptensio XR™ capsules will be moved to a higher tier based on net cost in comparison to other available products if the manufacturer chooses not to participate in supplemental rebates.
3. Move Quillivant XR® (methylphenidate ER suspension) and QuilliChew ER™ (methylphenidate ER chewable tablets) to Tier-2 based on net cost after rebates.
    a. Current Tier-2 criteria will apply.
    b. Quillivant XR® and QuilliChew ER™ will have an age restriction of ten years and younger. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
    c. Quillivant XR® suspension and QuilliChew ER™ chewable tablets have currently been placed in Tier-2 based on net cost; however, if the net cost changes, Quillivant XR® suspension and QuilliChew ER™ chewable tablets will be moved to a lower or higher tier based on net cost in comparison to other available products.
4. Move generic Metadate ER® (methylphenidate ER tablets), generic Methylin ER® (methylphenidate ER tablets), and generic Ritalin SR® (methylphenidate ER tablets) into Tier-3 based on net cost after rebates.
    a. Current Tier-3 criteria will apply.
5. Add a previously failed trial of Nuvigil® (armodafinil) for authorization of Provigil® (modafinil), due to a significantly lower net cost of Nuvigil® after rebates.

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

ADHD Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and

2. A previously failed trial with at least one long-acting Tier-1 stimulant that resulted in an inadequate response:
    a. Trials should have been within the last 180 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician; and
3. For Adzenys XR-ODT™, QuilliChew ER™, and Quillivant XR®, an age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Tier-3 Approval Criteria:

1. A covered diagnosis; and
2. A previously failed trial with at least one long-acting Tier-1 stimulant that resulted in an inadequate response; and
3. A previously failed trial with at least one long-acting Tier-2 stimulant that resulted in an inadequate response:
    a. Trials should have been within the last 365 days; and
    b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
    c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.
4. A clinical exception may apply for special formulation products when there is a patient-specific, clinically significant reason why the member cannot use the available long-acting lower tiered formulations.
5. Use of Kapvay® (clonidine extended-release tablets) requires:
    a. An FDA approved diagnosis; and
    b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, a long-acting Tier-2 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
    c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets.

ADHD Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.
2. Daytrana®, Dyanavel® XR, ~~QuilliChew ER™, Quillivant XR®,~~ and Methylin® Chewable Tablets and Solution Criteria:
    a. An FDA approved diagnosis; and

b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of long-acting stimulant medications that can be used for members who cannot swallow capsules or tablets; and
c. An age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior authorization is required for all tiers for members older than 20 years of age and for members younger than 5 years of age. All prior authorization requests for members younger than 5 years of age must be reviewed by an Oklahoma Health Care Authority (OHCA)-contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria: Binge Eating Disorder (BED)
   a. An FDA approved diagnosis of moderate-to-severe binge eating disorder (BED); and
   b. Member must be 18 years of age or older; and
   c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and
   d. Authorizations will not be granted for the purpose of weight loss without the diagnosis of BED or for the diagnosis of obesity alone. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
   e. A quantity limit of 30 capsules or chewable tablets per 30 days will apply; and
   f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

Narcolepsy Medications Approval Criteria:

1. An FDA approved diagnosis; and
2. Use of ~~Provigil® (modafinil) or~~ Nuvigil® (armodafinil) requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
   a. Nuvigil® is brand name preferred due to net cost after rebates; however, brand name preferred status may be removed if the net cost changes and brand name is more costly than generic; and
3. Use of Provigil® (modafinil) requires a previously failed trial (within the last 180 days) with Nuvigil® and a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime; and
4. Use of Xyrem® (sodium oxybate) requires previously failed trials (within the last 180 days) with Tier-1 and Tier-2 stimulants from different chemical categories, Provigil®, and Nuvigil®, unless contraindicated, that did not yield adequate results; and
5. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea; and
6. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Daytrana® (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) Dyanavel® XR (amphetamine ER susp) Evekeo® (amphetamine) Methylin® (methylphenidate soln & chew tabs) Zenzedi® (dextroamphetamine)
Short-Acting			
Adderall® (amphetamine/ dextroamphetamine)		**ProCentra® (dextroamphetamine)**	
Long-Acting			
Vyvanse® (lisdexamfetamine caps and chew tabs)+	**Adderall XR® brand name only (amphetamine/ dextroamphetamine ER)** **Adzenys XR-ODT™ (amphetamine ER-ODT)**	amphetamine/ dextroamphetamine ER (generic Adderall XR®)	
Methylphenidate			
Short-Acting			
Focalin® (dexmethylphenidate) Methylin® (methylphenidate) Ritalin® (methylphenidate)			
Long-Acting			
Aptensio XR™ (methylphenidate ER) **Metadate CD® (methylphenidate ER)** **Ritalin LA® (methylphenidate ER)**	Focalin XR® (dexmethylphenidate ER) **QuilliChew ER™ (methylphenidate ER chew tabs)** **Quillivant XR® (methylphenidate ER susp)**	Concerta® (methylphenidate ER) **Metadate ER® (methylphenidate ER)** **Methylin ER® (methylphenidate ER)** **Ritalin SR® (methylphenidate ER)**	
Non-Stimulants			
Intuniv® (guanfacine ER) Strattera® brand name only (atomoxetine)		Kapvay® (clonidine ER)	

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. **Proposed changes due to supplemental rebate participation are shown in blue. Products may be moved to a higher tier based on net cost if the manufacturer chooses not to participate in supplemental rebates.**

+Unique criteria applies for the diagnosis of binge eating disorder (BED).

ER = extended-release, Caps = capsules, ODT = orally disintegrating tablet, Chew Tabs = chewable tablets, Soln = solution, Susp = suspension

Recommendation 9: 30-Day Notice to Prior Authorize Radicava™ (Edaravone)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Atopic Dermatitis (AD) Medications and 30-Day Notice to Prior Authorize Eucrisa™ (Crisaborole 2% Ointment), Dupixent® (Dupilumab Injection), & Prudoxin™ and Zonalon® (Doxepin 5% Cream)

NO ACTION REQUIRED.

Recommendation 11: 30-Day Notice to Prior Authorize Vimizim® (Elosulfase Alfa)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Natpara® (Parathyroid Hormone Injection) and 30-Day Notice to Prior Authorize Rayaldee® (Calcifediol), Parsabiv™ (Etelcalcetide), Zemplar® (Paricalcitol Capsules), and Hectorol® (Doxercalciferol Capsules)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Opioid Analgesics and Opioid Medication Assisted Treatment (MAT) Medications & 30-Day Notice to Prior Authorize Arymo™ ER (Morphine Sulfate Extended-Release), Troxyca® ER (Oxycodone/Naltrexone Extended-Release), Vantrela™ ER (Hydrocodone Extended-Release), Oxaydo® (Oxycodone), and RoxyBond™ (Oxycodone)

NO ACTION REQUIRED.

Recommendation 14: 30-Day Notice to Prior Authorize Brineura™ (Cerliponase Alfa)

NO ACTION REQUIRED.

Recommendation 15: Annual Review of Antidepressants and 30-Day Notice to Prior Authorize Marplan® (Isocarboxazid) and Desyrel® (Trazodone 300mg Tablets)

NO ACTION REQUIRED.

Recommendation 16: Annual Review of Fibric Acid Derivative Medications and 30-Day Notice to Prior Authorize Choline Fenofibrate Delayed-Release (Trilipix®) 135mg Capsules and Fenofibrate Micronized (Lofibra®) 200mg Capsules

NO ACTION REQUIRED.

Recommendation 17: Annual Review of Fibromyalgia Medications

NO ACTION REQUIRED.

Recommendation 18: Annual Review of Ocaliva® (Obeticholic Acid)

NO ACTION REQUIRED.

Recommendation 19: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 20: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

ST. ANTHONY DERMATOLOGY CTR OF EXCELLENCE
9720 Broadway Extension
Oklahoma City OK 73114-9998
405-280-7546

7/6/2017

To Whom It May Concern:

I am a dermatologist at Saint Anthony Dermatology Center of Excellence in Oklahoma City. I have been in practice since 2010. During this time, I have seen thousands of patients struggle with eczema. I have seen my other patients with psoriasis enjoy the benefits of therapeutic advances with biologic medications. For most, it can significantly clear them and this has been life changing for my psoriasis patients. I have often wished for the same therapeutic options for my chronic eczema patients. I see them struggle with chronic itch and skin disfigurement. The majority of them suffer social embarrassment. They get frustrated that the topical medications do not really make a difference (and they don't!). As one patient put it, its like a "drop in the bucket".

When I first read the medical journals and learned of dupilumab, I was hopeful this would be something I could, for the first time ever, offer my patients that may actually work and make a difference in their lives. Since it was FDA approved early this year, I quickly have enrolled many patients on it. Some of my worst eczema patients have government insurance and we have been successful getting three (so far) on this. These are my most severe eczema patients that have had several ER visits, numerous rounds of antibiotics for secondary infections, and a significant amount of money spent on therapies that just did not make a difference. Of the three, one reported 80% improvement, the other reported 50% improvement, and I have not followed up with the third yet. They are hopeful for the first time. I have also been able to get those three off a immunosuppressant medication called cyclosporine which can have long term side effects of renal insufficiency and hypertension (which could cost more money to treat in the future if those side effects manifested). They also required lab monitoring on these immunosuppressant medications and with dupilumab, no lab monitoring is required. This will save an enormous amount of money alone.

I am writing in support of insurance coverage of this medication for all patients since it is the first of its kind with no other alternatives for this chronic disease.

Sincerely,

Tiffany Brazeal, MD.

St. Anthony Hospital

ST. ANTHONY DERMATOLOGY CTR OF EXCELLENCE
9720 Broadway Extension
Oklahoma City
OK 73114-9998
405-280-7546

Renee Hamel Grau, MD
SSM Health

7/5/2017

RE: [redacted]

To Whom it May Concern:

[redacted] has been my patient for over 9 years. He has struggled with Hyper IgE syndrome and severe, recalcitrant eczema. We have been managing his condition with aggressive immunosuppressive agents (cyclosporine, Cellcept) at great overall health risk.

My experience with Dupixent with adults with the same condition has been astounding and life changing. I desire this for [redacted] not only for his quality of life, but also for his overall risk of future infections and cancers which can be side effects of his current immunosuppressant management. Since Dupixent has no laboratory monitoring, I suspect the cost in the long term would be equivalent to the cost of his current management when lab cost for monitoring are factored in.

I would strongly urge your acceptance of his medication for him.

Please feel free to contact my office if you have any questions or concerns. Thank you for your assistance in this matter.

Sincerely,

Renee Grau, MD

Renee Hamel Grau, MD

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
Michael F. Stanton		Ped	Muskogee	918-441-0073	Happybabydoc@Hughesnet.net				✓	
Kain Wade md.		Ped	MUSK.	918 23)-6540	wadepeds@suddenlink mail.com				✓	
Helen M Bumpass		Ped.	Bartlesville	918 338-3777	hbumpas@jpmc		✓	✓	✓	
Jeremy Jones		Peds	Tulsa	918 630 8422	jeremy.jones@okstate.edu		✓	✓	✓	✓
Edward Co		Neo	OKC	405 204 7707	Edward-co@mednax.com	✓	✓	✓		
Janet Jones		Peds	Tulsa	918-688-5914	janetjonesmd@gmail.com	✓	✓	✓	✓	
Santiago Reyes		Pedo pulm.	OKC.	405-[illegible]	Reyerespidis@coxinet-net	✓	✓	✓	✓	
R. Whittaker MD	Rungko Whittaker	Peds	Tulsa	918 812-3104	rwhittakermd@westviewpediatrics.com	✓	✓	✓	✓	
NAILA Paul MD	MD	Peds	Tulsa	918 752-9776	Oknpedsesbcglobal.net	✓	✓	✓		
Jonathan C. Baker MD		Peds	Tulsa	—	rspeds1@gmail.com	✓	✓	✓	✓	
Julie Sullivan	Julie Sullivan	Peds	Broken Arrow	816-2895336	juliesullivanokc@gmail.com	✓	✓	✓	✓	
JULIE WATSON		NICU	OKC	405 513 4355	juliedwatson@gmail.com	✓	✓	✓	✓	
James Pinkerton MD		NICU	OKC	405-830-2461	james_pinkerton@mednax.com	✓	✓	✓	✓	
Brooke Burks ARNP		NICU	OKC	—	brooke-burks@mednax.com	✓	✓	✓	✓	
Jennifer Hunter		NICU	OKC	405 410 2[illegible]	jennifer-hunter@mednax.com	✓	✓	✓	✓	

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
PATRICE ASTANDO	Patrice Astando	Peds	OKC	405 641 8046	pastan1046@aol.com	✓	✓	✓	✓	
Jeanne Schaefer	J Schaefer	PEDS	EDMond		drjeanneschaefer@cox.net	✓	✓	–	–	
Katie Heitmann	Katie Heitmann APRN-CNP	Family/ Peds	Edmond	405 473-8914	heitmann2011@gmail.com	✓	✓	✓	✓	
Ashley Hebert	Ashley Hebert, APRN	Peds	Edmond		ahebert1219@gmail.com	✓	✓	✓	✓	
Scott S. Cyrus	Scott S Cyrus	Pediatrics	Tulsa	(918) 625-3536	CANISKIDDS@AOL.COM	✓	✓	✓		
Lisa Siswanto		Peds	Tulsa		lisa@mykiddsdoc.com	✓	✓	✓		
Carrie McCracken	Carrie McCracken NP-C	PCCls	Tulsa		carrie@mykiddsdoc.com	✓	✓	✓		
Paulette L. Jordan	Paulette L Jordan	Pediatrics	Claremore	281 840-3690	paulette.jordan@cibs.gov	✓	✓	✓	✓	

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
RC WELLIVER SR	[illegible]	PEDS ID	OKC	716 848-9251	ROBERT-WELLIVER @ OUHSC EDU	✓	✓	✓	✓	
Michael McCoy APRN-CNP	[illegible]	Neonatology	OKC	405 990-7815	mike-mccoy@ ouhsc.edu	✓	✓	✓		
STEFAN IORGA	[illegible]	Peds	Ada	580-399-7760	STEFAN.IORGA@ MERCY.NET	✓	✓	✓	✓	
Sharon Weirick APRNCNP	Shan Weirl	Peds	Ada	580 332-7337	sweirickpnp @yahoo.com	✓	✓	✓	✓	
Ruth Weesner MD	Ruth Weesner MD	Peds	Ada	580 421-8233	drweesner@yahoo.com	✓	✓	✓	✓	
Tiffany McCrabb APRN	[illegible]	Peds Pulmonary	OKC	405 271-2234	tiffany-mccrabb@ouhsc.edu	✓	✓	✓	✓	
Janislynn Dorris PA-C	Janislynn Dorris PA-C	Peds Pulmonary	OKC	406 366-3442	janislynn-dorris@ ouhsc.edu	✓	✓	✓	✓	
Andrea Willeitner	[illegible]	Peds NICU	OKC	405 605 2028	awilleit@ ouhsc.edu	✓	✓	✓	✓	
Sarah Smith	[illegible]	Peds Primary	Norman	405 609-9591	sarahsmithou @gmail.com	✓	✓	✓	✓	
Glen Diaz	[illegible]	Peds	Moore	405 412-6510	glen-d2@ yahoo.com	✓	✓	✓	✓	
Brian Ellis	[illegible]	Peds	Norman	405 2908017	monotungo@ yahoo.com	✓	✓	✓	✓	
Ginger Thebault	[illegible]	Peds	Norman	405 802-7769	GThebault77@gmail.com	✓	✓	✓	✓	
James Fields, MD	[illegible] MD	Pediatrics	Norman	405 [illegible]		✓	✓	✓	✓	
[illegible], DO	Cynthia West, DO	Peds	Norman	405 226 2652	drcindywest@ gmail.com	✓	✓	✓	✓	
Katrin Green, PAC	[illegible]	Peds	Yukon	405-921-1062	wecare@yukonpediatrics.com	✓	✓	✓	✓	✓

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
Alecia Haines		Peds	Yukon	405 414 9320	DrAleciaHaines@aol.com	✓	✓	✓		
Catherine Flores MD		Peds	Yukon	405 314 4800	fbrepeds2@yahoo.com	✓	✓	✓		
Javier Flores MD		Peds	Yukon	405 514-4997	"	✓	✓	✓	✓	
Amanda Lowry		Peds	Norman	405 816-4484	aLowry@normanpediatrics.com	✓	✓	✓	✓	✓
Tadd Stacy MD		Peds	Norman	405-321-5114	tstacy@normanpediatrics.com	✓	✓	✓		
Tina Stinson PA		Peds	Norman	405 321-5114	tstinson@normanpediatrics.com	✓	✓	✓	✓	
Leslie Whisenhunt		Peds	Yukon	405 201-2043	jenwhiz@cox.net	✓	✓	✓	✓	✓
Diana Farrow		Peds	Yukon	918-939-6664	dianafarrow@gmail.com	✓	✓	✓	✓	
Trinity Loveless		Peds	Yukon	405 203-2506	trinitymloveless@gmail.com	✓	✓	✓	✓	
INDIRA SINGH		Peds	OKC	405 630 0266	Indira.Singh@sbcglobal.net	✓	✓	✓	✓	
Rose Trigg		Peds	OKC	405-760-5726	rose.trigg@yahoo.com	✓	✓	✓	✓	✓
Brian Sharp		Peds	Del City	405 760 5010	bsharp@varietycare.org	✓	✓	✓	✓	
Jihan Abdul-Hagg		Peds	Pelcity	678 592 1297	DrJihan@peaceofmindpediatrics.com	✓	✓	✓	✓	
Brian Lepley, DO		Peds	Norman	405-632-6688	blepley3@cox.net	✓	✓	✓	✓	
Sarah Eggers APRN		Peds	Norman	405 626 1312	seggers@varietycare.org	✓	✓	✓	✓	✓

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
Reem Shawar	[signature]	Pediatric	OKC	6463004031	rshawar@varietycare.org	✓	✓	✓	✓	
Tawfik Ramadan	[signature]	Ped.	ADA	580-399-4714	tzramadan@hotmail.com	✓	✓	✓	✓	✓
Paul Thomas	[signature]	Ped	MCA	918 421849	thomas_psu(s) hotmail.com	✓	✓	✓	✓	
Cynthia Sanford	[signature]	Peds	McAlester	918 6984740	KIDZCHOICE @ SBCGlobal.net	✓	✓	✓	✓	
Michael O'Quin	[signature]	Peds	Enid	234 7070	Blacklab12131961@yahoo.com	✓	✓	✓		
Eve Switzer	[signature]	Peds	Enid	580 402-4554	kidoctr@hotmail.com	✓	✓	✓	✓	✓
Clark Hamilton	[signature]	Peds	OKC	570-0430	CNCI.gov.com	✓	✓	✓	✓	✓
Michael Simulescu	[signature]	Peds	Durant	920-1980	msimulescu@texomapediatrics.com	✓	✓	✓	✓	✓
Jamie Akin DO	[signature]	Peds	Durant	580 920 1980	KBZDOC@Gmail.com texomapediatrics@gmail.com	✓	✓	✓	✓	✓
Derek Landis, MD	[signature]	Peds	Ardmore	580 2206092	derek.landis@mercy.net	✓	✓	✓	✓	
Scott Cooper PA-C	[signature]	Peds	Ardmore	903-449-2230	scott.cooper2@mercy.net	✓	✓	✓	✓	
Shelley Bohn MD	[signature]	Peds	OK	(405)271-7447	shelley-bohn@ouhsc.edu	✓	✓	✓	✓	
Pastor Gomez	[signature]	Peds	Lawton	580-277-5544	Pastor.gomez@ihs.gov	✓	✓	✓	✓	✓
Lilachar Kgdy	[signature]	Pd	OU		Lilachar.kgdy@ouhsc...	✓	✓	✓		
Horelie Efhong MD	[signature]	Peds	Altus		Horelie.efhong@jcmh.org	✓	✓	✓	✓	

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
Secunda Charlton, APRN CNP	Secunda Charlton, APRN CNP	Peds	Spencer	405-227-6360	leah.charlton@cmchokc.org	✓	✓	✓	✓	
Brian J Bauer		Peds	Norman	405-412-7257	JacobBauer24@yahoo.com	✓	✓	✓	✓	✓
Stephen O'Grady		Peds	Ada	580-399-8709	rpz0128@yahoo.com	✓	✓	✓	✓	✓
Jody Wilson MD		Peds	McAlester	918-916-3659	jmwind@hotmail.com	✓	✓	✓	✓	
JACQUELINE GILLESPIE APRN CNP		PEDS	DUNCAN	580-512-9133	jacque.gillespie@sanfordhealth.org	✓	✓	✓	✓	
Roger Thompson MD		Peds	OKC	405 8206676	roger1824@aol.com	✓	✓	✓	✓	✓
Mark Maloney MD		Pediatrics	Norman		mark.maloney@gmail.com	✓	✓	✓	✓	
Donna Jackson MD		Pediatrics	Norman	(405) 818-3688	djackson@normanpediatrics.com	✓	✓	✓	✓	
Martha Royall APRN		Peds	Norman	405 820-6364	mroyall1e cox.net	✓	✓	✓	✓	
Bridget Bryan DO	Bridget Bryan DO	Peds	Chickasha	405 880-6784	bridget.d.bryan@gmail.com	✓	✓	✓	✓	
Laura Kadechuk		Peds	Chickasha	405 826-8893	Lkadechuk@gmail.com	✓	✓	✓	✓	
Diadra Larsen PAC		Peds	Chickasha	405 3170056	diadra.dgre@gmail.com	✓	✓	✓	✓	
Nancy Collazo Bonilla		Peds	Lawton	580-354-5509	nancy.collazo@ihs.gov	✓	✓	✓	✓	✓
Barbara Cardona		Peds	Lawton	580 354 5500	barbara.cardona@ihs.gov.	✓	✓	✓	✓	✓
Sharon McKie		Peds	Lawton	580-354-5500	sharon.mckie@ihs.gov	✓	✓	✓	✓	

RSV Prophylaxis Petition to improve guidelines based on the current literature:

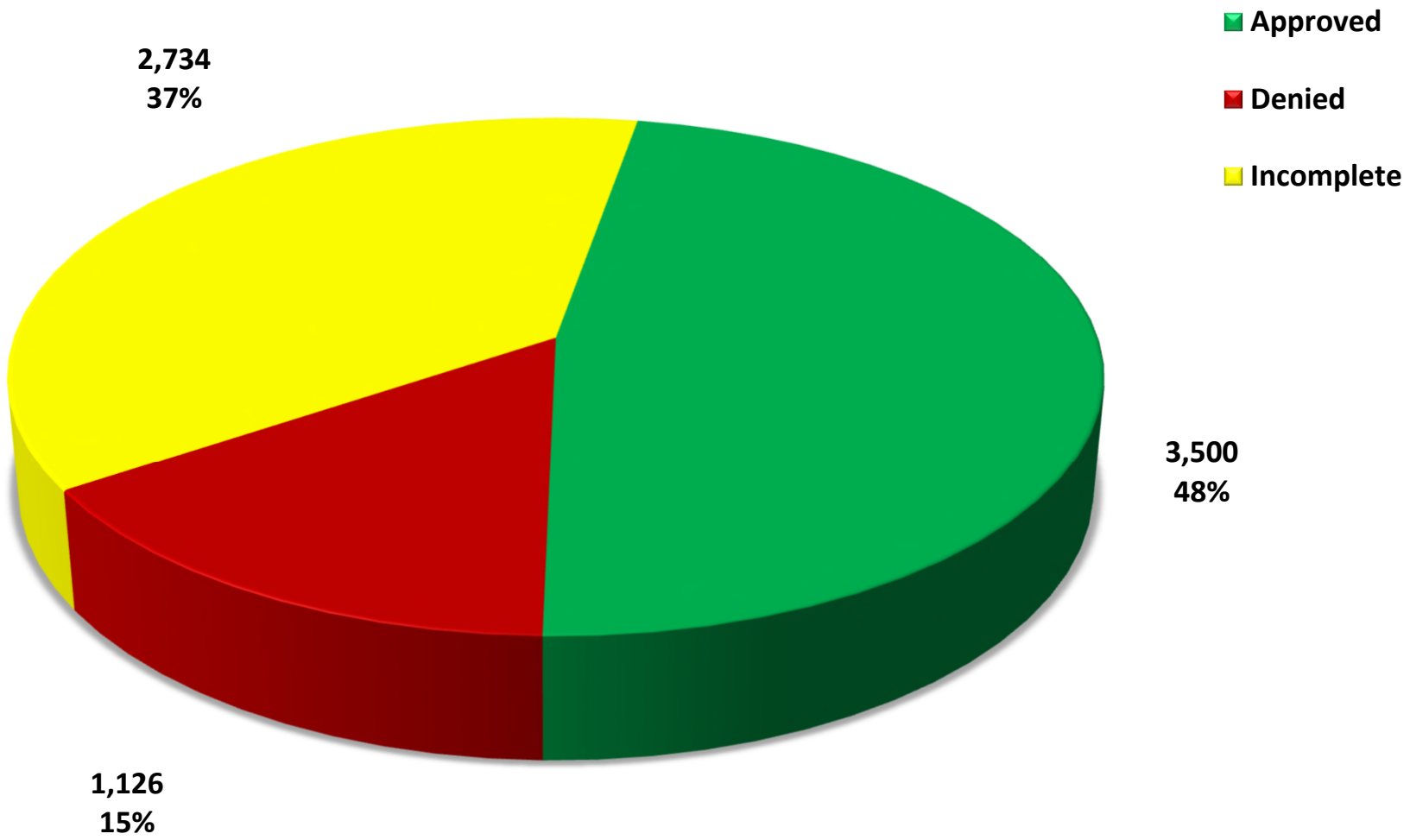
Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of age)	29 to 32 GA (<3 months of age)	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of age)	32 to 35 GA (3 to 6 months of age)
Melissa Lindeman		Peds	OKC	405 [illegible]	melissa-lindeman@ouhsc.edu	✓	✓	✓	✓	
Shawn Cochrane		Peds	OKC	405 205-0770	shawn-cochrane@ouhsc.edu	✓	✓	✓		
Micah Marshall		Peds	OKC	405 255-[illegible]	micah-marshall@ouhsc.edu	✓	✓	✓	✓	
Ken Jackson		Peds	OKC	4056307050	Kenneth-c-jackson@ouhsc.edu	✓	✓	✓	✓	
DARIN BRANNON		PEDS	OKC	405 922-4[illegible]	DBRANNON@KIDSOKC.ORG	✓	✓	✓	✓	
Victor Wilson		Peds	Nolmn	405 [illegible]	vicwilson@[illegible]	✓	✓	✓	✓	
Eileen Poe		Peds	Norman	405-[illegible]	eileenfpa@cox.net	✓	✓	✓	✓	

RSV Prophylaxis Petition to improve guidelines based on the current literature:

Provider's Name PRINTED	Provider's Name SIGNATURE	Specialty	City	Mobile Number	Email Address	<29 GA (<6 months of	29 to 32 GA (<3 months of	29 to 32 GA (3 to 6 months of age)	32 to 35 GA (<3 months of	32 to 35 GA (3 to 6 months of
Jennifer Unruh	Jennifer Unruh	Peds	Norman	8207640	jjunruh@pldi.net	✓	✓	✓		
Julianne Clark	Julianne Clark	Peds	Shawnee	405-550-3203	julesclarko@yahoo.com	✓	✓	✓	✓	✓
Amy Meiser	Amy Meiser	Peds	Norman	405 990-1569	ameiser@normanpediatric.com	✓	✓	✓		
JOAnn Rosenberger	JOAnn Rosenberger	Peds	Tahlequah	918-207-6922	joann-13@yahoo.com	✓	✓	✓		
Kandi Cunningham		Peds	Altus	580 471-6119	KandiCunningham@jcmh.com	✓	✓	✓		

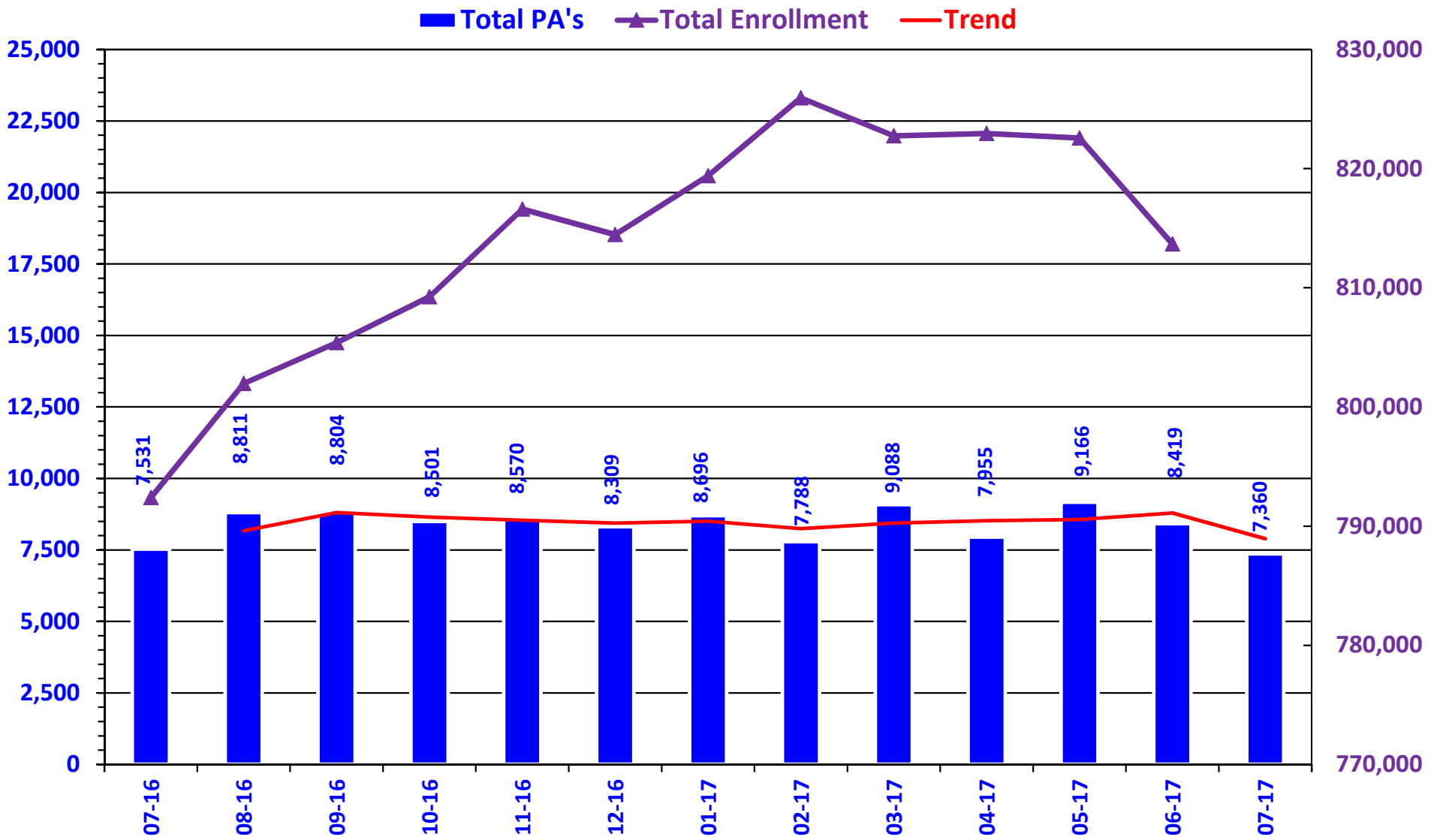
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JULY 2017



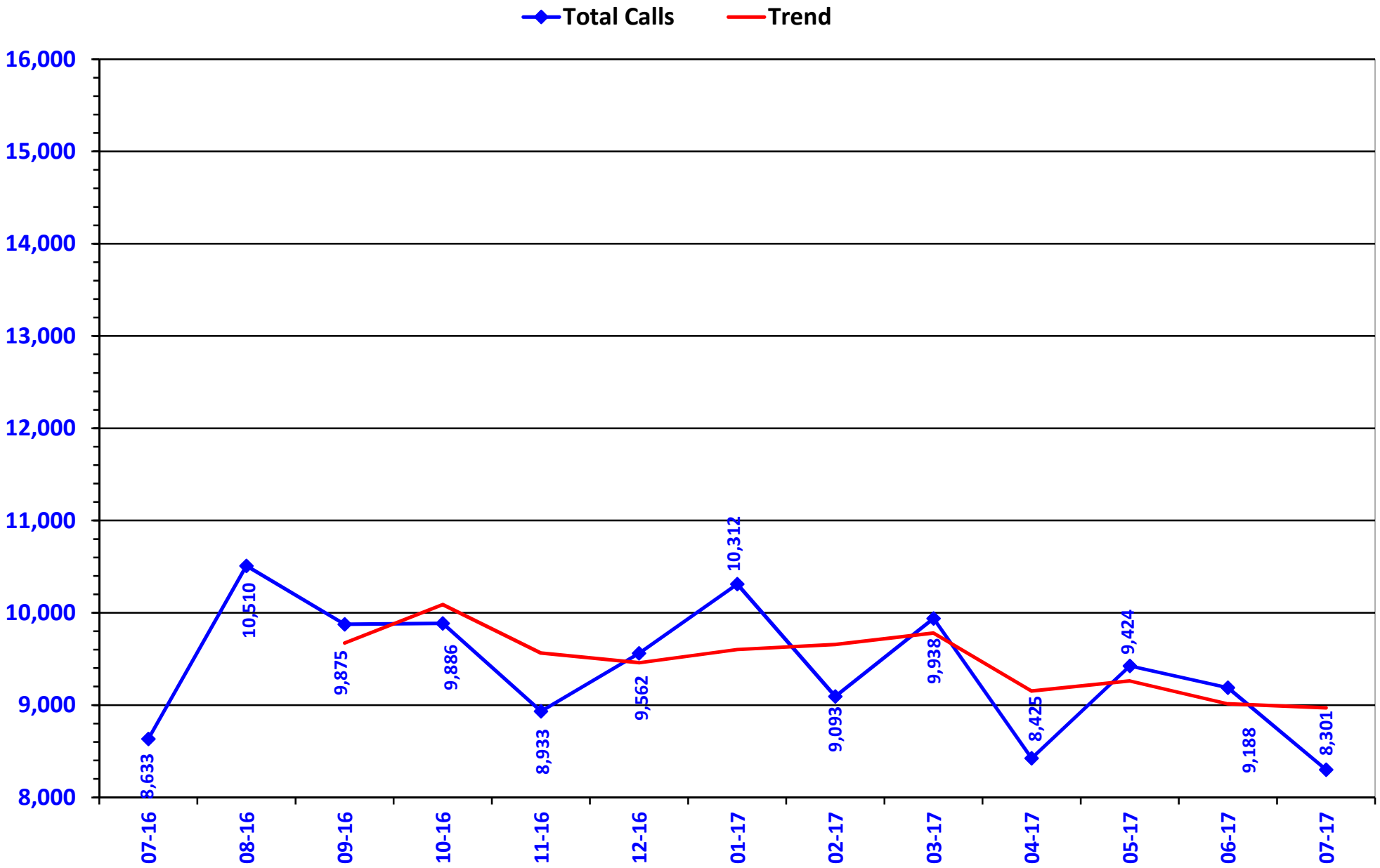
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JULY 2016 – JULY 2017



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JULY 2016 – JULY 2017



Prior Authorization Activity

7/1/2017 Through 7/31/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	128	16	25	87	302
Analgesic - NonNarcotic	15	0	2	13	0
Analgesic - Narcotic	428	219	47	162	171
Angiotensin Receptor Antagonist	19	7	5	7	359
Antiasthma	36	5	12	19	358
Antibiotic	15	5	0	10	287
Anticonvulsant	96	41	14	41	300
Antidepressant	103	26	17	60	345
Antidiabetic	207	86	30	91	349
Antigout	16	8	0	8	325
Antihistamine	163	124	15	24	355
Antimigraine	32	5	9	18	288
Antineoplastic	45	28	3	14	159
Antiparasitic	11	0	2	9	0
Antiulcers	132	24	51	57	172
Anxiolytic	64	37	4	23	248
Atypical Antipsychotics	209	114	17	78	319
Biologics	96	55	12	29	319
Bladder Control	52	18	11	23	342
Blood Thinners	179	106	14	59	334
Botox	28	15	8	5	322
Buprenorphine Medications	359	266	18	75	70
Cardiovascular	116	52	20	44	330
Chronic Obstructive Pulmonary Disease	181	28	48	105	293
Constipation/Diarrhea Medications	149	20	58	71	192
Contraceptive	36	25	4	7	318
Dermatological	151	23	69	59	235
Diabetic Supplies	464	284	21	159	182
Endocrine & Metabolic Drugs	108	81	9	18	172
Erythropoietin Stimulating Agents	18	10	5	3	99
Fibromyalgia	158	17	79	62	357
Fish Oils	16	1	6	9	356
Gastrointestinal Agents	106	21	30	55	144
Glaucoma	11	4	2	5	305
Growth Hormones	60	45	2	13	154
Hepatitis C	197	114	27	56	9
HFA Rescue Inhalers	46	13	11	22	305
Insomnia	32	6	7	19	175
Insulin	65	22	11	32	346
Miscellaneous Antibiotics	22	2	1	19	7
Multiple Sclerosis	47	15	10	22	217
Muscle Relaxant	48	5	16	27	89
Nasal Allergy	50	8	13	29	251
Neurological Agents	46	17	9	20	357
Neuromuscular Agents	19	3	15	1	238
NSAIDs	170	28	46	96	291
Ocular Allergy	25	4	6	15	87
Ophthalmic Anti-infectives	17	4	0	13	14
Osteoporosis	15	3	5	7	356
Other*	272	58	64	150	250
Otic Antibiotic	40	5	9	26	9
Pediculicide	12	1	1	10	5
Respiratory Agents	14	9	1	4	168
Statins	48	12	8	28	284
Stimulant	597	291	45	261	340
Testosterone	56	13	19	24	332
Topical Antifungal	23	2	9	12	54
Topical Corticosteroids	115	3	35	77	163
Vitamin	50	11	23	16	359

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

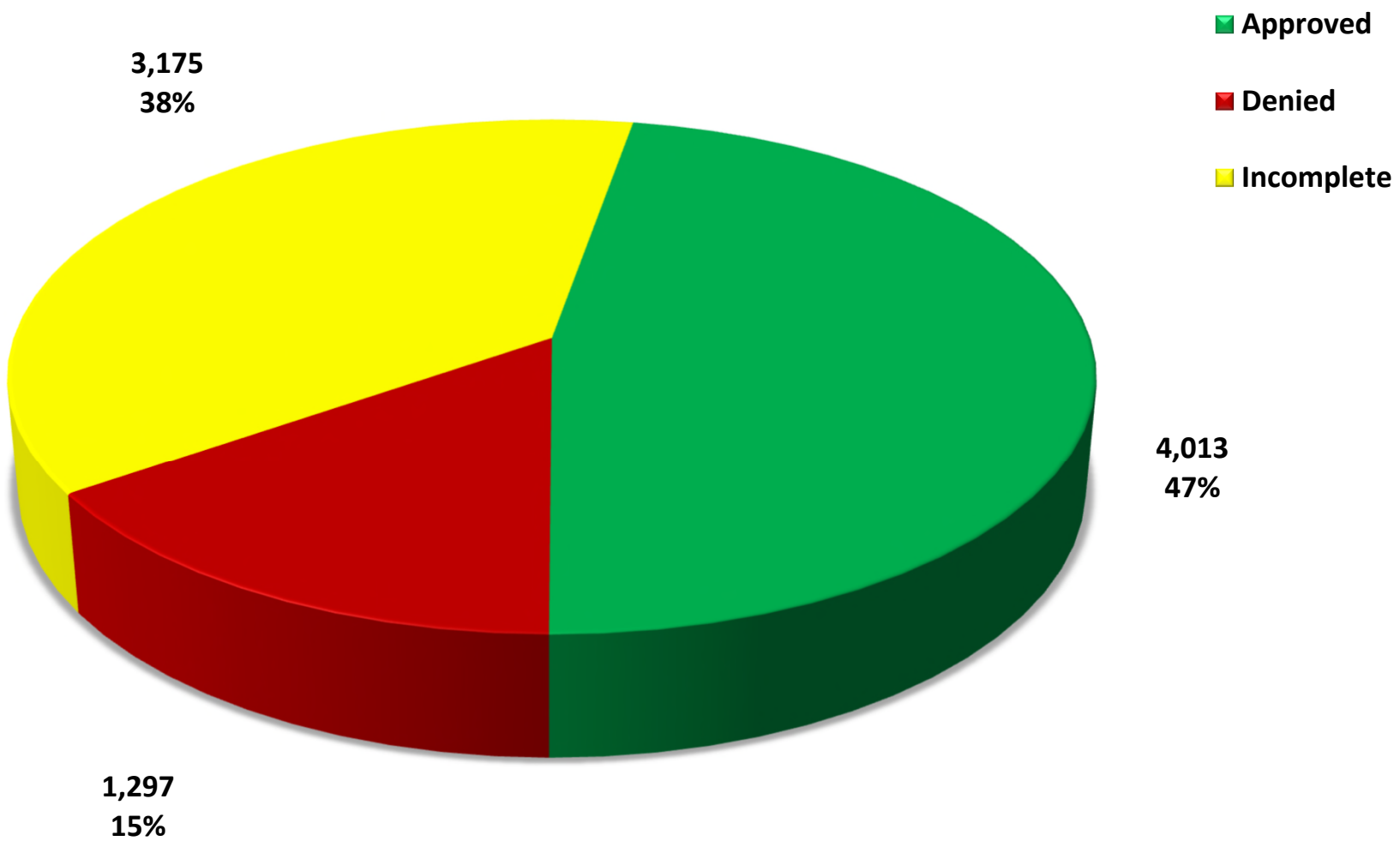
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Emergency PAs	1	1	0	0	
Total	**6,129**	**2,549**	**1,060**	**2,520**	
Overrides					
Brand	38	26	4	8	321
Cumulative Early Refill	3	3	0	0	180
Diabetic Supplies	2	1	0	1	360
Dosage Change	300	271	3	26	12
High Dose	4	4	0	0	272
Ingredient Duplication	23	15	1	7	11
Lost/Broken Rx	62	58	1	3	11
NDC vs Age	164	110	20	34	276
Nursing Home Issue	49	45	0	4	11
Opioid Quantity	19	15	0	4	132
Other*	22	21	0	1	11
Quantity vs. Days Supply	531	374	35	122	250
STBS/STBSM	7	5	0	2	41
Stolen	6	4	0	2	11
Temporary Unlock	1	1	0	0	28
Third Brand Request	24	17	2	5	16
Overrides Total	**1,231**	**951**	**66**	**214**	
Total Regular PAs + Overrides	**7,360**	**3,500**	**1,126**	**2,734**	

Denial Reasons	
Unable to verify required trials.	2,007
Does not meet established criteria.	1,151
Lack required information to process request.	692

Other PA Activity	
Duplicate Requests	561
Letters	8,163
No Process	6
Changes to existing PAs	583
Helpdesk Initiated Prior Authroizations	647
PAs Missing Information	43

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

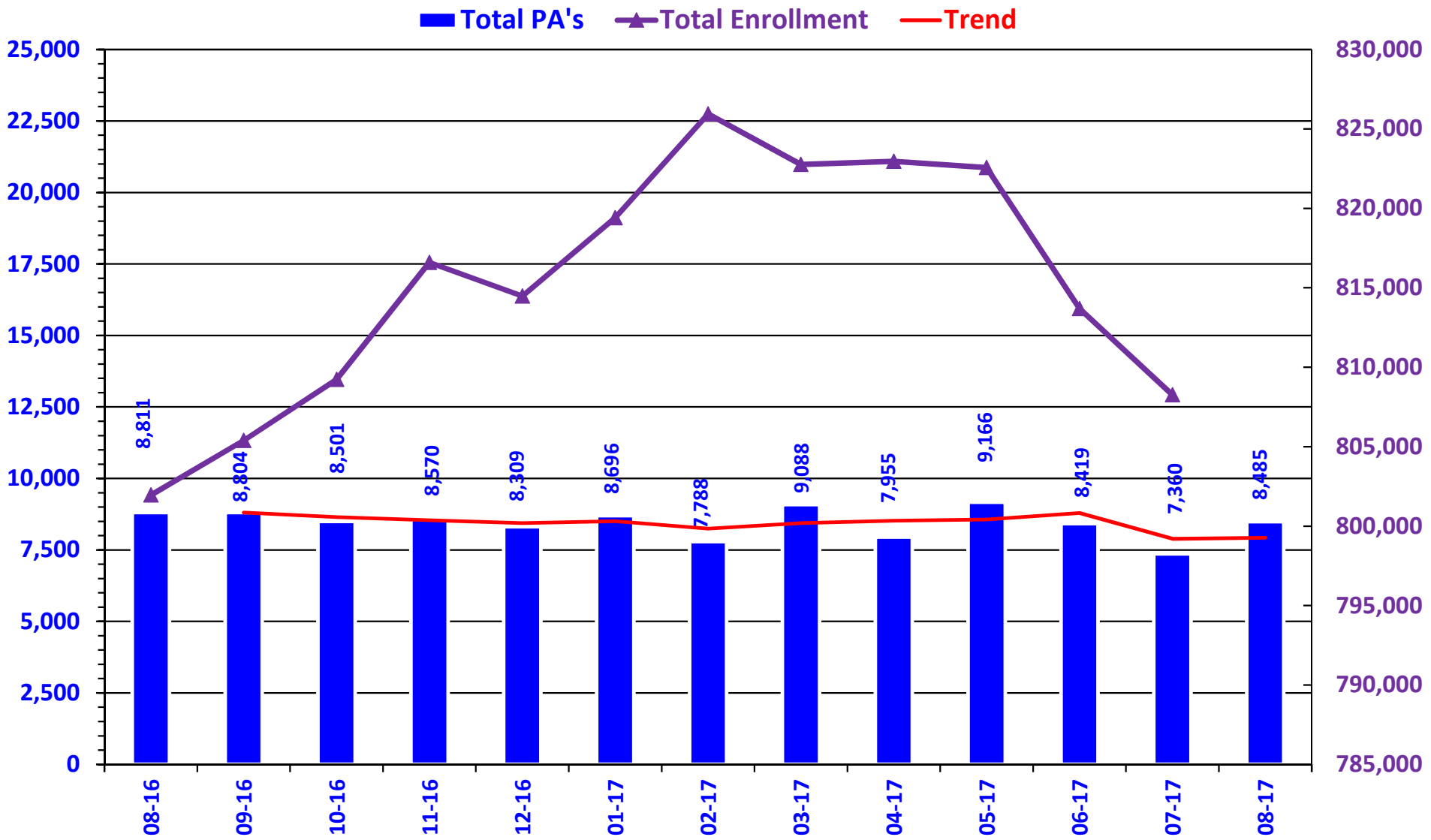
PRIOR AUTHORIZATION ACTIVITY REPORT: AUGUST 2017



As of August 30, 2017. August numbers will be updated in the October DUR packet to reflect the full month.

PA totals include approved/denied/incomplete/overrides

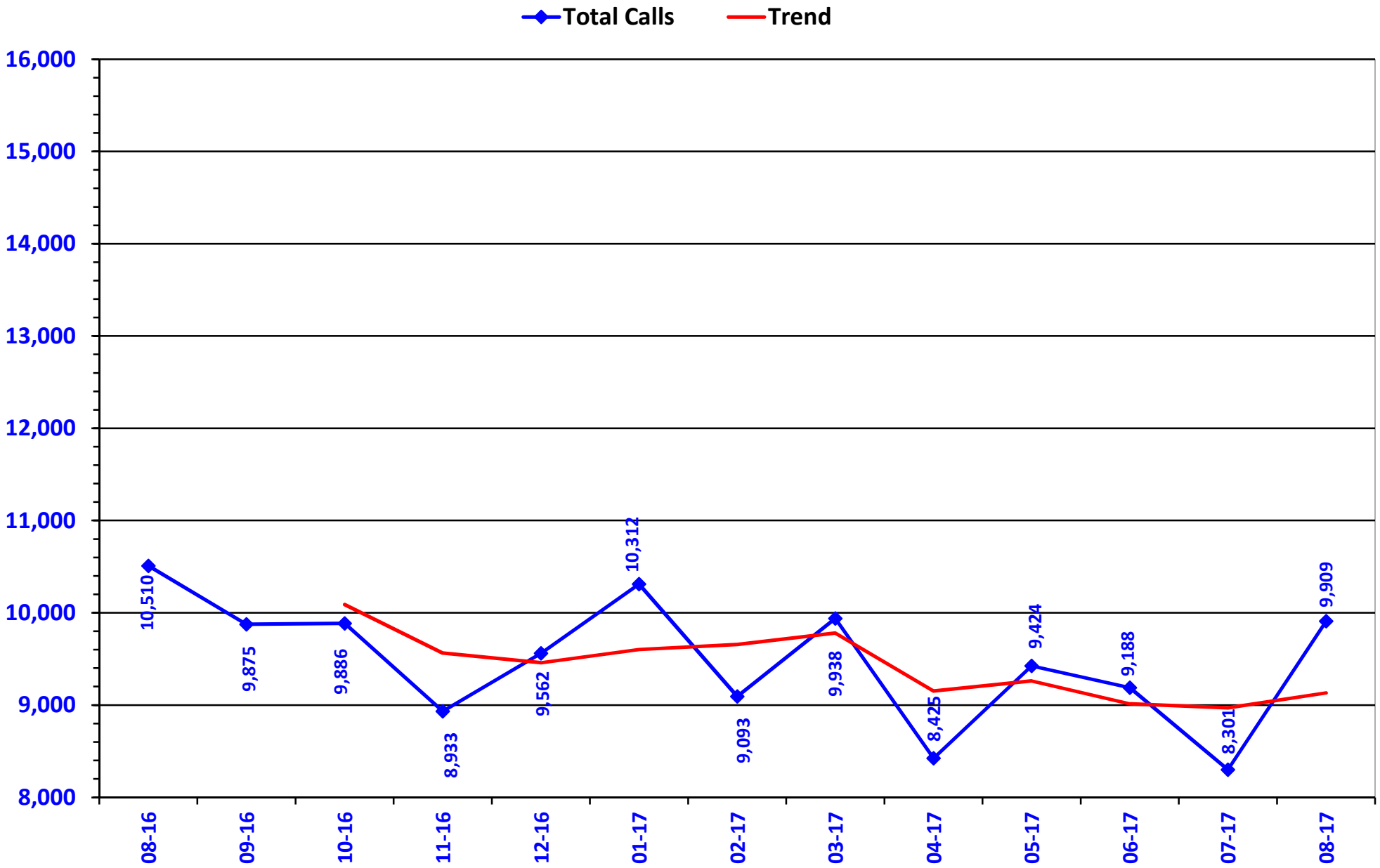
PRIOR AUTHORIZATION REPORT: AUGUST 2016 – AUGUST 2017



As of August 30, 2017. August numbers will be updated in the October DUR packet to reflect the full month.

PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
AUGUST 2016 – AUGUST 2017



As of August 30, 2017. August numbers will be updated in the October DUR packet to reflect the full month.

Prior Authorization Activity

8/1/2017 Through 8/30/2017

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	142	13	33	96	358
Analgesic - NonNarcotic	36	0	9	27	0
Analgesic, Narcotic	415	226	54	135	161
Antiasthma	36	12	5	19	306
Antibiotic	25	11	2	12	314
Anticonvulsant	117	48	16	53	313
Antidepressant	123	26	24	73	338
Antidiabetic	215	82	30	103	357
Antigout	13	5	2	6	323
Antihistamine	221	178	7	36	356
Antimigraine	40	9	10	21	129
Antineoplastic	58	32	8	18	167
Antiulcers	129	26	44	59	167
Anxiolytic	75	37	6	32	221
Atypical Antipsychotics	241	111	45	85	344
Biologics	96	56	16	24	311
Bladder Control	53	10	20	23	345
Blood Thinners	211	120	22	69	319
Botox	51	35	9	7	356
Buprenorphine Medications	371	249	25	97	73
Cardiovascular	132	56	19	57	315
Chronic Obstructive Pulmonary Disease	182	37	39	106	350
Constipation/Diarrhea Medications	147	22	52	73	182
Contraceptive	19	15	2	2	310
Dermatological	167	35	70	62	241
Diabetic Supplies	576	317	20	239	187
Endocrine & Metabolic Drugs	132	91	4	37	163
Erythropoietin Stimulating Agents	17	8	1	8	111
Fibromyalgia	166	19	92	55	279
Fish Oils	12	2	9	1	360
Gastrointestinal Agents	117	33	26	58	134
Growth Hormones	93	58	4	31	155
Hepatitis C	203	122	24	57	9
HFA Rescue Inhalers	81	26	18	37	322
Insomnia	49	8	14	27	191
Insulin	102	35	20	47	300
Miscellaneous Antibiotics	19	1	1	17	8
Multiple Sclerosis	49	31	4	14	185
Muscle Relaxant	59	14	21	24	81
Nasal Allergy	48	7	13	28	128
Neurological Agents	50	23	12	15	317
NSAIDs	201	22	62	117	244
Ocular Allergy	37	9	12	16	117
Osteoporosis	17	6	4	7	312
Other*	296	65	65	166	230
Otic Antibiotic	54	11	5	38	11
Pediculicide	18	0	4	14	0
Respiratory Agents	32	24	1	7	277
Statins	56	15	10	31	316
Stimulant	867	400	101	366	342

As of August 30, 2017. August numbers will be updated in the October DUR packet to reflect the full month.

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Topical Antifungal	40	6	6	28	77
Topical Corticosteroids	157	3	57	97	355
Vitamin	57	13	22	22	318
Pharmacotherapy	51	47	0	4	297
Emergency PAs	0	0	0	0	
Total	**7,021**	**2,881**	**1,220**	**2,920**	
Overrides					
Brand	51	40	3	8	296
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	4	3	0	1	46
Dosage Change	384	352	2	30	13
High Dose	5	4	0	1	194
Ingredient Duplication	38	35	0	3	13
Lost/Broken Rx	80	75	0	5	10
NDC vs Age	220	134	27	59	257
Nursing Home Issue	73	72	0	1	9
Opioid Quantity	15	13	2	0	137
Other*	41	36	4	1	14
Quantity vs. Days Supply	503	332	37	134	239
STBS/STBSM	24	18	0	6	46
Stolen	9	7	1	1	7
Third Brand Request	36	27	3	6	14
Overrides Total	**1,464**	**1,132**	**77**	**255**	
Total Regular PAs + Overrides	**8,485**	**4,013**	**1,297**	**3,175**	

Denial Reasons	
Unable to verify required trials.	2,482
Does not meet established criteria.	1,330
Lack required information to process request.	640
Other PA Activity	
Duplicate Requests	614
Letters	8,889
No Process	7
Changes to existing PAs	641
Helpdesk Initiated Prior Authorizations	680
PAs Missing Information	59

As of August 30, 2017. August numbers will be updated in the October DUR packet to reflect the full month.

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

Medicaid Opioid Utilization Comparison

Oklahoma Health Care Authority
September 2017

Introduction[1,2*]

The Oklahoma Health Care Authority (OHCA) is committed to curbing the opioid epidemic and is continually monitoring SoonerCare utilization of opioid analgesics. In October 2016, Express Scripts (ESI), one of the largest pharmacy benefit managers (PBM) in the United States, released a report focusing on opioid analgesic utilization in Medicaid enrollees during calendar year (CY) 2015. The ESI report evaluated a population of 3.1 million members enrolled in Medicaid managed care plans across 14 states. These include the same case mix as covered by the OHCA: Temporary Assistance for Needy Families (TANF) children and their parents; Aged, Blind, and Disabled adults and children; and Children's Health Insurance Program (CHIP) children. The following data compare opioid analgesic utilization among Oklahoma Medicaid members and ESI Medicaid members.

Background[3,4]

Opioid overdose deaths have become a significant public health concern both nationally and in Oklahoma. From 1999 to 2012, drug overdose deaths increased eightfold in Oklahoma and since 2013 have exceeded the number of fatalities due to auto accidents. In a May 2017 editorial, Oklahoma Attorney General, Mike Hunter, estimated the number of opioid-related overdose deaths in Oklahoma to be 2,684 over the past three years, with the caveat that the actual figure could be higher.

Overall Medicaid Opioid Analgesic Utilization[1,2]

Table 1: Medicaid Population Overall

Plan/Year	# of Eligible Members	# of Members Filling Any Rx	% of Members Who Fill Any Rx	% of Members Filling Opioids	% of Rx Utilizers* Filling Opioids
SC 2015	945,694	552,057	58.4%	13.3%	22.8%
ESI 2015	3,103,339	2,005,571	64.6%	14.9%	22.9%
SC 2016	1,088,591	548,602	50.4%	11.0%	21.9%

SC = SoonerCare, ESI = Express Scripts, Rx = prescription
*Rx utilizers are members who filled any prescription during the calendar year.

During CY 2015, 13.3% of SoonerCare members had a paid claim for an opioid analgesic. This is slightly less than the 14.9% seen in the ESI population. This number continued to decline for SoonerCare members to 11.0% in CY 2016. Similar numbers were seen between SoonerCare and ESI in the percentage of utilizers with paid claims for opioid analgesics in CY 2015 (22.8% vs

SoonerCare data compiled by Timothy Pham, Pharm.D., Ph.D. and Corby Thompson, Pharm.D.

22.9%). Percentage of opioid analgesic utilizers who took opioid analgesics for more than 30 days:

- **SoonerCare CY15:** 26.5% of opioid analgesic utilizers
- **ESI CY15:** Specific data not provided; "nearly one third" of opioid analgesic utilizers took opioid analgesics for more than 30 days
- **SoonerCare CY16:** 26.6% of opioid analgesic utilizers

Table 2: Other Measures of Opioid Analgesic Utilization

Plan/Year	# of Opioid Claims	Opioids as a % of All Rx	Opioid Total Cost	Opioid Costs as a % of All Rx Spend	Opioid Cost per Claim
SC 2015	457,189	7.6%	$21,084,563	4.3%	$46.11
ESI 2015	1,831,974	6%	$90,179,002	4.1%	$49.22
SC 2016	436,368	7.2%	$22,351,601	4.3%	$51.22

SC = SoonerCare, ESI = Express Scripts, Rx = prescription
Costs do not reflect rebated prices or net costs.

A larger percentage of SoonerCare prescription claims were for opioid analgesics in both CY 2015 and CY 2016 compared to ESI correlating with a slightly larger percentage of opioid analgesic costs as a percentage of the total prescription spend. Alternatively, the opioid analgesic cost per claim was slightly less for SoonerCare compared to ESI in CY 2015. CY 2016 data were not available for ESI.

Gender Factors[1,2]

Table 3: Members Using Opioid Analgesics

Plan/Year	Gender	# of Members with Opioids	% of Members Who Fill Opioids	# of Opioid Rx per Opioid Utilizer
SC 2015	Male	39,489	31.3%	3.5
	Female	86,725	68.7%	3.7
ESI 2015	Male	171,578	37.3%	4.1
	Female	288,901	62.7%	3.9
SC 2016	Male	37,466	31.2%	3.6
	Female	82,620	68.8%	3.7

SC = SoonerCare, ESI = Express Scripts, Rx = prescription

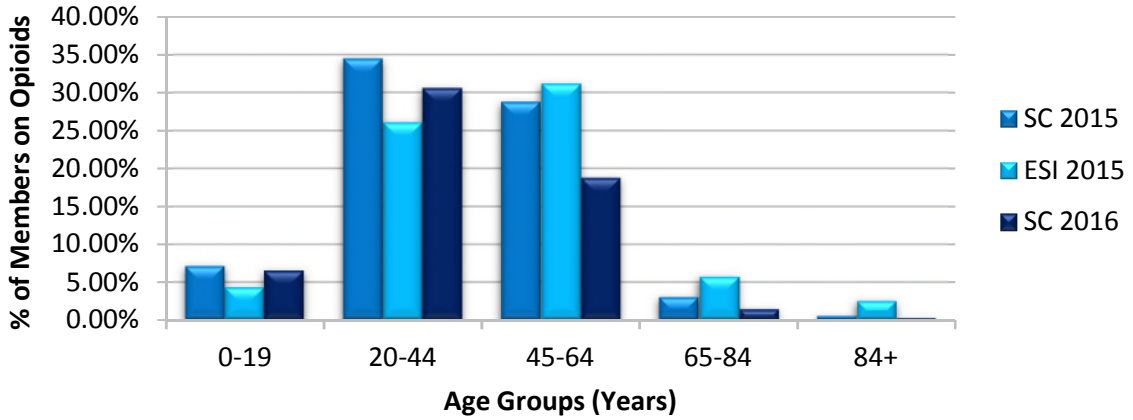
- Relative risk (95% confidence interval [CI]) of receiving an opioid analgesic prescription if female compared to male:
  - **SoonerCare CY15:** 1.68 (1.66 to 1.70)
  - **ESI CY15:** Specific data not provided; "prevalence of opioid use among Medicaid enrollees is 68% higher in women"
  - **SoonerCare CY16:** 1.69 (1.67 to 1.71)

The number of opioid analgesic claims per opioid analgesic utilizer was less for both men and women in CY 2015 and CY2016 for SoonerCare members compared to ESI members. SoonerCare also differed from ESI in the proportion of female members who filled opioid

analgesics compared to male members, with a larger percentage of female members compared to male members having paid claims for opioid analgesics.

Age Factors[1,2]

Percentage of Members with a Paid Claim for an Opioid Analgesics by Age Group



- Overall average age of opioid analgesic utilizers:
  - **SoonerCare CY15:** 28.7 years of age
  - **ESI CY15:** 41 years of age
  - **SoonerCare CY16:** 29.4 years of age

The overall average age of SoonerCare members utilizing opioid analgesics was notably younger than ESI (28.7 years vs 41 years). This can be accounted for by the larger percentage of SoonerCare members in the 20 to 44 year old age group utilizing opioid analgesics. The largest percentage of ESI members utilizing opioid analgesics were in the 45 to 64 year old age group.

Drug Types[1,2]

Table 4: Long-Acting Opioid Analgesic Utilization

Plan/Year	% of Eligible Members	% of All Rx	% of All Opioid Rx	% of All Rx Costs	% of All Opioid Costs
SC 2015	0.75%	0.77%	10.2%	2.4%	65.0%
ESI 2015	4.5%	Not Provided	7.3%	1.0%	24.0%
SC 2016	0.68%	0.83%	11.6%	2.8%	56.7%

SC = SoonerCare, ESI = Express Scripts, Rx = prescription
Percentages of cost do not reflect rebated prices or net costs.

The percentage of SoonerCare eligible members utilizing long-acting opioid analgesics was lower than the percentage for ESI; however, the percentage of long-acting opioid analgesics as a percentage of all opioid analgesics was greater for SoonerCare than ESI. These results indicate a smaller number of members had a larger number of claims for long-acting opioid analgesics in the SoonerCare population. The larger percentage of claims corresponded with a larger percentage of total prescription and total opioid costs. The opioid analgesic category is a SoonerCare supplementally rebated category, and some brand formulation long-acting opioid

analgesics are in Tier-1 as a result of a supplemental rebate. Specific data regarding preferred product status was not specified in the ESI report. Percentages of cost do not reflect rebated prices or net costs.

The top 10 opioid analgesics prescribed to Medicaid members by number of claims were similar across populations and CY with hydrocodone/acetaminophen being the most common followed by oxycodone/acetaminophen and tramadol in all three groups.

Table 5: Top 10 Opioid Analgesics Prescribed to Medicaid Members by Number of Claims

Rank	SC 2015	ESI 2015	SC 2016
1	Hydrocodone/Acetaminophen	Hydrocodone/Acetaminophen	Hydrocodone/Acetaminophen
2	Oxycodone/Acetaminophen	Oxycodone/Acetaminophen	Oxycodone/Acetaminophen
3	Tramadol	Tramadol	Tramadol
4	Codeine/Acetaminophen	Oxycodone	Oxycodone
5	Oxycodone	Suboxone®	Codeine/Acetaminophen
6	Morphine Sulfate	Codeine/Acetaminophen	Morphine Sulfate
7	Fentanyl	Buprenorphine/Naloxone	Buprenorphine/Naloxone
8	Buprenorphine/Naloxone	Morphine Sulfate ER	Fentanyl
9	Methadone	Fentanyl	Methadone
10	Hydromorphone	Buprenorphine	Hydromorphone

SC = SoonerCare, ESI = Express Scripts, ER = extended-release

Prevalence by Enrollment Category[2]

Medicaid provides coverage for a diverse group of individuals. Members are covered under different enrollment categories based on age, gender, disease severity, and socioeconomic status. The following are some of the different enrollment categories covered by Medicaid:

- Temporary Assistance for Needy Families (TANF)
- Aged, Blind, and Disabled (ABD)
- Children's Health Insurance Program (CHIP)
- Dual Eligible

SoonerCare and ESI should cover a similar case mix of members in their Medicaid populations. The following are tables evaluating opioid utilization among SoonerCare members by enrollment category for CY 2016.

Table 6: Comparative Utilization by Enrollment Category

Medicaid Category	# of All Rxs Filled by Enrollment Category	% of All Rxs Filled by Enrollment Category	% of All Rxs for Opioids	% of Rx Utilizers* Filling an Opioid Rx
ABD	2,049,050	33.6%	9.2%	42.2%
TANF	3,925,936	64.5%	6.0%	18.9%
Others	115,565	1.9%	9.6%	33.1%
Total	6,090,551	100%	7.2%	21.9%

Rx = prescription; *Rx utilizers are members who filled any prescription during the calendar year.

The enrollment category with the largest percentage of utilizers filling an opioid analgesic was the ABD population which has an older average age (see table 7) than the other populations and is more associated with chronic disease. ABD members also had a longer average opioid

analgesic prescription day supply compared to the other eligibility categories which reflects more chronic use and may correlate to more chronic disease. Many TANF members receive Medicaid coverage due to pregnancy; opioid prescriptions in this eligibility group may be largely accounted for by prescriptions following labor and delivery.

Table 7: Other Measures of Comparative Utilization by Enrollment Category

Medicaid Category	Average Opioid Rx Day Supply	Average Member Age for Any Rx	Average Member Age Receiving an Opioid Rx
ABD	24.4	40.5	47.1
TANF	15.1	40.3	23.6
Others	22.1	12.8	45.1
Total	19.3	16.5	29.4

Rx = prescription; Age is in years

Conclusions[1,2,5,6]

Overall opioid analgesic utilization in the SoonerCare population was similar to the ESI population. ESI differed from SoonerCare in the percentage of long-acting opioid analgesic utilizers. Long-acting opioid analgesics are only recommended in chronic pain; therefore the current analysis of utilizers and claims may not be a fair indication of appropriate use without corresponding diagnosis data. Another notable difference between the two populations was the average age of opioid analgesic users. The average SoonerCare opioid analgesic user was younger by more than 10 years. Differences may be a result of plan restrictions on pediatric patients or excluding analysis of liquid dosage formulation claims. Neither of which were mentioned in the ESI report. Additionally, some states included in the ESI analysis may have expanded Medicaid; expansion populations typically include a higher percentage of adults and may alter the overall average age of the population.

Many opioid analgesic parameters appeared to improve in the SoonerCare population from CY 2015 to CY 2016 with declines in the percentage of eligible members with paid claims for opioid analgesics and the percentage of opioid analgesics of all prescription claims. The College of Pharmacy and the OHCA will continue efforts to ensure clinically appropriate utilization of opioid analgesics.

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[1] Ward, Krista. A Nation in Pain: The Medicaid Opioid Crisis. Express Scripts®. Available online at: http://lab.express-scripts.com/lab/insights/government-programs/a-nation-in-pain-the-medicaid-opioid-crisis. Issued 06/21/2017. Last accessed 07/18/2017.

[2] Express Scripts®. Data Insights: A Nation in Pain: The Medicaid Opioid Crisis. Available online at: http://lab.express-scripts.com/lab/insights/government-programs/~/media/44e8de2c68b84ad9b122a1715ee1375a.ashx. Last revised 10/2016. Last accessed 07/18/2017.

[3] Oklahoma Highway Safety Office. Crash Data and Statistics. Available online at: https://www.ok.gov/ohso/Data/Crash_Data_and_Statistics/index.html. Last revised 07/26/2016. Last accessed 08/09/2017.

[4] The *Oklahoman* Opinion. Epidemic not too strong a word where opioids are concerned. The *Oklahoman* Editorial Board. Available online at: http://newsok.com/article/5547297. Issued 05/01/2017. Last accessed 08/09/2017.

[5] Centers for Disease Control and Prevention (CDC). CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. *Recommendations and Reports.* March 2016: 65(1); 1-49.

[6] National Association of Medicaid Directors. State Medicaid Operations Survey. Available online at: http://medicaiddirectors.org/wp-content/uploads/2016/12/NAMD_OpsSurveyReport_FINAL.pdf. Issued 12/2016. Last accessed 08/22/2017.

Appendix C

Vote to Prior Authorize Radicava™ (Edaravone)

Oklahoma Health Care Authority
September 2017

Introduction[1,2,3,4,5,6,7,8,9,10]

Amyotrophic lateral sclerosis (ALS; Lou Gehrig's disease) is a rapidly progressive neurodegenerative disease that affects motor neurons in the brain and spinal cord that control voluntary muscle movement. The progressive degeneration of motor neurons in ALS eventually leads to their demise, and thus the ability of the brain to initiate and control muscle movement is lost. With voluntary muscle action progressively affected, people with ALS may lose the ability to speak, eat, move, and breathe. Most people with ALS die from respiratory failure, usually within 3 to 5 years from the onset of symptoms. There is currently no cure for ALS, and treatment typically consists of symptomatic and supportive care. Rilutek® (riluzole) was approved by the U.S. Food and Drug Administration (FDA) in 1995 for the treatment of ALS and may prolong survival by a few months, but does not reverse the damage already done to motor neurons.

Radicava™ (edaravone) was FDA approved in May 2017 as an orphan drug for the treatment of ALS and has been shown to slow the clinical decline in daily functioning of people with ALS. Edaravone is the first new treatment for ALS approved by the FDA in over 20 years. Edaravone is a free radical scavenger that is thought to reduce oxidative stress, a likely factor in the onset and progression of ALS. Radicava™ is supplied for intravenous (IV) infusion in single-dose bags containing 30mg of edaravone in 100mL of clear, colorless aqueous solution. The recommended dosage regimen is an IV infusion of 60mg edaravone administered over a 60 minute period. The initial dosing cycle should consist of daily dosing for 14 days, followed by a 14-day drug-free period. Subsequent dosing cycles should consist of daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods. The efficacy of edaravone for the treatment of ALS was established in a six month randomized placebo-controlled double-blind study conducted in 137 Japanese patients with ALS who were living independently and had a disease duration of 2 years or less at screening. The primary efficacy endpoint was a comparison of change between treatment arms in the ALS functional rating scale – revised (ALSFRS-R) scores from baseline to week 24. The ALSFRS-R measure is used in ALS clinical studies, but it is important to note that a clinically meaningful change in the ALSFRS-R score remains undefined. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS and each item is scored from 0 to 4, with higher scores representing greater functional ability. ALSFRS-R scores may not be directly comparable since different motor features have different influences on activities of daily living. The decline in ALSFRS-R scores from baseline was statistically significantly less in the edaravone-treated patients as compared to placebo (p=0.0013). Therefore, edaravone-treated ALS patients meeting the inclusion criteria for the study had less functional loss at 6 months compared to those receiving standard of care.

Cost: Radicava™ became available in the United States in August 2017; the wholesale acquisition cost (WAC) of Radicava™ is shown in the table below.

Medication	Cost/Infusion	Cost/Treatment Cycle	Cost/Year
Radicava™ (edaravone)	$1,086.00	$10,860.00	$141,180.00

Costs based on WAC and do not reflect rebated prices or net costs. Cost per treatment cycle based on 10 infusions per 28-day treatment cycle (maintenance dosing). Cost per year based on 13 treatment cycles (every 28 days) of maintenance dosing.

Recommendations

The College of Pharmacy recommends the prior authorization of Radicava™ (edaravone) with the following criteria:

Radicava™ (Edaravone) Approval Criteria:

1. An FDA approved diagnosis of amyotrophic lateral sclerosis (ALS); and
2. Member must have been evaluated by a physician specializing in the treatment of ALS within the last three months; and
3. Disease duration of two years or less (for initial approval); and
    a. A prior authorization request with patient-specific information may be submitted for consideration of edaravone for members with disease duration greater than two years, including but not limited to disease progression, specific symptoms related to the disease, activities of daily living currently affected by the disease, or prognosis; and
4. Approvals will be for the duration of six months. For each subsequent approval, the prescriber must document that the member is responding to the medication, as indicated by a slower progression in symptoms and/or slower decline in quality of life compared to the typical ALS disease progression.

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[1] National Institutes of Health. National Institute of Neurological Disorders and Stroke: Amyotrophic Lateral Sclerosis (ALS) Fact Sheet. Available online at: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet#Treatment. Last accessed 08/21/2017.

[2] National Institutes of Health. National Institute of Neurological Disorders and Stroke: Amyotrophic Lateral Sclerosis (ALS) Information Page. Available online at: https://www.ninds.nih.gov/Disorders/All-Disorders/Amyotrophic-Lateral-Sclerosis-ALS-Information-Page. Last accessed 08/21/2017.

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Appendix D

Vote to Prior Authorize Eucrisa™ (Crisaborole 2% Ointment), Dupixent® (Dupilumab Injection), & Prudoxin™ and Zonalon® (Doxepin 5% Cream)

Oklahoma Health Care Authority
September 2017

Introduction[1,2,3,4]

- **Eucrisa™ (crisaborole ointment)** was approved by the U.S. Food and Drug Administration (FDA) in December 2016. It is a phosphodiesterase 4 (PDE-4) inhibitor indicated for topical treatment of mild-to-moderate atopic dermatitis (AD) in patients 2 years of age and older. It is recommended to apply a thin layer of crisaborole twice daily to the affected areas. Crisaborole is for topical use only and is not for ophthalmic, oral, or intravaginal use.
- **Dupixent® (dupilumab injection)** was approved by the FDA in March 2017. It is an interleukin-4 (IL-4) alpha antagonist indicated for the treatment of adult patients with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupilumab can be used with or without topical corticosteroids (TCS). The recommended dose is an initial dose of 600mg (two 300mg injections in different injection sites), followed by 300mg given every other week. Dupilumab is administered by subcutaneous injection.
- **Prudoxin™ and Zonalon® (doxepin 5% cream)** were approved by the FDA in 2015. Doxepin cream is indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with AD or lichen simplex chronicus. It is recommended to apply a thin film of cream four times each day with at least a 3 to 4 hour interval between applications. There are no data to establish the safety and effectiveness of doxepin cream when used for greater than 8 days. Chronic use beyond 8 days may result in higher systemic levels and should be avoided. Use of doxepin cream for longer than 8 days may result in an increased likelihood of contact sensitization.

Cost:

Medication	Recommended Dosing Regimen	Cost/Unit	Cost/Month
Dupixent® (dupilumab injection)	300mg subQ Q2W	$1,423.08	$2,846.16
Eucrisa™ (crisaborole ointment), 60gm	Apply twice daily	$561.60	$561.60
doxepin cream, 45gm	Apply 4 times daily	$479.70	$479.70

SubQ = subcutaneous; gm = gram; Q2W = every other week
Costs based on National Average Drug Acquisition Cost (NADAC), State Maximum Allowable Cost (SMAC), or Wholesale Acquisition Cost (WAC) if NADAC unavailable. Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Eucrisa™ (crisaborole), Dupixent® (dupilumab), and Prudoxin™ and Zonalon® (doxepin cream) with the following criteria:

Eucrisa™ (Crisaborole Ointment) Approval Criteria:

1. An FDA approved indication for treatment of mild-to-moderate atopic dermatitis (eczema); and
2. Member must be at least 2 years of age or older; and
3. Member must have documented trials within the last six months for a minimum of two weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
    a. One Tier-1 topical corticosteroid; and
    b. One topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. A quantity limit of one tube per 30 days will apply.
5. Initial approvals will be for the duration of one month. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Dupixent® (Dupilumab Injection) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies; and
2. Member must be 18 years of age or older; and
3. Member must have documented trials within the last six months for a minimum of two weeks that resulted in failure with both of the following therapies (or have a contraindication or documented intolerance):
    a. One medium potency to very-high potency Tier-1 topical corticosteroid; and
    b. One topical calcineurin inhibitor [e.g., Elidel® (pimecrolimus), Protopic® (tacrolimus)]; and
4. Dupixent® must be prescribed by a dermatologist, allergist, or immunologist or the member must have been evaluated by a dermatologist, allergist, or immunologist within the last twelve months (or be an advanced care practitioner with a supervising physician who is a dermatologist, allergist, or immunologist); and
5. Initial approvals will be for the duration of 16 weeks. Reauthorization may be granted if the prescriber documents the member is responding well to treatment. Additionally, compliance will be evaluated for continued approval.

Prudoxin™ and Zonalon® (Doxepin Cream) Approval Criteria:

1. An FDA approved diagnosis for the short-term (up to eight days) management of moderate pruritus in patients with atopic dermatitis or lichen simplex chronicus; and
2. Requests for longer use than eight days will not generally be approved. Chronic use beyond eight days may result in higher systemic levels and should be avoided.

[1] Eucrisa™ Prescribing Information. Anacor Pharmaceuticals. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=5331. Last revised 12/2016. Last accessed 07/26/2017.
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[3] Zonalon® (doxepin hydrochloride cream) Prescribing Information. *DailyMed*. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ea3b314f-473f-45cb-bab2-8a89ef632030. Last revised 03/11/2015. Last accessed 07/26/2017.
[4] Prudoxin™ (doxepin hydrochloride cream) Prescribing Information. *DailyMed*. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9756deca-4d3f-4b8f-bbdc-5f3d61793c34. Last revised 06/01/2015. Last accessed 07/26/2017.

Appendix E

Vote to Prior Authorize Vimizim® (Elosulfase Alfa)

Oklahoma Health Care Authority
September 2017

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

Vimizim® (elosulfase alfa) was approved by the U.S. Food and Drug Administration (FDA) in 2014 as an enzyme replacement therapy for patients with Morquio A, also known as mucopolysaccharidosis type IVA or MPS IVA. Morquio syndrome is a progressive condition that is characterized by skeletal involvement, but is also associated with significant non-skeletal manifestations including respiratory disease, spinal cord compression, cardiac disease, impaired vision, hearing loss, and dental problems. Morquio syndrome is inherited in an autosomal recessive pattern and there are two forms with similar clinical findings. Morquio A results from mutations in the gene encoding galactosamine-6-sulfatase, and Morquio B (MPS IVB) results from a deficiency of beta-galactosidase. The clinical features of the syndrome result from accumulation of chondroitin-6-sulfate (C6S) and keratan sulfate (KS). Elosulfase alfa is intended to provide the exogenous enzyme *N*-acetylgalactosamine-6-sulfatase (GALNS) that will be taken up into the lysosomes and increase catabolism of KS and C6S. Elosulfase alfa has a boxed warning for the risk of life-threatening anaphylactic reactions. The recommended dosage regimen of elosulfase alfa is 2mg per kilogram (kg) of body weight administered once weekly as an intravenous (IV) infusion.

Cost: The wholesale acquisition cost (WAC) of Vimizim® (elosulfase alfa) is $1,111.00 per 5mg/5mL single-use vial for IV use.

Patient Weight	Dosing Regimen	Vials Per Infusion	Cost Per Weekly Infusion	Cost Per Year
10kg	20mg once weekly	4	$4,444.00	$231,088.00
20kg	40mg once weekly	8	$8,888.00	$462,176.00
55kg	110mg once weekly	22	$24,442.00	$1,270,984.00

Costs based on WAC and do not reflect rebated prices or net costs. Cost per year based on 52 weekly infusions.

Recommendations

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

Vimizim® (Elosulfase Alfa) Approval Criteria:

1. An FDA approved diagnosis of Morquio A syndrome (mucopolysaccharidosis type IVA; MPS IVA) confirmed by:
    a. Enzyme assay demonstrating a deficiency of *N*-acetylgalactosamine-6-sulfatase (GALNS) enzyme activity; or
    b. Molecular genetic testing to confirm biallelic pathogenic variants in *GALNS*; and

2. Vimizim® 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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[1] Vimizim® Prescribing Information. Biomarin Pharmaceutical Inc. Available online at: http://www.vimizim.com/hcp/. Last revised 02/2014. Last accessed 07/26/2017.

[2] Hendriksz CJ, Berger KI, Giugliani R, et al. International Guidelines for the Management and Treatment of Morquio A Syndrome. *American Journal of Medical Genetics Part a*. 2015; 167(1):11-25. doi:10.1002/ajmg.a.36833.

[3] Morquio Answers. Biomarin Pharmaceuticals. Available online at: http://www.morquioanswers.com/?bm=bm1. Last accessed 07/26/2017.

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[5] National Institutes of Health. Morquio Syndrome. *U.S. National Library of Medicine: Medline Plus*. Available online at: https://medlineplus.gov/ency/article/001206.htm. Last reviewed 04/20/2015. Last accessed 07/26/2017.

[6] Wynn R. Mucopolysaccharidoses: Clinical features and diagnosis. *UpToDate®*. Available online at: http://www.uptodate.com/contents/mucopolysaccharidoses-clinical-features-and-diagnosis?source=search_result&search=mps+iv&selectedTitle=1%7E22#H14. Last revised 06/10/2016. Last accessed 07/26/2017.

[7] Mucopolysaccharidosis IV. National Organization for Rare Disorders (NORD). Available online at: https://rarediseases.org/rare-diseases/morquio-syndrome/. Last accessed 07/26/2017.

Appendix F

Vote to Prior Authorize Rayaldee® (Calcifediol), Parsabiv™ (Etelcalcetide), Zemplar® (Paricalcitol Capsules), and Hectorol® (Doxercalciferol Capsules)

Oklahoma Health Care Authority
September 2017

Introduction[1,2,3,4]

- **Rayaldee® (calcifediol extended-release [ER] capsules)** is a vitamin D_3 analog indicated for the treatment of secondary hyperparathyroidism (SHPT) in adults with chronic kidney disease (CKD) stage 3 or 4 and serum total 25-hydroxyvitamin D levels less than 30ng/mL.
    - Limitations of Use: Rayaldee® is not indicated in patients with CKD stage 5 or end-stage renal disease on dialysis.
- **Parsabiv™ (etelcalcetide injection)** is a calcium-sensing receptor agonist indicated for SHPT in adult patients with CKD on hemodialysis.
    - Limitations of Use: Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism (PHPT), or in patients with CKD who are not on hemodialysis, and Parsabiv™ is not recommended for use in these populations.
- **Zemplar® (paricalcitol capsules)** is a vitamin D analog indicated in adults and pediatric patients 10 years of age and older for the prevention and treatment of SHPT associated with CKD stages 3 and 4 and CKD stage 5 in patients on hemodialysis or peritoneal dialysis.
- **Hectorol® (doxercalciferol capsules)** is a synthetic vitamin D_2 analog indicated for the treatment of SHPT in patients with CKD on dialysis and indicated in pre-dialysis patients for the treatment of SHPT in patients with CKD stage 3 or stage 4.

Recommendations

The College of Pharmacy recommends the prior authorization of Rayaldee® (calcifediol ER capsules), Parsabiv™ (etelcalcetide injection), Zemplar® (paricalcitol capsules), and Hectorol® (doxercalciferol capsules) with the following criteria:

Rayaldee® (Calcifediol ER Capsules) Approval Criteria:

1. An FDA approved indication for treatment of secondary hyperparathyroidism (SHPT) in adults with chronic kidney disease (CKD) stage 3 or 4; and
2. Member must not have CKD stage 5 or end-stage renal disease on dialysis; and
3. Member should have a serum total 25-hydroxyvitamin D level less than 30ng/mL before starting treatment; and
4. Member should have a serum calcium level below 9.8mg/dL before initiating treatment; and

5. Rayaldee® must be prescribed by a nephrologist, endocrinologist, or provider who specializes in the treatment of SHPT; and
6. Member must have a documented failure or clinically-significant reason why the member cannot use available generic vitamin D analogs including calcitriol; and
7. Initial approval will be for 30mcg daily for three months; and
    a. After three months, approval for 60mcg daily for 12 months can be considered if intact parathyroid hormone (iPTH) is above the treatment goal and serum calcium is below 9.8mg/dL, phosphorus is below 5.5mg/dL, and 25-hydroxyvitamin D is below 100ng/mL.
    b. Additional approvals will not be granted if iPTH is persistently abnormally low, serum calcium is consistently above the normal range, or serum 25-hydroxyvitamin D is consistently above 100ng/mL.
8. A quantity limit of 60 capsules per 30 days will apply.

Parsabiv™ (Etelcalcetide Injection) Approval Criteria:

1. An FDA approved indication for the treatment of secondary hyperparathyroidism (SHPT) in adult patients with chronic kidney disease (CKD) on hemodialysis; and
2. Parsabiv™ will not be approved for parathyroid carcinoma, primary hyperparathyroidism, or in patients with CKD who are not on hemodialysis and is not recommended for use in these populations; and
3. Member's corrected serum calcium should be at or above the lower limit of normal (≥ 8.3mg/dL) prior to initiation, dose increase, or re-initiation of Parsabiv™; and
4. Parsabiv™ must be prescribed by a nephrologist, endocrinologist, or provider who specializes in the treatment of SHPT; and
5. Member must have a documented failure or a clinically-significant reason why the member cannot use available generic vitamin D analogs including calcitriol; and
6. Member must have a documented failure or a clinically-significant reason why the member cannot use Sensipar® (cinacalcet); and
7. A quantity limit of 12 vials per month will apply.

Zemplar® (Paricalcitol Capsules) Approval Criteria:

1. Member must be 10 years of age or older; and
2. An FDA approved indication for the prevention and treatment of secondary hyperparathyroidism (SHPT) associated with one of the following:
    a. Chronic kidney disease (CKD) stage 3 or 4; or
    b. CKD stage 5 in patients on hemodialysis or peritoneal dialysis; and
        i. Members with CKD stage 5 should have a corrected total serum calcium equal to or less than 9.5mg/dL before initiating treatment; and
3. Zemplar® must be prescribed by a nephrologist, endocrinologist, or provider who specializes in the treatment of SHPT; and
4. Member must have a documented failure or a clinically-significant reason why the member cannot use other generic vitamin D analogs available without prior authorization including calcitriol and Zemplar® injection; and
5. A quantity limit of 30 capsules per 30 days will apply.

Hectorol® (Doxercalciferol Capsules) Approval Criteria:

1. An FDA approved diagnosis; and
2. Member must have a documented failure or a clinically-significant reason why the member cannot use calcitriol.

[1] Rayladee® Prescribing Information. OPKO Ireland Global Holdings Ltd. Available online at: http://www.rayaldee.com/docs/Rayaldee_PI.pdf. Last revised 06/2016. Last accessed 08/07/2017.
[2] Parsabiv™ Prescribing Information. KAI Pharmaceuticals, Inc. Available online at: http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/parsabiv/parsabiv_pi.ashx. Last revised 02/2017. Last accessed 08/07/2017.
[3] Zemplar® Prescribing Information. AbbVie Inc. Available online at: http://www.rxabbvie.com/pdf/Zemplarcappi.pdf. Last revised 10/2016. Last accessed 08/07/2017.
[4] Hectorol® Prescribing Information. Genzyme Co. Available online at: http://products.sanofi.us/Hectorol_Capsule/Hectorol_Capsule.pdf. Last revised 12/2010. Last accessed 08/07/2017.

Appendix G

Vote to Prior Authorize Marplan® (Isocarboxazid) and Desyrel® (Trazodone 300mg Tablets)

Oklahoma Health Care Authority
September 2017

Introduction[1]

Marplan® (isocarboxazid) is a non-selective hydrazine monoamine oxidase inhibitor (MAOI) indicated for the treatment of depression. Because of its potentially serious side effects, isocarboxazid is not an antidepressant of first choice in the treatment of newly diagnosed depressed patients. Isocarboxazid is supplied as a 10mg oral tablet and the recommended initial dose of isocarboxazid is 10mg twice daily. If tolerated, the dosage may be increased by increments of 10mg every two to four days to achieve a dosage of 40mg daily by the end of the first week of treatment. The maximum recommended dose is 60mg/day. Isocarboxazid should not be administered to patients with hypersensitivity to isocarboxazid, cerebrovascular disorders, pheochromocytoma, liver disease, or renal impairment.

Cost Comparison:

Medication	Cost Per Unit	Cost Per 30 days
Marplan® (isocarboxazid) 10mg tablet	**$4.31**	**$517.20***
Cymbalta® (duloxetine) 60mg capsule	$0.26	7.80^{\Delta}$
Nardil® (phenelzine) 15mg tablet	$0.48	57.60^{\Delta}$

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.
Unit = tablet or capsule
*Cost per 30 days based on 40mg daily dose as caution is indicated in patients for whom a dose of 40mg/day is exceeded.
$^{\Delta}$Cost per 30 days based on typical treatment dose of 60mg daily.

Trazodone 300mg (Desyrel®) is one of several strengths of trazodone available for the treatment of major depressive disorder (MDD); however, the cost of trazodone 300mg differs greatly from the cost of other strengths of trazodone. The national average drug acquisition cost (NADAC) of trazodone 300mg is $2.90 per tablet. This results in a 30-day supply costing $87.00. As shown below a 30-day supply of the other available strengths of trazodone, at an equivalent dose, is significantly less.

Cost Comparison:

Medication	Cost Per Tablet	Cost for 30 Days of Therapy*
Desyrel® 300mg (trazodone tablet)	**$2.90**	**$87.00**
Desyrel® 150mg (trazodone tablet)	$0.20	$12.00
Desyrel® 100mg (trazodone tablet)	$0.09	$8.10
Desyrel® 50mg (trazodone tablet)	$0.05	$9.00

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.
*30 days of therapy based on 300mg/day of trazodone.

Recommendations

The College of Pharmacy recommends the following:

1. The placement of Marplan® (isocarboxazid) into the Special Prior Authorization (PA) Tier of the Antidepressant Product Based Prior Authorization (PBPA) category based on wholesale acquisition cost (WAC). The following criteria will apply:
    a. **Marplan® (Isocarboxazid) Approval Criteria:**
        i. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan®. Tier structure rules still apply.
2. The placement of Desyrel® (trazodone) 300mg into the Special PA Tier of the Antidepressant PBPA category based on national average drug acquisition cost (NADAC) compared to other trazodone strengths. The following criteria will apply:
    a. **Desyrel® (Trazodone 300mg Tablets) Approval Criteria:**
        i. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including two trazodone 150mg tablets or three trazodone 100mg tablets to achieve a 300mg dose.
3. Move desvenlafaxine (generic Pristiq®) from Tier-3 to Tier-2 based on NADAC. Current Tier-2 criteria will apply.

Antidepressant Medications Tier-2 Approval Criteria:

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

Antidepressant Medications Tier-3 Approval Criteria:

1. Member must have a documented, recent (within six months) trial with two Tier-1 medications (one medication from the SSRI category and one trial with duloxetine) and a trial of a Tier-2 medication at least four weeks in duration each and titrated to recommended dosing, that did not provide an adequate response; or
2. Prior stabilization on the Tier-3 medication documented within the last 100 days. A past history of success on the Tier-3 medication will also be considered with adequate documentation; or
3. A unique FDA-approved indication not covered by a lowered tiered medication or other medications from a different therapeutic class; or

4. A petition may be submitted for consideration whenever a unique patient-specific situation exists.

Antidepressant Medications Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 medications; or
2. A petition may be submitted for consideration whenever a unique patient-specific situation exists.
3. Tier structure rules still apply.
4. When Irenka™ (duloxetine 40mg) is being requested for non-depression related diagnoses, the criteria below will apply:
    a. An FDA approved diagnosis of diabetic peripheral neuropathy or chronic musculoskeletal pain; and
    b. A patient-specific, clinically significant reason why the member cannot use two duloxetine 20mg capsules in place of Irenka™ 40mg capsules; and
    c. A quantity limit of 30 capsules per 30 days will apply.
5. **Marplan® (Isocarboxazid) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use any of the Tier-3 monoamine oxidase inhibitors (MAOIs) or other cost-effective, lower tiered alternatives in place of Marplan®. Tier structure rules still apply.
6. **Desyrel® (Trazodone 300mg Tablets) Approval Criteria:**
    a. A patient-specific, clinically significant reason why the member cannot use other available generic Tier-1 products including two trazodone 150mg tablets or three trazodone 100mg tablets to achieve a 300mg dose.

Antidepressants*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Selective Serotonin Reuptake Inhibitors (SSRIs)			
citalopram (Celexa®)			fluoxetine 60mg tablets
escitalopram (Lexapro®)			fluoxetine DR (Prozac® Weekly™)
fluoxetine (Prozac®, Sarafem®)			fluvoxamine CR (Luvox CR®)
fluvoxamine (Luvox®)			paroxetine CR (Paxil CR®)
paroxetine (Paxil®)			paroxetine (Pexeva®)
sertraline (Zoloft®)			
Dual-Acting Antidepressants			
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	**desvenlafaxine (Pristiq®)**	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)	vilazodone (Viibryd®)	levomilnacipran (Fetzima®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron® SolTab™)		nefazodone (Serzone®)	duloxetine 40mg (Irenka™)
trazodone (Desyrel®)			**trazodone 300mg tablet (Desyrel®)**
venlafaxine (Effexor®, Effexor XR® capsules)			trazodone ER (Oleptro®)
			venlafaxine ER tablets (Effexor XR® tablets)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	**isocarboxazid (Marplan®)**
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
CR = Controlled-Release, DR = Delayed-Release, ER = Extended-Release

[1] National Institute of Health. Marplan® (Isocarboxazid). *U.S. National Library of Medicine: DailyMed*. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ac387aa0-3f04-4865-a913-db6ed6f4fdc5. Last revised 06/23/2016. Last accessed 08/04/2017.

Appendix H

Vote to Prior Authorize Choline Fenofibrate Delayed-Release (Trilipix®) 135mg Capsules and Fenofibrate Micronized (Lofibra®) 200mg Capsules

Oklahoma Health Care Authority
September 2017

Cost Comparison[1]

Fibric acid derivatives come in a variety of formulations (i.e. fenofibrate, fenofibrate micronized, fenofibric acid, and choline fenofibrate delayed-release) and strengths for the treatment of dyslipidemia, including hyperlipidemia and hypertriglyceridemia. The primary difference between the various products is that the different formulations vary in relation to food effect and are not equivalent on a milligram-to-milligram basis because of their bioavailability. The cost of choline fenofibrate delayed-release (Trilipix®) 135mg capsules and fenofibrate micronized (Lofibra®) 200mg capsules differs greatly from the cost of other comparable fibric acid derivative products. The national average drug acquisition cost (NADAC) of choline fenofibrate delayed-release (Trilipix®) 135mg capsules and fenofibrate micronized (Lofibra®) 200mg capsules is $1.61 and $1.75 per capsule, respectively. This results in a 30-day supply costing $48.30 and $52.50. As shown below, a 30-day supply of the other available comparable fibric acid derivative products is between $15.60 and $33.60, which is less by almost $15.00 or more per month.

Cost Comparison:

Medication	Cost Per Unit	Cost for 30 Days of Therapy*
choline fenofibrate delayed-release (Trilipix® capsules) 135mg	**$1.61**	**$48.30**
fenofibrate micronized (Lofibra® capsules) 200mg	**$1.75**	**$52.50**
fenofibrate (Lofibra® tablets) 160mg	$0.52	$15.60
fenofibrate (Tricor® tablets) 145mg	$0.91	$27.30
fenofibrate (Triglide® tablets) 160mg	$1.12	$33.60

*30 days of therapy based on usual dose of medication
Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC) or State Maximum Allowable Cost (SMAC) if NADAC unavailable.
Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

Recommendations

The College of Pharmacy recommends the following changes to the fibric acid derivative medication Product Based Prior Authorization (PBPA) category:

1. Move fenofibric acid (Fibricor®) 35mg tablets into Tier-1 based on low net cost.
2. Move choline fenofibrate delayed-release (Trilipix®) 135mg capsules and fenofibrate micronized (Lofibra®) 200mg capsules into Tier-2 based on net cost. Current Tier-2 criteria will apply.

Fibric Acid Derivative Medications	
Tier-1	**Tier-2**
choline fenofibrate delayed-release (Trilipix® capsules) 48mg	**choline fenofibrate delayed-release (Trilipix® capsules) 135mg**
fenofibrate (Tricor® tablets)	fenofibrate (Fenoglide® tablets)
fenofibrate (Triglide® tablets)	fenofibrate (Lipofen® capsules)
fenofibrate micronized (Lofibra® capsules) 67mg, 134mg	fenofibrate micronized (Antara® capsules)
fenofibric acid (Fibricor® tablets) 35mg	**fenofibrate micronized (Lofibra® capsules) 200mg**
gemfibrozil (Lopid® tablets)	fenofibric acid (Fibricor® tablets) 105mg

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

[1] Ling J, Luoma JT, Hilleman D. A Review of Currently Available Fenofibrate and Fenofibric Acid Formulations. *Cardiol Res*. 2013; 4(2): 47-55.

Appendix I

Vote to Prior Authorize Arymo™ ER (Morphine Sulfate Extended-Release), Troxyca® ER (Oxycodone/Naltrexone Extended-Release), Vantrela™ ER (Hydrocodone Extended-Release), Oxaydo® (Oxycodone), and RoxyBond™ (Oxycodone)

Oklahoma Health Care Authority
September 2017

Introduction[1,2,3,4,5,6,7,8,9,10]

- The U.S. Food and Drug Administration (FDA) issued a Drug Safety Communication regarding the use of **codeine pain and cough medicines or tramadol** in children and breastfeeding women. The FDA required several changes to the labels of all prescription medications containing codeine or tramadol. The label changes include the following:
    - Codeine and tramadol are now contraindicated for use in children younger than 12 years of age due to the risk of slowed or difficult breathing.
    - Tramadol is now contraindicated in children under 18 years of age when used to treat pain following surgery to remove the tonsils and/or adenoids.
    - Codeine or tramadol are not recommended in breastfeeding mothers due to the risk of excess sleepiness, difficulty breastfeeding, or serious breathing problems in the breastfed infant.
- The FDA has asked Endo Pharmaceuticals, the manufacturer of **Opana® ER (oxymorphone extended-release [ER])**, to remove the product from the market, stating the "benefits of the drug may no longer outweigh its risks."
- **Trezix® (dihydrocodeine/acetaminophen [APAP]/caffeine)** is supplied as 320.5mg APAP/30mg caffeine/16mg dihydrocodeine oral capsules and is indicated for the relief of moderate-to-severe pain; the recommended dosing is two capsules every four hours as needed for pain. The national average drug acquisition cost (NADAC) of the generic formulation is $2.74 per capsule.
- **ConZip® (tramadol ER capsules)** is supplied as 100mg, 200mg, and 300mg ER oral capsules and is indicated for the treatment of pain severe enough to require daily around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The recommended dosing is one capsule by mouth once daily. ConZip® is available in a generic formulation with a wholesale acquisition cost (WAC) of $7.65 per 100mg capsule. The ER tablet formulation of tramadol is also available as a generic formulation with a NADAC of $1.71 per 100mg tablet.
- **Arymo™ ER (morphine sulfate ER tablets)** is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Arymo™ ER is available as 15mg, 30mg, and 60mg ER oral tablets recommended to be dosed every 8 or 12 hours. Arymo™ ER is formulated with inactive ingredients that make the tablet more difficult to manipulate for misuse and abuse. The WAC of Arymo™ ER 30mg is $8.65 per capsule resulting in a monthly cost of $519.00.

- **Troxyca® ER (morphine/naltrexone ER capsules)** is a combination opioid agonist/opioid antagonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Troxyca® ER is formulated with a sequestered opioid antagonist, naltrexone, which is released with manipulation by crushing. Troxyca® ER is available as ER oral capsules to be administered every 12 hours. Troxyca® ER is supplied in the following strengths (oxycodone/naltrexone): 10mg/1.2mg, 20mg/2.4mg, 30mg/3.6mg, 40mg/4.8mg, 60mg/7.2mg, and 80mg/9.6mg. The cost information for Troxyca® ER is not yet available.
- **Vantrela™ ER (hydrocodone ER tablets)** is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Vantrela™ ER is supplied as ER oral tablets in the following strengths: 15mg, 30mg, 45mg, 60mg, and 90mg and is administered every 12 hours. Vantrela™ ER is formulated with physicochemical properties intended to make the tablet more difficult to manipulate for misuse and abuse. The cost information for Vantrela™ ER is not yet available.
- **Oxaydo® (oxycodone immediate-release [IR] tablets)** is indicated for the management of acute and chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Oxaydo® is supplied as IR oral tablets in the following strengths: 5mg and 7.5mg and is administered every 4 to 6 hours. The WAC of Oxaydo® 5mg is $6.08 per tablet resulting in a monthly cost of $729.60.
- **RoxyBond™ (oxycodone IR tablets)** is an opioid agonist indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. RoxyBond™ is supplied as IR oral tablets in the following strengths: 5mg, 15mg, and 30mg and is administered every 4 to 6 hours. RoxyBond™ is formulated with inactive ingredients that make the tablet more difficult to manipulate for misuse and abuse. The cost information for RoxyBond™ is not yet available.

Recommendations

The College of Pharmacy recommends the following:

1. The implementation of an age restriction for all tramadol and codeine products for members younger than 12 years of age. Members younger than 12 years of age would require prior authorization approval for reimbursement of these products. This restriction would include both liquid and solid dosage forms. Authorization would require a patient-specific, clinically significant reason for use of these products despite the medication being contraindicated for the member's age.
2. The movement of Opana® ER (oxymorphone ER) from Tier-3 to the Special Prior Authorization (PA) Tier of the Opioid Analgesics Product Based Prior Authorization (PBPA) category based on FDA recommendations to remove the medication from the market. Authorization would require a patient-specific, clinically significant reason why the member could not use any other available extended-release opioid analgesic.
3. The placement of ConZip® (tramadol ER capsules) into the Special PA Tier of the Opioid Analgesics PBPA category based on net cost. Authorization would require a patient-specific, clinically significant reason why the member could not use the extended-release tablet formulation. Tier structure rules would apply.

4. The placement of Oxaydo® (oxycodone), RoxyBond™ (oxycodone), and Trezix® (dihydrocodeine/APAP/caffeine) into Tier-3 of the Opioid Analgesics PBPA category. Current short-acting Tier-3 criteria would apply.
5. The placement of Arymo™ ER (morphine sulfate ER), Troxyca® ER (morphine/naltrexone ER), and Vantrela™ ER (hydrocodone ER) into Tier-3 of the Opioid Analgesics PBPA category. Current long-acting Tier-3 criteria would apply.

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting: oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®)◊ **Short-Acting:** ASA/butalbital/caff/cod (Fiorinal with Codeine®) codeine codeine/APAP dihydrocodone/ASA/caff (Synalgos-DC®) hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) morphine IR (MSIR®) oxycodone IR (Oxy IR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone/IBU (Combunox™) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** buprenorphine (Butrans®) fentanyl patches (Duragesic®) hydrocodone ER (Hysingla™ ER) morphine ER tablets (MS Contin®) oxycodone ER (Oxycontin®)◊ **Short-Acting:** oxymorphone IR (Opana®) tapentadol IR (Nucynta®)	**Long-Acting:** buprenorphine ER buccal film (Belbuca™) **hydrocodone ER (Vantrela™ ER)** hydrocodone ER (Zohydro™ ER) hydromorphone ER (Exalgo®) methadone (Dolophine®) **morphine sulfate ER (Arymo™ ER)** morphine sulfate ER capsules (Kadian®) morphine sulfate ER (MorphaBond™) morphine/naltrexone ER (Embeda®) **morphine/naltrexone ER (Troxyca® ER)** oxycodone ER (Xtampza™ ER) tapentadol ER (Nucynta® ER) tramadol ER tablets (Ultram ER®, Ryzolt®) **Short-Acting:** **dihydrocodeine/APAP/caff (Trezix®)** hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) oxycodone (Oxecta®) **oxycodone (Oxaydo®)** **oxycodone (RoxyBond™)** oxycodone/APAP (Primlev™, Xolox®)	**Long-Acting:** **oxymorphone ER (Opana® ER)+** oxycodone/APAP ER (Xartemis™ XR) **tramadol ER capsules (ConZip®)** **Oncology Only:** fentanyl transmucosal lozenge (Actiq®) fentanyl buccal tablet (Fentora®) fentanyl buccal film (Onsolis®) fentanyl sublingual tablet (Abstral®) fentanyl nasal spray (Lazanda®) fentanyl sublingual spray (Subsys™)

APAP = Acetaminophen, ASA = Aspirin, IR = Immediate-Release, ER = Extended-Release, IBU = Ibuprofen, Cod = Codeine, Caff = Caffeine

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

◊Brand name preferred.

+Brand name Opana® ER preferred. Generic oxymorphone ER tablets require special authorization as they are not abuse-deterrent.

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[2] ConZip®. Vertical Pharmaceuticals, LLC. Available online at: http://www.verticalpharma.com/vertical-products/conzip/. Last accessed 08/21/2017.

[3] U.S. Food and Drug Adminstration (FDA). FDA News Release: FDA requests removal of Opana ER for risks related to abuse. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm562401.htm. Issued 06/08/2017. Last accessed 08/21/2017.

[4] Lowes, R. Don't Use Tramadol and Codeine in Kids Under 12, FDA Warns. *Medscape*. Available online at: http://www.medscape.com/viewarticle/878880. Issued 04/20/2017. Last accessed 08/21/2017.

[5] U.S. Food and Drug Adminstration (FDA). FDA Drug Safety Communication: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women. Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm. Issued 04/20/2017. Last accessed 08/21/2017.

[6] Arymo™ ER Prescribing Information. Egalet Corporation. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e60552c9-06ce-4790-95e7-aadd4df12b2a. Last revised 01/2017. Last accessed 08/21/2017.

[7] Troxyca® ER Prescribing Information. Pfizer Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/207621s000lbl.pdf. Last revised 08/2016. Last accessed 08/21/2017.

[8] Vantrela ER™ Prescribing Information. Teva Pharmaceuticals Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/207975s000lbl.pdf. Last revised 01/2017. Last accessed 08/21/2017.

[9] Oxaydo® Prescribing Information. Egalet US Inc. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=cff0c64a-63f5-4b3c-909a-cdecf6755cbe. Last revised 07/2017. Last accessed 08/21/2017.

[10] RoxyBond™ Prescribing Information. Inspirion Delivery Sciences LLC. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209777lbl.pdf. Last revised 04/2017. Last accessed 08/21/2017.

Appendix J

Vote to Prior Authorize Brineura™ (Cerliponase Alfa)

Oklahoma Health Care Authority
September 2017

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

Ceroid lipofuscinosis 2 (CLN2) is caused by mutations in the tripeptidyl-peptidase-1 (TPP-1) gene; TPP-1 mutations lead to reduced TPP-1 enzyme activity and impaired breakdown of peptides in lysosomes, peptide accumulation, and subsequent nerve cell damage. The diagnosis of CLN2 is based on the presence of typical symptoms and reduced activity of TPP-1 enzyme confirmed via an assay of enzymatic activity. Symptoms of CLN2 disease, classic late infantile, typically appear between the ages of 2 and 4 years starting with delayed language development and epilepsy. This is followed by regression of developmental milestones and myoclonic ataxia. Visual impairment appears at 4 to 6 years of age and rapidly progresses to blindness. Affected children are usually bedridden by 6 years of age and life expectancy ranges from 6 years to early teens. Motor and language functional abilities for patients with CLN2 disease are assessed via the CLN2 Clinical Rating Scale (CCRS). The CCRS can be used to quantitatively assess disease progression and track loss of function over time. CLN2 has an estimated incidence of approximately 0.5 per 100,000 live births.

In April 2017, the U.S. Food and Drug Administration (FDA) approved Brineura™ (cerliponase alfa) to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal CLN2. Cerliponase alfa, the first FDA approved treatment for CLN2, is a recombinant form of TPP-1, serving as an enzyme replacement therapy in TPP-1 deficient patients. Prior to the approval of cerliponase alfa, the treatment of CLN2 disease was symptomatic and palliative care only.

Brineura™ is supplied as a 150mg/5mL solution for intraventricular infusion. The recommended dosage of cerliponase alfa is 300mg administered once every other week as an intraventricular infusion followed by an infusion of intraventricular electrolytes over approximately 4.5 hours. Cerliponase alfa is administered to the cerebrospinal fluid (CSF) via a surgically implanted reservoir and catheter. The intraventricular access device must be implanted prior to the first infusion. It is recommended that the first dose be administered at least 5 to 7 days after device implantation.

The efficacy of cerliponase alfa was assessed in a non-randomized, single-arm clinical study of pediatric patients with late infantile CLN2 disease. Cerliponase alfa-treated patients were compared to untreated patients from a natural history cohort. The motor domain of the CCRS was used to assess disease progression. Decline was defined as having an unreversed (sustained) 2-category decline or an unreversed score of 0. The results demonstrated the odds of cerliponase alfa-treated patients not having a decline by 96 weeks were 13 times the odds of natural history cohort patients not having a decline (Odds Ratio [95% CI]: 13.1 [1.2, 146.9]).

The efficacy and safety of cerliponase alfa were also evaluated in an open-label, single arm study. Cerliponase alfa was evaluated by comparing CLN2 disease progression in the treatment group to a historical cohort. At 48 weeks the percentage of treated subjects who experienced less than 2-point decline on the motor/language CLN2 score was 87% (p=0.0002) and 65% of patients experienced no decline in motor/language CLN2 score (13 no change, 2 improved by one point). At 48 weeks the cortical gray matter volume measured by MRI scans was 408.3 cm^3 (vs. baseline 452.0 cm^3). A total of 9.7% of gray matter volume loss occurred in treated patients vs. 14.5% in historically untreated patients. The statistical significance of this was not reported.

Cost:

Product	Cost per Treatment	Cost per Month	Annual Cost
Brineura™ (cerliponase alfa) 300mg	**$18,000.00**	**$36,000.00**	**$468,000.00**

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

Recommendations

The College of Pharmacy recommends the prior authorization of Brineura™ (cerliponase alfa) with the following criteria:

Brineura™ (Cerliponase Alfa) Approval Criteria:

1. An FDA-approved diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) also known as tripeptidyl peptidase-1 (TPP-1) deficiency; and
2. Member must have confirmed TPP-1 enzymatic deficiency via enzyme assay, confirmed by molecular analysis; and
3. Member must be at least 3 years of age or older; and
4. Brineura™ must be prescribed by a specialist with expertise in treatment of CLN2 (or be an advanced care practitioner with a supervising physician who is a specialist with expertise in treating CLN2); and
5. Brineura™ must be administered in a healthcare facility by a prescriber who is knowledgeable in intraventricular administration; and
6. Member must not have ventriculoperitoneal shunts or acute intraventricular access device-related complications; and
7. Member must not have documented generalized status epilepticus within 4 weeks of initiating treatment; and
8. Prescriber must verify member's blood pressure and heart rate will be monitored prior to each infusion, during infusion, and post-infusion; and
9. Prescriber must be willing to perform regular 12-lead electrocardiogram (ECG) evaluation at baseline and at least every 6 months and verify that they are acceptable to the prescriber; and
10. A baseline assessment must be performed to assess the Motor plus Language CLN2 score; and
11. Initial authorizations will be for the duration of six months, at which time compliance will be required for continued approval. After 12 months of utilization, the prescriber

must verify the member is responding to the medication as demonstrated by a two point or less decline in Motor plus Language CLN2 score from baseline; and

12. Approval quantity will be based on Brineura™ prescribing information and FDA approved dosing regimen.

[1] Mole SE, Williams RE. Neuronal Ceroid-Lipofuscinoses. *GeneReviews®*. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK1428/. Last revised 08/01/2013. Last accessed 08/21/2017.

[2] BioMarin Pharmaceuticals. CLN2 Connection. Available online at: http://www.cln2connection.com/. Last accessed 08/21/2017.

[3] U.S. National Library of Medicine. CLN2 disease. *Genetics Home Reference*. Available online at: https://ghr.nlm.nih.gov/condition/cln2-disease. Last revised 11/2016. Last accessed 08/11/2017.

[4] Chang CH. Neuronal Ceroid Lipofuscinoses. *Medscape*. Available online at: http://emedicine.medscape.com/article/1178391-overview. Last revised 05/04/2017. Last accessed 08/11/2017.

[5] U.S. Food and Drug Administration (FDA). FDA approves first treatment for a form of Batten disease. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm555613.htm. Issued 04/27/2017. Last accessed 08/14/2017.

[6] Brineura™ Prescribing Information. BioMarin Pharmaceutical USA, Inc. Available online at: http://brineura.com/downloads/Brineura_PI.pdf. Last revised 04/2017. Last accessed 08/14/2017.

[7] Reyes E, Schulz A, Specchio N, et al. Intracerebroventricular cerliponase alfa (BMN 190) in children with CLN2 disease: Results from a Phase 1/2, open-label, dose-escalation study. Forty-Fifth CNS Annual Meeting. October 26-29, 2016. Vancouver, BC.

Appendix K

Fiscal Year 2017 Annual Review of Breast Cancer Medications and 30-Day Notice to Prior Authorize Kisqali® (Ribociclib), Kisqali® Femara® Co-Pack (Ribociclib/Letrozole), and Nerlynx™ (Neratinib)

Oklahoma Health Care Authority
September 2017

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

According to the National Cancer Institute, in 2017 there will be an estimated 252,710 new cases of breast cancer, making it the most common cancer found in women, and an estimated 40,610 deaths. The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Breast cancer can also begin in the cells of the lobules and in other tissues in the breast. Invasive breast cancer is breast cancer that has spread from where it began in the ducts or lobules to surrounding tissue. Traditional chemotherapy has long been used to treat breast cancer, but in more recent years targeted chemotherapy is being developed to specifically take advantage of gene changes in cells that cause cancer [e.g., drugs that target Human Epidermal Receptor Type 2 (HER2), anti-angiogenesis drugs, cyclin-dependent kinase inhibition, etc.].

Use of evidence-based expert consensus guidelines is imperative in the treatment of cancers. The National Comprehensive Cancer Network (NCCN) Compendium contains authoritative, scientifically derived information designed to support decision-making about the appropriate use of drugs and biologics in patients with cancer. These evidence-based guidelines should be used for optimal outcomes of cancer patients.

Current Prior Authorization Criteria

Kadcyla® (Ado-Trastuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Diagnosis of metastatic breast cancer; and
3. Member has previously received trastuzumab and a taxane, separately or in combination; and
4. Members should also have either:
    a. Received prior therapy for metastatic disease; or
    b. Developed disease recurrence during or within six months of completing adjuvant therapy.
5. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ado-trastuzumab therapy.

Halaven® (Eribulin) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of metastatic breast cancer; and

2. Previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on eribulin therapy.

Halaven® (Eribulin) Approval Criteria [Liposarcoma Diagnosis]:

1. Diagnosis of unresectable or metastatic liposarcoma; and
2. Previously received an anthracycline-containing chemotherapy regimen.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on eribulin therapy.

Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:

1. Diagnosis of advanced breast cancer; and
2. Negative expression of Human Epidermal Receptor Type 2 (HER2); and
3. Hormone receptor-positive (ER positive); and
4. Used in combination with exemestane; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.
6. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Neuroendocrine Tumors of Pancreatic Origin (PNET) or Neuroendocrine Tumors (NET) of Gastrointestinal or Lung Origin Diagnosis]:

1. Diagnosis of unresectable, locally advanced, or metastatic neuroendocrine tumors of pancreatic (PNET), gastrointestinal, or lung (NET) origin; and
2. Progressive disease from a previous treatment.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Renal Cell Carcinoma Diagnosis]:

1. Diagnosis of advanced renal cell carcinoma; and
2. Failure of treatment with sunitinib or sorafenib.
3. Everolimus may also be approved to be used in combination with lenvatinib for advanced renal cell carcinoma.
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Renal Angiomyolipoma and Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC); and
2. Not requiring immediate surgery; and

3. Used in pediatric and adult patients with age ≥ 1 year.
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Afinitor® (Everolimus) Approval Criteria [Subependymal Giant Cell Astrocytoma (SEGA) with Tuberous Sclerosis Complex (TSC) Diagnosis]:

1. Diagnosis of subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC); and
2. Requires therapeutic intervention but cannot be curatively resected.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on everolimus therapy.

Ixempra® (Ixabepilone) Approval Criteria:

1. Diagnosis of metastatic or locally advanced breast cancer; and
2. Usage as either:
    a. In combination with capecitabine after failure of an anthracycline and a taxane; or
        i. May be used in combination in taxane only resistance if anthracyclines not indicated; or
    b. Monotherapy after failure of an anthracycline, a taxane, and capecitabine.
3. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ixabepilone therapy.

Tykerb® (Lapatinib) Approval Criteria:

1. An FDA approved diagnosis of metastatic or recurrent breast cancer; and
2. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
3. Lapatinib must be used in combination with one of the following:
    a. Herceptin® (trastuzumab); or
    b. Xeloda® (capecitabine); or
    c. An aromatase inhibitor [e.g. Aromasin® (exemestane), Femara® (letrozole), or Arimidex® (anastrozole)] if also estrogen receptor positive (ER positive).
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on lapatinib therapy.

Ibrance® (Palbociclib) Approval Criteria:

1. A diagnosis of advanced metastatic, hormone receptor positive, Human Epidermal Receptor Type 2 (HER2)-negative breast cancer in combination with:
    a. Letrozole as initial endocrine-based therapy in postmenopausal women; or
    b. Fulvestrant in women with disease progression following endocrine therapy.
2. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on palbociclib therapy.

Perjeta® (Pertuzumab) Approval Criteria:

1. Positive expression of Human Epidermal Receptor Type 2 (HER2); and
2. Usage for either:
   a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease; or
   b. Neoadjuvant treatment of patients with locally advanced, inflammatory, or early stage breast cancer (either greater than 2cm in diameter or node positive); and
3. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents as well in addition to trastuzumab and docetaxel).
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on pertuzumab therapy.

Utilization of Breast Cancer Medications: Fiscal Year 2017

Comparison of Fiscal Years: Breast Cancer Medications (Pharmacy Claims)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	44	222	$2,366,474.52	$10,659.80	$373.97	7,058	6,328
2017	38	176	$2,077,442.66	$11,803.65	$413.09	4,957	5,029
% Change	**-13.60%**	**-20.70%**	**-12.20%**	**10.70%**	**10.50%**	**-29.80%**	**-20.50%**
Change	**-6**	**-46**	**-$289,031.86**	**$1,143.85**	**$39.12**	**-2,101**	**-1,299**

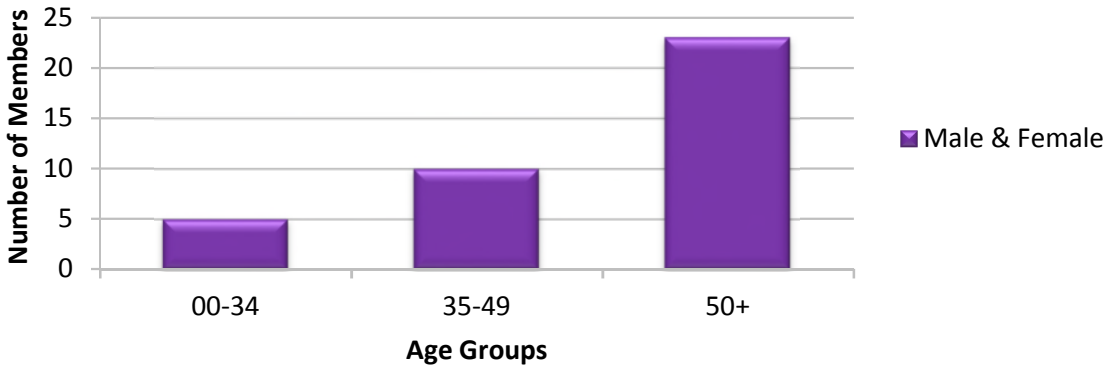
*Total number of unduplicated members.
Cost do not reflect rebated prices or net costs.

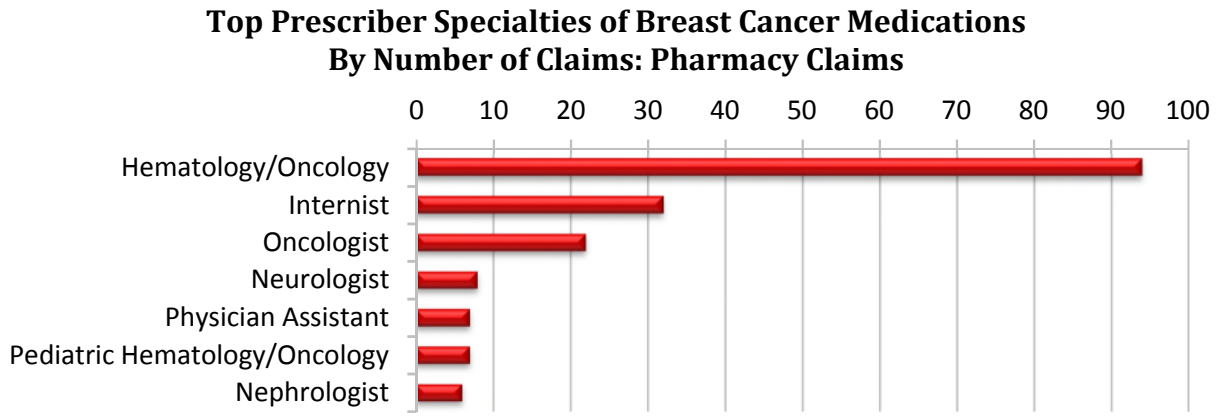
Fiscal Year 2017 Utilization of Breast Cancer Medications: Medical Claims

*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units
127	822	$4,039,116.14	$4,913.77	125,695

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

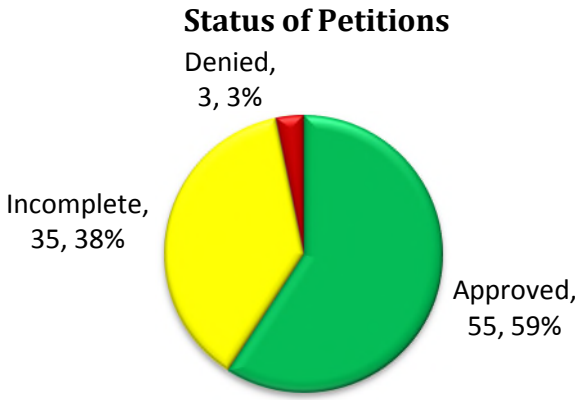
Demographics of Members Utilizing Breast Cancer Medications: Pharmacy Claims





Prior Authorization of Breast Cancer Medications

There were 93 prior authorization requests submitted for breast cancer medications during fiscal year 2017. The following chart shows the status of the submitted petitions.



Market News and Updates[6,7,8,9,10,11,12,13]

New Drug Approval(s):

- **March 2017:** The U.S. Food and Drug Administration (FDA) approved ribociclib (Kisqali®) in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone-receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-negative) advanced or metastatic breast cancer.
- **May 2017:** The FDA approved ribociclib/letrozole (Kisqali® Femara® Co-Pack) for the treatment of postmenopausal women with HR+, HER2-negative advanced or metastatic breast cancer. The Co-Pack is the first and only combination pack with two prescription products in advanced breast cancer.
- **July 2017:** The FDA approved neratinib (Nerlynx®) for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.

Pipeline:

- **February 2016:** The FDA granted breakthrough and fast track designations to sacituzumab govitecan (IMMU-132), an investigational, first-in-class antibody-drug conjugate, for the treatment of triple-negative breast cancer in patients who have failed at least two therapies.
- **December 2016:** Approval of the first PI3-kinase inhibitor, buparlisib, may be on the horizon following the results of the BELLE-2 trial. Buparlisib in combination with fulvestrant showed significant improvements in progression free survival (PFS) compared to placebo in postmenopausal women with HR+, HER2-negative locally advanced or metastatic breast cancer. Toxicities seen in the buparlisib arm included increased transaminases, depression, and anxiety.
- **January 2017:** Tucatinib (ONT-380), an oral tyrosine kinase inhibitor, received fast track designation by the FDA in HER2-negative overexpressed breast cancer.
- **March 2017:** Eli Lilly announced abemaciclib, a cyclin-dependent kinase (CDK) 4 and CDK 6 inhibitor, in combination with fulvestrant met the primary endpoint of PFS in a Phase 3 study of women with HR+, HER2-negative, advanced breast cancer who have relapsed or progressed after endocrine therapy. The data demonstrated the addition of abemaciclib to fulvestrant resulted in a statistically significant improvement in PFS, when compared to the control arm of placebo plus fulvestrant. The most common adverse events observed in the abemaciclib arm were diarrhea, neutropenia, nausea, and fatigue.
- **July 2017:** MYL-1401O, an investigational trastuzumab (Herceptin®) biosimilar, has been recommended for approval by the FDA's Oncologic Drugs Advisory Committee (ODAC) in a 16 to 0 vote. The Biologics License Application (BLA) will now be reviewed by the FDA for final approval.

Product Summaries[14,15,16]

Kisqali® (Ribociclib):

- **Therapeutic Class:** Kinase Inhibitor
- **Indication(s):** In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with HR+, HER2-negative advanced or metastatic breast cancer
- **How Supplied:** 200mg oral tablets
- **Dose:** 600mg (three 200mg tablets) orally once daily for 21 consecutive days followed by 7 days off treatment
- **Cost:** 600mg for 21 days (63 tablets): $10,950.03

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole):

- **Therapeutic Class:** Kinase Inhibitor/Aromatase Inhibitor
- **Indication(s):** As initial endocrine-based therapy for the treatment of postmenopausal women with HR+, HER2-negative advanced or metastatic breast cancer
- **How Supplied:**
    - Kisqali®: 200mg oral tablets
    - Femara®: 2.5mg oral tablets

- **Dose:**
    - Kisqali®: 600mg (three 200mg tablets) orally once daily for 21 consecutive days followed by 7 days off treatment
    - Femara®: 2.5mg (one tablet) orally once daily throughout the 28-day cycle
- **Cost:** 600mg Kisqali® for 21 days (63 tablets) plus Femara® 2.5mg for 28 days (28 tablets): $10,950.03

Nerlynx™ (Neratinib):

- **Therapeutic Class:** Kinase Inhibitor
- **Indication(s):** The extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy
- **How Supplied:** 40mg oral tablets
- **Dose:** 240mg (6 tablets) orally once daily with food, continuously for one year
- **Cost:** 240mg for 30 days (180 tablets): $10,499.40

Recommendations

The prior authorization of Nerlynx™ (neratinib), Kisqali® (ribociclib), and Kisqali® Femara® Co-Pack (ribociclib/letrozole) with the following criteria:

Nerlynx™ (Neratinib) Approval Criteria:

1. For adjuvant treatment in early stage breast cancer; and
2. Member must have Human Epidermal Receptor Type 2 (HER2)-overexpressed breast cancer; and
3. Neratinib must be used to follow adjuvant trastuzumab-based therapy.
4. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on neratinib therapy.

Kisqali® (Ribociclib) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the co-packaged formulation with letrozole; and
2. A diagnosis of advanced or metastatic breast cancer, initial therapy; and
3. Member must be Hormone Receptor (HR)-positive; and
4. Member must be Human Epidermal Receptor Type 2 (HER2)-negative; and
5. Ribociclib must be given in combination with an aromatase inhibitor; and
6. Ribociclib must be used in postmenopausal women only.
7. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ribociclib therapy.

Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria:

1. A diagnosis of advanced or metastatic breast cancer, initial therapy; and
2. Member must be Hormone Receptor (HR)-positive; and
3. Member must be Human Epidermal Receptor Type 2 (HER2)-negative; and
4. Ribociclib must be used in postmenopausal women only.

5. Authorizations will be for the duration of three months. Reauthorization may be granted if the patient does not show evidence of progressive disease while on ribociclib/letrozole therapy.

Utilization Details of Breast Cancer Medications: Fiscal Year 2017

Pharmacy Claims: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
PALBOCICLIB PRODUCTS					
IBRANCE CAP 125MG	74	19	$810,174.56	3.89	$10,948.30
IBRANCE CAP 100MG	29	6	$317,608.56	4.83	$10,952.02
IBRANCE CAP 75MG	19	4	$207,962.88	4.75	$10,945.41
SUBTOTAL	**122**	**29**	**$1,335,746.00**	**4.21**	**$10,948.74**
EVEROLIMUS PRODUCTS					
AFINITOR TAB 10MG	26	8	$333,917.76	3.25	$12,842.99
AFINITOR TAB 5MG	7	1	$181,013.07	7	$25,859.01
AFINITOR TAB 7.5MG	7	1	$90,310.25	7	$12,901.46
AFINITOR TAB 2.5MG	6	1	$72,483.44	6	$12,080.57
AFINITOR DIS TAB 5MG	2	1	$25,439.58	2	$12,719.79
SUBTOTAL	**48**	**12**	**$703,164.10**	**4**	**$14,649.25**
LAPATINIB PRODUCTS					
TYKERB TAB 250MG	6	4	$38,532.56	1.5	$6,422.09
SUBTOTAL	**6**	**4**	**$38,532.56**	**1.5**	**$6,422.09**
TOTAL	**176**	**38***	**$2,077,442.66**	**4.63**	**$11,803.65**

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

Medical Claims: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9355 TRASTUZUMAB INJECTION	650	85	$2,852,229.22	$4,388.05
J9306 PERTUZUMAB INJECTION	190	37	$962,721.00	$5,066.95
J9354 ADO-TRASTUZUMAB INJECTION	17	2	$132,179.60	$7,775.27
J9179 ERIBULIN MESYLATE INJECTION	24	3	$68,709.32	$2,862.89
J9207 IXABEPILONE INJECTION	8	1	$23,277.00	$2,909.63
TOTAL	**822+**	**127***	**$4,039,116.14**	**$4,913.77**

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

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Appendix L

Fiscal Year 2017 Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] and Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated]

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

Eloctate™, Adynovate®, Alprolix®, and Idelvion® Approval Criteria:

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
    a. Hemophilia A: Advate® or current factor VIII replacement product; or
    b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approval will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of one year.

Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence] Approval Criteria:

1. An FDA approved indication; and
2. Obizur® must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use Feiba® (anti-inhibitor coagulant complex) or NovoSeven® RT [coagulation factor VIIa (recombinant)]; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approval will be for the duration of the half-life study. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Corifact® [Factor XIII Concentrate (Human)] and Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)] Approval Criteria:

1. An FDA approved indication; and
2. Corifact® or Tretten® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and

3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Coagadex® [Coagulation Factor X (Human)] Approval Criteria:

1. An FDA approved indication; and
2. Coagadex® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

Standards of Care for Pharmacies Providing Factor Replacement Products:

1. The Provider/Pharmacy must be licensed as a pharmacy by the Oklahoma State Board of Pharmacy. The Pharmacist-in-Charge must be licensed as a pharmacist in Oklahoma.
2. The Provider/Pharmacy agrees that it will provide the following services:
    a. The provider/pharmacy shall be capable to provide a full range of factor products including all available vial sizes.
    b. The provider/pharmacy must have 24 hours per day, 7 days per week "24/7" support in the event of an after-hours emergency.
    c. The provider/pharmacy shall deliver within 24 hours (with a delivery goal of 4 hours) of notification of a need due to current bleeding episode. If the patient is not having an emergency/current bleeding episode the provider/pharmacy must deliver factor within 3 days of notification of need.
    d. The provider/pharmacy shall provide all necessary supplies for appropriate preparation and administration of the factor product as well as appropriate sharps and bio-hazardous disposal unit which includes retrieval and destruction of disposal unit. If the items are SoonerCare compensable, they must be billed as durable medical equipment (DME) via a DME contract.
    e. The provider/pharmacy must provide access to multilingual interpreters for those patients and families where English is not the primary language. The interpreters must be available "24/7", in order to assure availability in the event of an after-hours emergency.
    f. Case Management:
        i. Case Management can be performed by a pharmacist, nurse, social worker, or case manager.
        ii. An in-home patient assessment must be performed upon initiation of services and at least yearly thereafter:
            1. In-home assessments will include but not be limited to the following:
                a. Verification of appropriate and adequate storage
                b. A current inventory of factor product and supplies

c. Verification of access to a bio-hazardous waste disposal unit
d. A review of current treatment records/logs
e. An assessment of educational opportunities to be performed by appropriately trained staff (please refer to 3, b, ii below)
f. Identification of adverse events

2. In the event a patient or caregiver refuses entry to the home, the pharmacy must re-attempt the in-home assessment within three months. If the patient or caregiver continues to deny access, the pharmacy must discuss this issue with the prescribing provider and develop an action plan to verify items set forth in subparagraph 2, f, ii, 1 above. Documentation must be kept of any refusal, re-attempt, and action plan.

iii. Regular follow up with the patient either via telephone, video call, or in-person. This contact should be quarterly and should include but not be limited to the following:
1. All recent bleed episodes reported should be forwarded to the prescribing practitioner immediately.
2. Current inventory
a. Number of factor doses on hand
b. Expiration dates of vials on hand
3. Confirmation of factor storage
4. Adverse events
a. If adverse events are reported to a non-clinical case manager, a clinician should become involved immediately.

iv. Coordination of care including nursing, DME, treating practitioner, and all medications, regardless of source.

3. Educational requirements:
a. Staff Education:
i. Staff having contact with the patient via telephone, video calling, or in-person, must be knowledgeable about hemophilia and other bleeding disorders.
ii. Two hours of Continuing Education (CE) on hemophilia or other related bleeding disorders must be completed each year. Licensed staff must use accredited CE based on their license type. Non-licensed staff may use non-accredited CE performed by a licensed professional.
1. Staff members, whether employed or contracted by the pharmacy, required to complete CE include but are not limited to the following:
a. Pharmacist in Charge
b. Nurse Manager
c. Nurse Performing Direct Patient Care
d. Social Worker
e. Case Manager (including customer service representatives)
2. Documentation of educational activity completed must be kept at the pharmacy and must include the CE certificate or date of activity, staff in attendance, and name and license of professional providing activity.

b. Member and Caregiver Education:

i. Pharmacy staff must encourage engagement with the Oklahoma Comprehensive Hemophilia Treatment Center. Studies have shown better clinical outcomes for those patients engaged with a comprehensive hemophilia treatment center.
ii. Pharmacy staff must discuss educational needs of the patient with the treating practitioner. Once educational opportunities are identified, the pharmacy staff must provide training for the patients and family members in accordance with the treating physician or mid-level practitioner. All patient efforts must be documented. Areas of education may include but are not limited to the following:
    1. Proper storage for factor products and ancillary supplies
    2. Proper disposal of bio-hazardous waste
    3. Preparation of factor and supplies
    4. Training on self-infusion
        a. Prescriber to provide order
            i. Professional licensed nurse (LPN or RN) to train patients or caregivers for peripheral venous access.
            ii. Licensed RN to train patients or caregivers on central line care (e.g., PICC line, InfusaPort, etc.) which includes but is not limited to access, flushing, infusions, and dressing changes.
        b. Training must be in accordance with the MASAC guidelines
    5. Treatment record keeping
    6. Factor and supply management

4. Factor Product Dispensing and Delivery:
    a. Prescriptions cannot be filled without an expressed need from the patient, caregiver, or prescribing practitioner. Auto-filling is not allowed.
    b. Factor products must be packaged in such a way that a patient or caregiver can easily determine what is to be used for each dose.
        i. If the factor dose to be infused only consists of one vial/box then the vial/box should be labeled as such.
        ii. If the factor dose to be infused consists of two or more vials/boxes then each dose should be packaged as a group of appropriate vials/boxes and labeled as an individual dose.
    c. Factor dose must be within 5% of the prescribed dose
        i. If unable to provide factor dosing within 5% of prescribed dose, then pharmacy must provide proof of all available vial sizes from the manufacturer at the time dispensing occurred.
        ii. Any dose requiring more than 3 vials/boxes to be used must be approved by the prescribing practitioner and documented.
        iii. Pharmacy staff must, by the 10th of every month, fax or email to the Oklahoma Health Care Authority (OHCA) a record of dispensing for the previous month, to include but not limited to the member's name, SoonerCare ID, date dispensed, prescriber name, product, prescribed dose, units per vial dispensed, quantity of each vial size, how the doses were packaged if more than one vial was to be used per dose, type of treatment

(prophylaxis, episodic, or breakthrough), and delivery confirmation with member or caregivers' signature.

d. Any factor product which is short-dated (expiring within six months) may only be dispensed after approval from the prescribing practitioner and must be documented.
e. The pharmacy staff must assure appropriate storage of the factor products and supplies including cold chain supply shipping and delivery. The pharmacy must be able to trace the supply chain from manufacturer to patient delivery.
f. The pharmacy must keep records of all lots of factor products dispensed to each patient and notify patient and treating practitioner of any recalls of dispensed factor products. The pharmacy must participate in the National Patient Notification System for clotting factor recalls.
g. The pharmacy provider must have a plan in place for delivery of factor products to the patient in the event of a natural disaster.

5. The Provider/Pharmacy must originally attest to the OHCA these standards of care will be followed and must re-attest yearly.
6. The OHCA Auditing:
   a. The OHCA has the right to audit records of the Blood Clotting Factor Providers to assure all requirements are being met. The OHCA will audit these records which include but is not limited to the following:
      i. In-home assessment records
      ii. Educational information and training provided
      iii. Adverse Event records including reports to other state and federal agencies
      iv. Sharps and bio-hazardous waste disposal units delivery proof and education on proper disposal in patient record.
      v. Patient records
         1. Original Prescriptions
         2. Dispensing records (including lot numbers and expiration dates)
   b. The pharmacy will be excluded from providing blood factor products if the OHCA finds that the pharmacy is out of compliance with the requirements as outlined.

Utilization of Factor Replacement Products: Fiscal Year 2017

Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units	Cost Per Utilizer Per Year
2016	77	583	$13,091,519.73	$22,455.44	10,031,439	$170,019.74
2017	73	643	$13,666,981.82	$21,255.03	9,679,981	$187,218.93
% Change	**-5.20%**	**10.30%**	**4.40%**	**-5.30%**	**-3.50%**	**10.12%**
Change	**-4**	**60**	**$575,462.09**	**-$1,200.41**	**-351,458**	**$17,199.19**

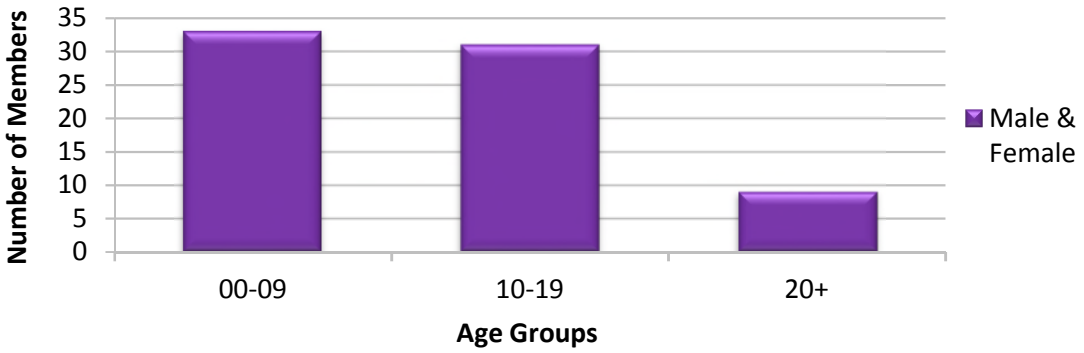
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Fiscal Year 2017 Utilization of Factor Replacement Products: Medical Claims

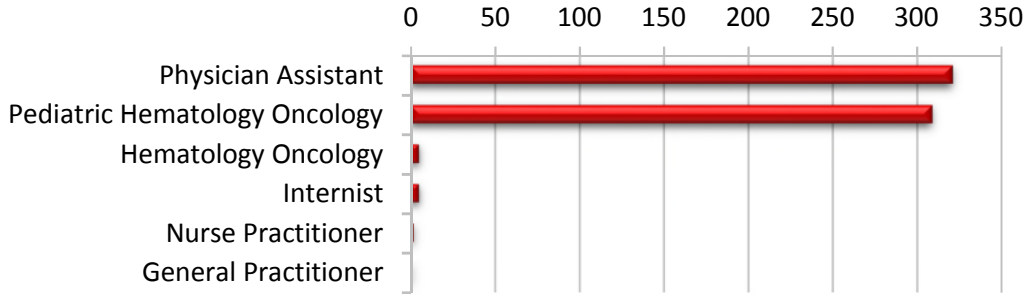
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units	Cost Per Utilizer Per Year
2017	9	36	$1,430,098.34	$39,724.95	762,469	$158,899.82

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

Demographics of Members Utilizing Factor Replacement Products: Pharmacy Claims



Top Prescriber Specialties of Factor Replacement Products by Number of Claims: Pharmacy Claims



Prior Authorization of Factor Replacement Products

There were 18 prior authorization requests for 13 unique members submitted for factor replacement products during state fiscal year (SFY) 2017. All submitted requests were approved.

There were 18 pharmacies with attestations for the Standards of Care (SOC) signed for SFY 2017. There are currently 18 pharmacies with attestations for the SOC signed for SFY 2018.

There were 60 members with a Patient Consent to Treat (PCT) agreement signed in SFY 2017. There are currently 7 patients with signed PCT agreement for SFY 2018. As SFY 2018 continues, the OHCA expects more PCT agreements to be signed and submitted. The pharmacies are required to obtain PCT agreements yearly.

Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14]

New Drug Approval(s):

- **May 2016:** Afstyla® [antihemophilic factor (recombinant), single chain]
- **May 2017:** Rebinyn® [coagulation factor IX (recombinant), glycoPEGylated]

New Indication Approval(s):

- **December 2016:** The U.S. Food and Drug Administration (FDA) approved an expanded indication for Adynovate® [antihemophilic factor (recombinant), PEGylated] to include children less than 12 years of age for the on-demand treatment and control of bleeding episodes, routine prophylaxis to prevent or reduce frequency of bleeding episodes, and perioperative management in adults and children.

Pipeline Update(s):

- **Eptacog Beta (rFVIIa):** In January 2017, LFB S.A. announced the FDA accepted for review the Biological License Application (BLA) for recombinant factor VIIa product, eptacog beta, a treatment for patients with hemophilia A and B with inhibitors. A response from the FDA is expected in November 2017.
- **Emicizumab:**
  - **December 2016:** Genentech reported the primary endpoint had been met in the Phase 3 HAVEN 1 trial evaluating emicizumab (ACE910) prophylaxis in people 12 years of age or older with hemophilia A and inhibitors to factor VIII.
  - **April 2017:** Genentech reported interim results which were positive from the Phase 3 HAVEN 2 trial evaluating emicizumab prophylaxis in children less than 12 years of age with hemophilia A and inhibitors to factor VIII.
  - **May 2017:** Baxalta filed a complaint in the United States District Court for the District of Delaware against Genentech and Chugai Pharmaceutical Co. alleging that the defendants' bispecific monoclonal antibody, emicizumab, infringes on several patents.
  - **August 2017:** Genentech announced the FDA granted priority review for emicizumab for hemophilia A with inhibitors. The application was based on results from the HAVEN1 Phase 3 study and interim results from the HAVEN2 Phase 3 study. The FDA is expected to make a decision by February 2018.
- **Fiturisan:** In July 2017, Alnylam announced positive results from a Phase 2 clinical trial studying fiturisan, an investigational RNA interference (RNAi) agent that reduces levels of circulating antithrombin which promotes clotting function in people with hemophilia A or B.
- **Factor IX Gene Therapy:**
  - **December 2016:** At the American Society of Hematology annual meeting, an update with positive results was presented on the Phase 1/2 trial for SPK-9001, a gene therapy for factor IX deficiency.
  - **July 2017:** UniQure announced positive results in an update to an ongoing Phase 1/2 trial for AMT-060, a gene therapy for patients with severe hemophilia B.
- **Factor VIII Gene Therapy:**
  - **January 2017:** Sangamo announced the FDA has cleared the Investigational New Drug (IND) application for SB-525, a gene therapy for patients with hemophilia A.

- **July 2017:** BioMarin Pharmaceuticals announced positive results in an update to its open-label Phase 1/2 study of BMN 270, an investigational gene therapy treatment for severe hemophilia A. A Phase 3 study is expected to begin in the fourth quarter of 2017.

Guideline Update(s):

- **June 2016:** The Medical and Scientific Advisory Committee (MASAC) released a recommendation regarding the doses of clotting factor concentrate in the home. The recommendations included the following:
  - Patients should be able to refill their clotting factor prescription when the home supply reaches a one-week supply
  - Emergency doses should be in the home even for patients who require infrequent infusions
  - Patients using on-demand therapy should be allowed to have a monthly dispensing supply reflective of their bleeding history
  - Patients on prophylaxis therapy require extra doses at home to treat breakthrough bleeding episodes
  - Patients and families should track expiration dates monthly, and doses about to expire should be used first to prevent waste

Afstyla® [Antihemophilic Factor (Recombinant), Single Chain] Product Summary[15]

FDA Approval: May 2016

Indication(s): Afstyla® [antihemophilic factor (recombinant), single chain] is indicated in adults and children with hemophilia A (congenital factor VIII deficiency) for the following:

- On-demand treatment and control of bleeding episodes
- Routine prophylaxis to reduce the frequency of bleeding episodes
- Perioperative management of bleeding

Dosing: One unit of Afstyla® per kilogram (kg) of body weight will raise the factor VIII level by 2 IU/dL; therefore, the recommended dose is calculated by the following equation:

- Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL)
  - Example: 50kg x 40 IU/dL (%) x 0.5 IU/kg per IU/dL = 1,000 IU per dose
- <u>Bleeding Episodes/On-Demand Treatment:</u>
  - Minor bleeding episodes should be treated with 20% to 40% of normal every 12 to 24 hours until bleeding resolves
  - Moderate bleeding episodes should be treated with 30% to 60% of normal every 12 to 24 hours until bleeding resolves
  - Major bleeding episodes should be treated with 60% to 100% of normal every 8 to 24 hours until bleeding resolves
- <u>Routine Prophylaxis:</u>
  - Adults and adolescents (≥12 years): The recommended starting regimen is 20 to 50 IU per kg administered 2 to 3 times weekly
  - Children (<12 years): The recommended starting regimen is 30 to 50 IU per kg administered 2 to 3 times weekly; more frequent or higher doses may be required

in children younger than 12 years of age to account for the higher clearance in this age group

- Perioperative Management of Bleeding:
  - Minor procedures (e.g., tooth extractions) 30% to 60% of normal every 24 hours for at least 1 day until healing occurs
  - Major procedures (e.g., intra-abdominal, joint replacement) 80% to 100% of normal every 8 to 24 hours until adequate wound healing, then continue therapy for at least another 7 days to maintain a factor VIII activity of 30% to 60% of normal

Prolonged Half-Life: Afstyla® is a single-chain recombinant factor VIII, and is a construct where the B-domain occurring in wild type full-length factor VIII has been truncated. Afstyla® is expressed as a single-chain factor VIII molecule with covalent linkage between heavy and light chains; thereby keeping the molecule in the single chain form resulting in increased stability and increased von Willebrand Factor (VWF) affinity. Afstyla® has a half-life ranging from 10.2 to 14.3 hours depending on the age of the patient. Younger patients tend to have a shorter half-life for factor VIII as compared to their adult counterparts. Factor VIII has an average half-life of 12 hours.

Cost Comparison:

Factor Replacement Product	Cost per Unit*	Cost for 4 Weeks of Prophylaxis Therapy
Afstyla® [antihemophilic factor (recombinant), single chain]Ŧ	**$1.69**	**$50,700**
Advate® [antihemophilic factor (recombinant)]+	$1.52	$42,560

*Costs based on Wholesale Acquisition Cost (WAC) and do not reflect rebated prices or net costs.
ŦAfstyla® dosing using 50 IU/kg three times a week for a 50kg child.
+Advate® dosing using 40 IU/kg every other day for a 50kg child.

Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated] Product Summary[16]

FDA Approval: May 2017

Indication: Rebinyn® [coagulation factor IX (recombinant), glycoPEGylated] is indicated in adults and children with hemophilia B for the following:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

Dosing: One unit of Rebinyn® per kg of body weight will raise the factor IX level by 1% [IU/dL]; therefore, the following is an example of a how to calculate a dose:

- Example: 70kg x 30 IU/dL (%) x 1 IU/kg per IU/dL = 2,100 IU per dose
- Bleeding Episodes/On-Demand Treatment:
  - Minor-to-moderate bleeding episodes should be treated with 40% [IU/kg] of normal. A single dose should be sufficient for minor-to-moderate bleeds, but additional doses of 40 IU/kg can be given.
  - Major bleeding episodes should be treated with 80% [IU/kg] of normal. Additional doses of 40 IU/kg can be given.

- Perioperative Bleeding Management:
  - Minor procedures (e.g., skin biopsies, tooth extraction) should be treated with 40 IU/kg; a single pre-operative dose should be sufficient. Additional doses can be given if needed.
  - Major procedures (e.g., organ removal, body cavity entered) should be treated with 80 IU/kg; as clinically needed for the perioperative management of bleeding, repeated doses of 40 IU/kg (in 1 to 3 day intervals) within the first week after major surgery may be administered. Frequency may be extended to once weekly after the first week until bleeding stops and healing is achieved.

Prolonged Half-Life: Rebinyn® is a purified, recombinant, human factor IX (rFIX) with polyethylene-glycol (PEG) conjugated to the protein which slows down removal from the blood. Rebinyn® has a half-life ranging from 69.6 to 114.9 hours. Factor IX has an average half-life of 18 to 24 hours.

Cost: No cost information is currently available for Rebinyn®.

Recommendations

The Oklahoma Health Care Authority recommends the prior authorization of Afstyla® [antihemophilic factor (recombinant), single chain] and Rebinyn® [coagulation factor IX (recombinant), glycoPEGylated] with the following criteria:

Eloctate™, Adynovate®, Afstyla®, Alprolix®, Idelvion®, and Rebinyn® Approval Criteria:

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
   a. Hemophilia A: Advate® or current factor VIII replacement product; or
   b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of one year.

At this time the Oklahoma Health Care Authority does not recommend any changes to the current Standards of Care for pharmacies providing factor replacement products.

Utilization Details of Factor Replacement Products: Fiscal Year 2017

Pharmacy Claims: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
ADVATE PRODUCTS					
ADVATE INJ 1500UNIT	57	9	$1,338,179.26	$1,398.31	$23,476.83
ADVATE INJ 500UNIT	47	10	$581,249.60	$676.66	$12,367.01
ADVATE INJ 1000UNIT	36	9	$345,241.78	$928.07	$9,590.05
ADVATE INJ 2000UNIT	15	3	$288,878.72	$768.29	$19,258.58
ADVATE INJ 250UNIT	8	4	$30,931.26	$276.17	$3,866.41
SUBTOTAL	**163**	**18**	**$2,584,480.62**	**$965.80**	**$15,855.71**
KOGENATE PRODUCTS					
KOGENATE FS INJ 1000 UNIT	43	15	$936,846.43	$911.33	$21,787.13
KOGENATE FS INJ 2000 UNIT	43	10	$1,421,474.99	$1,278.30	$33,057.56
KOGENATE FS INJ 500 UNIT	41	14	$430,488.93	$505.27	$10,499.73
KOGENATE FS INJ 250 UNIT	8	5	$42,590.82	$211.89	$5,323.85
KOGENATE FS INJ 3000 UNIT	7	3	$323,745.46	$2,172.79	$46,249.35
KOGENATE FS INJ 500/BS	6	2	$38,695.11	$217.39	$6,449.19
KOGENATE FS INJ 2000/BS	5	2	$153,608.69	$1,066.73	$30,721.74
KOGENATE FS INJ 1000/BS	5	2	$72,628.35	$626.11	$14,525.67
SUBTOTAL	**158**	**19**	**$3,420,078.78**	**$904.78**	**$21,646.07**
FEIBA PRODUCTS					
FEIBA INJ 1750-3250 UNIT	22	3	$2,497,213.00	$8,160.83	$113,509.68
SUBTOTAL	**22**	**3**	**$2,497,213.00**	**$8,160.83**	**$113,509.68**
ELOCTATE PRODUCTS					
ELOCTATE INJ 1000 UNIT	19	3	$391,362.86	$1,078.13	$20,598.05
ELOCTATE INJ 2000 UNIT	13	1	$329,695.90	$5,072.24	$25,361.22
ELOCTATE INJ 500 UNIT	10	3	$99,142.99	$354.08	$9,914.30
ELOCTATE INJ 3000 UNIT	9	1	$323,619.69	$7,191.55	$35,957.74
ELOCTATE INJ 1500 UNIT	4	2	$123,172.98	$1,383.97	$30,793.25
ELOCTATE INJ 750 UNIT	4	2	$67,440.00	$602.14	$16,860.00
ELOCTATE INJ 250 UNIT	4	1	$15,213.96	$135.84	$3,803.49
SUBTOTAL	**63**	**4**	**$1,349,648.38**	**$1,266.09**	**$21,422.99**
WILATE PRODUCTS					
WILATE INJ 500-500 UNIT	17	2	$99,709.06	$280.08	$5,865.24
WILATE INJ 1000-1000 UNIT	10	2	$141,850.70	$497.72	$14,185.07
WILATE INJ 500-500 UNIT KIT	7	3	$63,006.20	$381.86	$9,000.89
WILATE INJ 1000-1000 UNIT KIT	5	3	$108,571.00	$804.23	$21,714.20
SUBTOTAL	**39**	**3**	**$413,136.96**	**$439.04**	**$10,593.26**
ALPROLIX PRODUCTS					
ALPROLIX INJ 2000 UNIT	16	2	$79,342.17	$187.13	$4,958.89
ALPROLIX INJ 1000 UNIT	14	2	$123,791.24	$365.17	$8,842.23
ALPROLIX INJ 500 UNIT	8	2	$72,268.39	$350.82	$9,033.55
ALPROLIX INJ 3000 UNIT	7	1	$281,775.77	$1,583.01	$40,253.68
ALPROLIX INJ 4000 UNIT	5	1	$131,298.58	$1,620.97	$26,259.72
SUBTOTAL	**50**	**3**	**$688,476.15**	**$560.65**	**$13,769.52**
HELIXATE PRODUCTS					
HELIXATE FS INJ 1000 UNIT	15	5	$246,130.10	$1,309.20	$16,408.67
HELIXATE FS INJ 500 UNIT	4	2	$58,775.17	$1,175.50	$14,693.79

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
HELIXATE FS INJ 3000 UNIT	1	1	$2,459.44	$2,459.44	$2,459.44
SUBTOTAL	**20**	**6**	**$307,364.71**	**$1,286.04**	**$15,368.24**
ALPHANATE PRODUCTS					
ALPHANATE INJ VWF/HUM 250 UNIT	12	3	$35,384.92	$124.59	$2,948.74
ALPHANATE INJ VWF/HUM 500 UNIT	11	2	$70,296.84	$250.17	$6,390.62
ALPHANATE INJ VWF/HUM 1000 UNIT	3	2	$19,260.05	$550.29	$6,420.02
SUBTOTAL	**26**	**4**	**$124,941.81**	**$208.24**	**$4,805.45**
XYNTHA PRODUCTS					
XYNTHA SOLOF INJ 2000 UNIT	11	1	$338,236.15	$1,162.32	$30,748.74
XYNTHA SOLOF INJ 1000 UNIT	1	1	$22,226.51	$793.80	$22,226.51
SUBTOTAL	**12**	**1**	**$360,462.66**	**$1,129.98**	**$30,038.56**
ADYNOVATE PRODUCTS					
ADYNOVATE INJ 2000 UNIT	10	1	$123,608.96	$420.44	$12,360.90
ADYNOVATE INJ 1000 UNIT	10	1	$98,256.72	$350.92	$9,825.67
ADYNOVATE INJ 500 UNIT	9	1	$43,401.76	$172.23	$4,822.42
ADYNOVATE INJ 250 UNIT	1	1	$1,264.94	$45.18	$1,264.94
SUBTOTAL	**30**	**1**	**$266,532.38**	**$312.10**	**$8,884.41**
NUWIQ PRODUCTS					
NUWIQ KIT 1000 UNIT	6	1	$96,220.45	$1,069.12	$16,036.74
NUWIQ KIT 500 UNIT	4	1	$54,383.38	$906.39	$13,595.85
NUWIQ KIT 250 UNIT	2	1	$7,940.00	$264.67	$3,970.00
NUWIQ KIT 2000 UNIT	1	1	$11,831.95	$2,366.39	$11,831.95
SUBTOTAL	**13**	**2**	**$170,375.78**	**$920.95**	**$13,105.83**
MONOCLATE PRODUCTS					
MONOCLATE-P INJ 1500 UNIT	5	1	$75,868.75	$1,517.38	$15,173.75
MONOCLATE-P INJ 1000 UNIT	3	1	$36,948.04	$1,944.63	$12,316.01
SUBTOTAL	**8**	**2**	**$112,816.79**	**$1,635.03**	**$14,102.10**
HUMATE PRODUCTS					
HUMATE-P SOL 250-600 UNIT	5	2	$5,017.34	$627.17	$1,003.47
HUMATE-P SOL 500-1200 UNIT	3	1	$5,838.92	$1,167.78	$1,946.31
SUBTOTAL	**8**	**2**	**$10,856.26**	**$835.10**	**$1,357.03**
RIXUBIS PRODUCTS					
RIXUBIS INJ 1000 UNIT	4	4	$8,900.07	$1,483.35	$2,225.02
RIXUBIS INJ 2000 UNIT	2	2	$4,937.24	$1,645.75	$2,468.62
RIXUBIS INJ 3000 UNIT	1	1	$3,805.66	$3,805.66	$3,805.66
RIXUBIS INJ 500 UNIT	1	1	$2,584.46	$1,292.23	$2,584.46
SUBTOTAL	**8**	**6**	**$20,227.43**	**$1,685.62**	**$2,528.43**
NOVOSEVEN PRODUCTS					
NOVOSEVEN RT INJ 8MG	4	1	$918,148.30	$15,302.47	$229,537.08
NOVOSEVEN RT INJ 2MG	3	2	$91,612.70	$9,161.27	$30,537.57
NOVOSEVEN RT INJ 5MG	1	1	$190,299.60	$6,796.41	$190,299.60
SUBTOTAL	**8**	**4**	**$1,200,060.60**	**$12,245.52**	**$150,007.58**
BENEFIX PRODUCTS					
BENEFIX INJ 2000 UNIT	4	3	$19,937.97	$2,848.28	$4,984.49
BENEFIX INJ 1000 UNIT	3	2	$2,064.82	$64.53	$688.27
BENEFIX INJ 3000 UNIT	1	1	$27,383.15	$9,127.72	$27,383.15
SUBTOTAL	**8**	**4**	**$49,385.94**	**$1,175.86**	**$6,173.24**
KOVALTRY PRODUCTS					
KOVALTRY INJ 1000 UNIT	3	1	$30,198.62	$1,312.98	$10,066.21

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
SUBTOTAL	**3**	**1**	**$30,198.62**	**$1,312.98**	**$10,066.21**
IDELVION PRODUCTS					
IDELVION SOL 1000 UNIT	2	1	$38,608.50	$19,304.25	$19,304.25
IDELVION SOL 2000 UNIT	1	1	$16,605.50	$16,605.50	$16,605.50
SUBTOTAL	**3**	**1**	**$55,214.00**	**$18,404.67**	**$18,404.67**
VONVENDI PRODUCTS					
VONVENDI INJ 1300UNIT	1	1	$5,510.95	$5,510.95	$5,510.95
SUBTOTAL	**1**	**1**	**$5,510.95**	**$5,510.95**	**$5,510.95**
TOTAL	**643**	**73***	**$13,666,981.82**	**$1,097.31**	**$21,255.03**

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

Medical Claims: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J7187 VON WILLEBRAND FACTOR COMPLEX	10	3	$24,624.46	$2,462.45
J7189 FACTOR VIIA RECOMBINANT	65	2	$1,287,871.74	$19,813.41
J7192 FACTOR VII RECOMBINANT	5	3	$17,306.40	$3,461.28
J7195 FACTOR IX RECOMBINANT	1	1	$1,396.75	$1,396.75
J7198 ANTI-INHIBITOR	9	1	$51,243.00	$5,693.67
TOTAL	**36+**	**9***	**$1,430,098.34**	**$39,724.95**

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

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Appendix M

Fiscal Year 2017 Annual Review of Growth Hormone

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

Growth Hormone Products	
Tier-1*	**Tier-2**
Genotropin® (Pfizer) - Cartridge, MiniQuick	**Humatrope®** (Eli Lilly) - Vials, Cartridge Kits
	Norditropin® (NovoNordisk) - FlexPro® Pens
	Nutropin® and Nutropin AQ® (Genentech) - Vials, Pen Cartridge, NuSpin®
	Omnitrope® (Sandoz) - Vials, Cartridge
	Saizen® (EMD Serono) - Vials, click.easy®
	Serostim® (EMD Serono) - Vials
	Zomacton™ and Zoma-Jet™ (Ferring) - Vials, Injection Device
	Zorbtive® (EMD Serono) - Vials

*Supplementally rebated product(s); tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Cost (NADAC), or Wholesale Acquisition Cost (WAC) if NADAC unavailable.
(All products contain the identical 191 amino acid sequence found in pituitary-derived human growth hormone [hGH].)

Growth Hormone Covered Indications *(prior to epiphyseal closure)*:

1. Classic human growth hormone (hGH) deficiency as determined by childhood hGH stimulation tests
2. Panhypopituitarism with history of pituitary or hypothalamic injury due to tumor, trauma, surgery, whole brain radiation, irradiation, hemorrhage or infarction, or a congenital anomaly, and one of the following:
    a. Deficiency of three or more pituitary hormones and insulin-like growth factor (IGF)-1 greater than or equal to 2.5 standard deviations (SD) below the mean for the member's age and gender; or
    b. No deficiency or deficiency in less than three pituitary hormones and IGF-1 less than 50th percentile and failure of a growth hormone stimulation test
3. Panhypopituitarism in children with height greater than or equal to 2.25 SD below the mean for age and gender and MRI evidence of pituitary stalk agenesis, empty sella, or ectopic posterior pituitary "bright spot"
4. Short stature associated with Prader-Willi Syndrome
5. Short stature associated with Noonan Syndrome
6. Short stature associated with chronic renal insufficiency (pre-transplantation)
7. History of intrauterine growth restriction who have not reached a normal height (greater than or equal to 2.25 SD below the mean for age and gender) by age two years
8. Idiopathic short stature (ISS) who are greater than or equal to 2.25 SD below the mean for height (based on age and gender) and are unlikely to catch up in height
9. Turner syndrome or 45X, 46XY mosaicism
10. Hypoglycemia with evidence for hGH deficiency

11. Short-stature homeobox-containing gene (SHOX) deficiency with genetic evidence for SHOX deficiency
12. Other evidence for hGH deficiency submitted for panel review and decision

Growth Hormone Tier-2 Approval Criteria:

1. Documented allergic reaction to non-active components of all available Tier-1 medications; or
2. A clinical exception applies to members with a diagnosis of acquired immunodeficiency syndrome (AIDS) wasting syndrome, in which case Serostim® can be used, regardless of its current Tier status.

Discontinuation of Therapy or Transition to Adult Therapy Criteria:

1. Failure to show improvement in height percentile on growth chart after one year of treatment; or
2. Growth velocity less than 2.5cm/year unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism); or
3. Epiphyseal closure; or
4. Covered height has been reached:
    a. 152.4cm (60 inches) for girls; or
    b. 165.1cm (65 inches) for boys; or
5. Inadequate compliance; or
6. Significant adverse effects.

Insulin-Like Growth Factor-1 (IGF-1) Analog Medications: Increlex® and Iplex™ (Mecasermin [rDNA Origin] Injection) Approval Criteria:

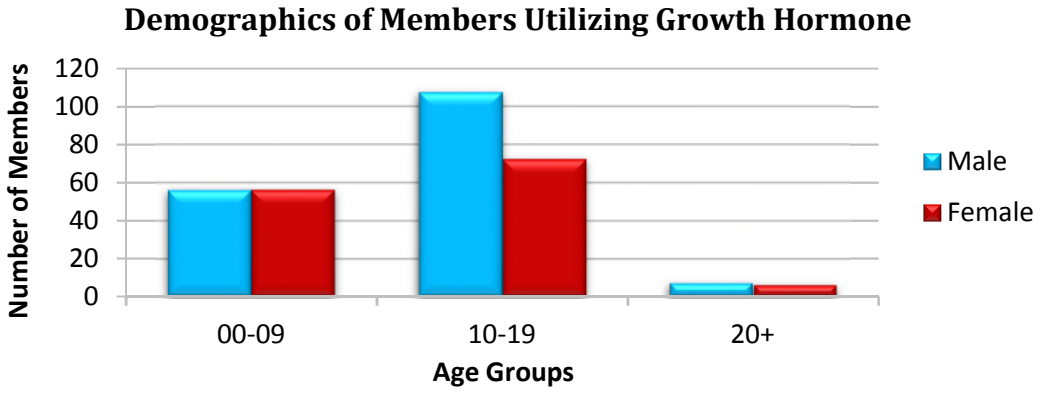
1. Therapy initiated by an endocrinologist; and
2. Diagnosis of Primary IGF-1 Deficiency with all of the following:
    a. Height greater than 3 standard deviations (SD) below the mean; and
    b. Basal IGF-1 greater than 3 SD below the mean; and
    c. Normal or elevated growth hormone (GH); and
3. Documentation of mutation in GH receptor (GHR) or mutation in post-GHR signaling pathway or IGF-1 gene defects (Laron Syndrome); and
4. IGF-1 analog medications will not be approved for use in secondary IGF-1 deficiencies related to GH deficiency, malnutrition, hypothyroidism, or chronic steroid therapy.

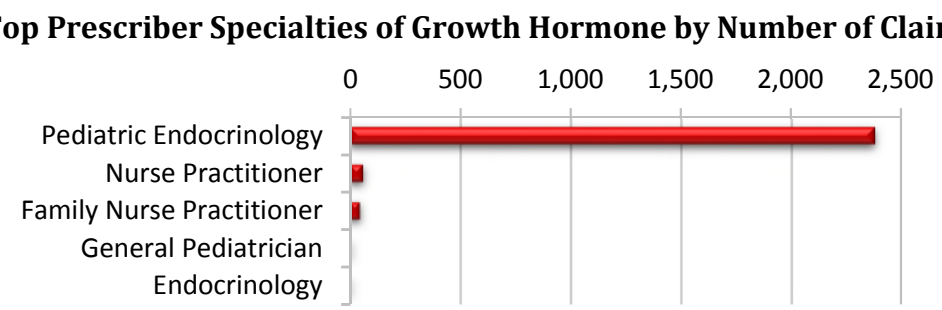
Utilization of Growth Hormone: Fiscal Year 2017

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost per Claim	Cost per Day	Total Units	Total Days
2016	272	2,326	$7,845,771.75	$3,373.07	$116.33	30,533	67,442
2017	301	2,503	$8,298,035.95	$3,315.24	$116.66	34,723	71,129
% Change	**10.70%**	**7.60%**	**5.80%**	**-1.70%**	**0.30%**	**13.70%**	**5.50%**
Change	**29**	**177**	**$452,264.20**	**-$57.83**	**$0.33**	**4,190**	**3,687**

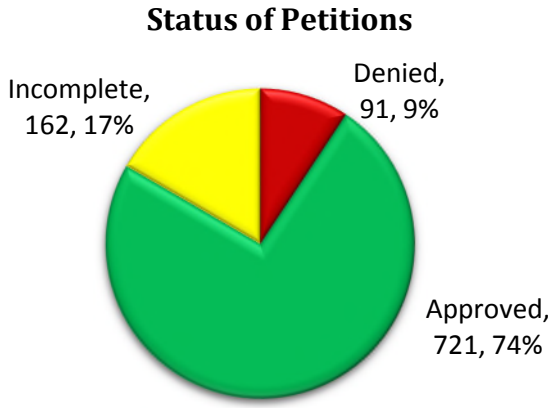
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
There was no utilization of insulin-like growth factor-1 (IGF-1) analog medications during fiscal year 2016 or 2017.





Prior Authorization of Growth Hormone

There were 974 prior authorization requests submitted for growth hormone during fiscal year 2017. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expiration(s):

- Norditropin® [somatropin (rDNA origin) for injection]: September 2027

Guideline Update(s):

- **November 2016:** The Pediatric Endocrine Society released updated guidelines for growth hormone (GH) and insulin-like growth factor-1 (IGF-1) treatment in children and adolescents with growth hormone deficiency (GHD), idiopathic short stature (ISS), and primary IGF-1 deficiency (PIGFD). This is the first update released since 2003. The authors stressed that in many instances, careful review of the published evidence

"revealed a paucity of evidence and highlighted areas that need further research." Recommendations include testing and diagnosis, shared decision making, counseling of risks, counseling of limited long-term safety data, and prescribers with expertise involvement. Select recommendations from the guidelines related to SoonerCare criteria include the following:

- For GH initiation after completion of tumor therapy with no evidence of ongoing tumor, a standard waiting period of 12 months to establish "successful therapy" of the primary lesion is reasonable (ungraded good practice statement). Although many of the intracranial tumors are not "malignant" (i.e., craniopharyngioma), they have the potential to recur. There are no data to suggest treating them differently than malignant tumors with regard to observation periods before initiation of GH treatment.
- Suggested sex steroid priming prior to provocative GH testing in prepubertal boys older than 11 years and in prepubertal girls older than 10 years with adult height prognosis within -2 Standard Deviations (SD) from the mean in order to prevent unnecessary GH treatment of children with constitutional delay of growth and puberty (conditional recommendation, low quality of evidence).
    - Boys can be primed with intramuscular testosterone (50mg to 100mg of depot formulation administered 1 week before the test).

Specialist(s) Input:

- The Oklahoma Health Care Authority (OHCA) and the College of Pharmacy actively seek specialist(s) input in updating and maintaining prior authorization criteria. Several pediatric endocrinologists in the state consulted with the OHCA to update the current SoonerCare GH criteria to reflect guideline recommendations and best practices. The specialists made the following recommendations:
    - Modify the growth velocity criteria from requiring a standard less than 5cm/year for most covered diagnoses to instead requiring less than 10% on a growth velocity curve for gender and age.
    - Be able to start GH for members with secondary panhypopituitarism due to tumor, trauma, or surgery once it has been determined the member will not start re-growing on their own.
    - Allow for testosterone prepubertal priming for boys prior to GH stimulation testing.
- A review of submitted prior authorization requests during fiscal year 2017 based on the specialist(s) recommendations determined these recommendations to be budget neutral.

Pipeline:

- **March 2017:** Novo Nordisk commenced a Phase 3 trial to evaluate a once-weekly formulation of somapacitan in adult growth hormone deficient patients, using Norditropin® as a comparator. Results are expected in the fall of 2018.

Recommendations

The College of Pharmacy recommends the following changes to the growth hormone prior authorization criteria based on specialist(s) input and guideline recommendations:

1. Modify the growth velocity criteria from requiring a standard less than 5cm/year for most covered diagnoses to instead requiring less than 10% on a growth velocity curve for gender and age.
2. Authorize reimbursement of growth hormone therapy for members with secondary panhypopituitarism due to tumor, trauma, or surgery 12 months post trauma or surgery if no evidence of tumor recurrence and growth has not restarted. The member must still meet all the other criteria; authorization would not require height greater than 2.25 SD below the mean for age in these circumstances.
3. Allow for one-time testosterone prepubertal priming for boys prior to growth hormone stimulation testing.

Utilization Details of Growth Hormone: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS						
GENOTROPIN PRODUCTS						
GENOTROPIN INJ 5MG	1,104	138	$3,083,423.41	8	$96.92	$2,792.96
GENOTROPIN INJ 12MG	316	46	$1,888,456.70	6.87	$211.40	$5,976.13
GENOTROPIN INJ 0.8MG	184	26	$480,886.70	7.08	$93.41	$2,613.51
GENOTROPIN INJ 0.6MG	149	26	$290,114.13	5.73	$68.86	$1,947.07
GENOTROPIN INJ 1MG	140	18	$478,893.89	7.78	$121.55	$3,420.67
GENOTROPIN INJ 0.4MG	124	19	$150,369.59	6.53	$43.21	$1,212.66
GENOTROPIN INJ 1.4MG	90	19	$414,331.43	4.74	$164.42	$4,603.68
GENOTROPIN INJ 0.2MG	80	14	$51,752.72	5.71	$23.10	$646.91
GENOTROPIN INJ 2MG	74	14	$497,471.35	5.29	$244.46	$6,722.59
GENOTROPIN INJ 1.2MG	61	14	$224,807.79	4.36	$131.62	$3,685.37
GENOTROPIN INJ 1.6MG	59	13	$319,134.27	4.54	$192.71	$5,409.06
GENOTROPIN INJ 1.8MG	44	11	$270,260.20	4	$218.66	$6,142.28
TIER-1 SUBTOTAL	**2,425**	**287**	**$8,149,902.18**	**8.45**	**$118.25**	**$3,360.78**
TIER-2 PRODUCTS+						
NORDITROPIN PRODUCTS						
NORDITROPIN INJ 10/1.5ML	19	3	$59,101.66	6.33	$119.16	$3,110.61
NORDITROPIN INJ 5/1.5ML	19	4	$9,487.65	4.75	$19.60	$499.35
NORDITROPIN INJ 15/1.5ML	11	2	$64,626.16	5.5	$238.47	$5,875.11
SUBTOTAL	**49**	**9**	**$133,215.47**	**5.44**	**$106.49**	**$2,718.68**
OMNITROPE PRODUCTS						
OMNITROPE INJ 5/1.5ML	21	3	$5,383.68	7	$8.85	$256.37
OMNITROPE INJ 5.8MG	2	1	$2,389.12	2	$45.08	$1,194.56
SUBTOTAL	**23**	**4**	**$7,772.80**	**5.75**	**$11.76**	**$337.95**
HUMATROPE PRODUCTS						
HUMATROPE INJ 12MG	5	3	$7,145.50	1.67	$27.07	$1,429.10
HUMATROPE INJ 24MG	1	1	$0.00	1	$0.00	$0.00

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
SUBTOTAL	6	4	$7,145.50	1.5	$24.22	$1,190.92
TIER-2 SUBTOTAL	78	16	$148,133.77	4.88	$67.12	$1,899.15
TOTAL	2,503	301*	$8,298,035.95	8.32	$116.66	$3,315.24

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
+Claims for Tier-2 products largely consist of claims for which SoonerCare is not the primary payer and therefore the reimbursed amount is not a true reflection of the cost of the medication.

[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 06/2017. Last accessed 07/31/2017.

[2] Grimberg A, DiVall SA, Polychronakos C, et al; on behalf of the Drug and Therapeutics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. *Horm Res Paediatr* 2016; 86:361–397.

[3] Pediatric Endocrine Society Provides Guidance for Growth Hormone Use in Pediatric Patients. *Endocrinology Advisor*. Available online at: http://www.endocrinologyadvisor.com/adrenal/growth-hormone-use-in-pediatric-patients/article/634909/. Issued 02/01/2017. Last accessed 07/31/2017.

[4] Children's Hospital of Philadelphia. When should doctors treat short children and teens with growth hormone? Endocrinologists issue new clinical guidelines for managing, treating children with growth failure. *ScienceDaily*. Available online at: www.sciencedaily.com/releases/2017/01/170125092600.htm. Issued 01/25/2017. Last accessed 07/31/2017.

[5] Pharmaceutical-Technology.com. Novo Nordisk's long-acting growth hormone somapacitan likely to conquer the adult GHD market in Japan. Available online at: http://www.pharmaceutical-technology.com/comment/commentnovo-nordisks-long-acting-growth-hormone-somapacitan-likely-to-conquer-the-adult-ghd-market-in-japan-5773191/. Issued 03/28/2017. Last accessed 08/16/2017.

Appendix N

Fiscal Year 2017 Annual Review of Synagis® (Palivizumab)

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

A prior authorization is required for all members who receive palivizumab in an outpatient setting. Palivizumab is approved for members who meet the established prior authorization criteria which is based on a modified version of the American Academy of Pediatrics (AAP) 2014 guidelines.

Synagis® (Palivizumab) Approval Criteria:

A. Member Selection:
   1. Infants less than 12 months of age at the start of respiratory syncytial virus (RSV) season:
      a. Born before 29 weeks, 0 days gestation; or
      b. Born before 32 weeks, 0 days gestation and develop chronic lung disease (CLD) of prematurity (require >21% oxygen supplementation for at least 28 days after birth); or
      c. Have hemodynamically significant congenital heart disease (acyanotic heart disease and receiving medication to control Congestive Heart Failure (CHF) and will require surgical procedures, or moderate-to-severe pulmonary hypertension); or
      d. May be considered for:
         i. Infants with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough
         ii. Infants who undergo cardiac transplantation during RSV season
         iii. Infants who are profoundly immunocompromised during RSV season
         iv. Infants with cystic fibrosis with clinical evidence of CLD and/or nutritionally compromised
   2. Infants 12 to 24 months of age at the start of RSV season:
      a. Born before 32 weeks, 0 days gestation and have CLD of prematurity (required at least 28 days of oxygen after birth) and continue to require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6 months before the start of the RSV season

B. Length of Treatment: Palivizumab is approved for use only during RSV season. Approval dates will be November 1st through March 31st.

C. Units Authorized: The maximum duration of therapy is five (5) doses, with a dose to be administered no more often than every 30 days. Members given doses more frequently than every 30 days will not be authorized for additional doses. Doses administered prior to the member's discharge from a hospital will be counted as one of the approved total.

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

Utilization of Synagis® (Palivizumab): Fiscal Year 2017

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	245	1,113	$2,543,042.20	$2,284.85	$76.16	945	33,391
2017	281	1,224	$2,786,474.72	$2,276.53	$75.89	1,046	36,716
% Change	**14.70%**	**10.00%**	**9.60%**	**-0.40%**	**-0.40%**	**10.70%**	**10.00%**
Change	**36**	**111**	**$243,432.52**	**-$8.32**	**-$0.27**	**101**	**3,325**

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

Pharmacy Claim Details for Respiratory Syncytial Virus (RSV) Season 2016-2017

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Cost/ Day	Cost/ Claim
SYNAGIS INJ 100MG/ML	815	259	$2,214,844.13	3.15	$90.60	$2,717.60
SYNAGIS INJ 50MG/0.5ML	409	193	$571,630.59	2.12	$46.59	$1,397.63
Total	**1,224**	**281***	**$2,786,474.72**	**4.36**	**$75.89**	**$2,276.53**

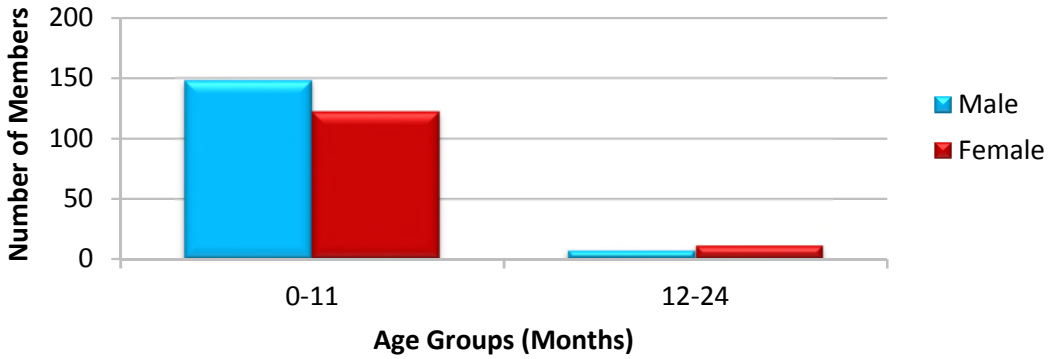
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Cost per Vial

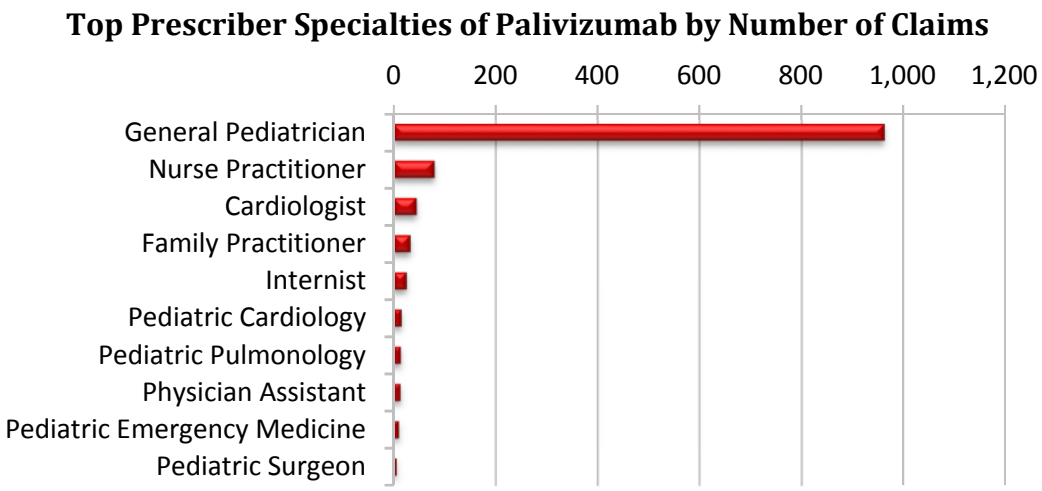
Vial Size	Cost per Vial
Synagis® (palivizumab) 100mg/mL vial	$2,697.32
Synagis® (palivizumab) 50mg/mL vial	$1,428.32

Costs do not reflect rebated prices or net costs.
Costs based on state maximum allowable cost (SMAC).

Demographics of Members Utilizing Palivizumab

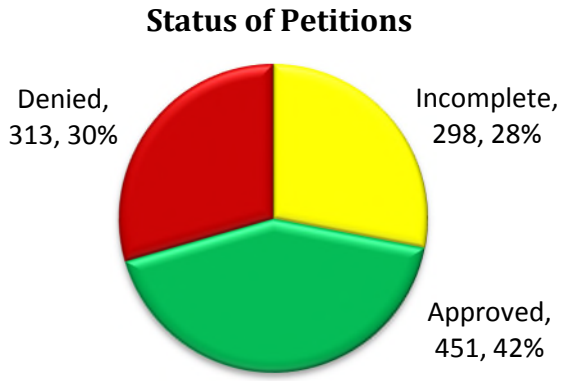


Both age groups saw an increase in utilization compared to the 2015 to 2016 respiratory syncytial virus (RSV) season. The 0 to 11 month age group saw a 10.20% increase in utilization, and the 12 to 24 month age group saw a 125.00% increase in utilization.

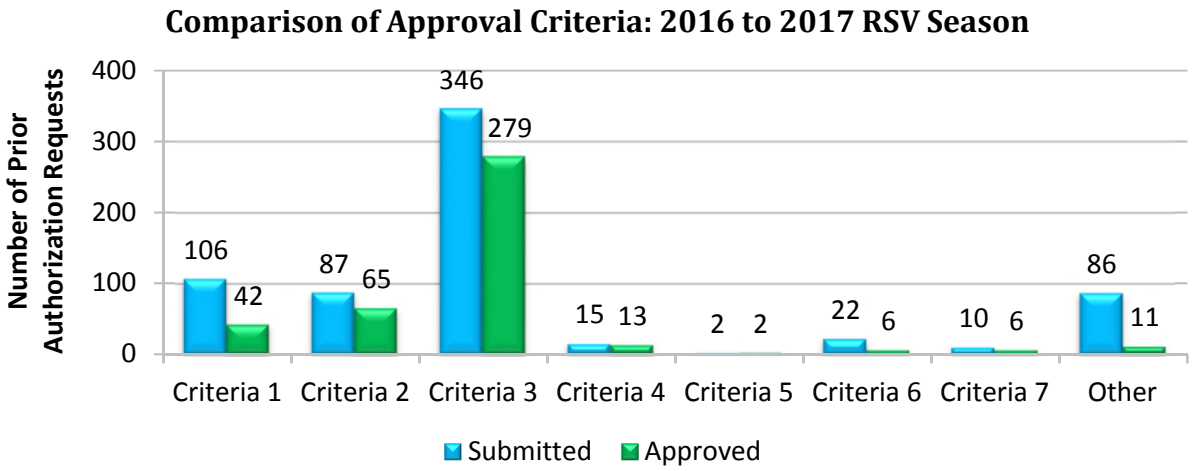


Prior Authorization of Synagis® (Palivizumab)

There were 1,062 palivizumab prior authorization requests submitted for 521 unique members during fiscal year 2017. This is a decrease in both submitted petitions and number of members requesting palivizumab compared to fiscal year 2016 when there were 1,110 palivizumab prior authorization requests submitted for 571 unique members. The following chart shows the status of the submitted petitions for fiscal year 2017.



The following graph shows the number of submissions and approvals for each prior authorization criteria. The graph is followed by a numbered list in which the list number corresponds to the criteria number in the graph. The most commonly requested and approved criteria selection during the 2016 to 2017 RSV season was criteria number three: infants born before 29 weeks, 0 days gestation. Infants born before 32 weeks, 0 days gestation and who had CLD of prematurity was also a commonly requested and approved criteria selection.



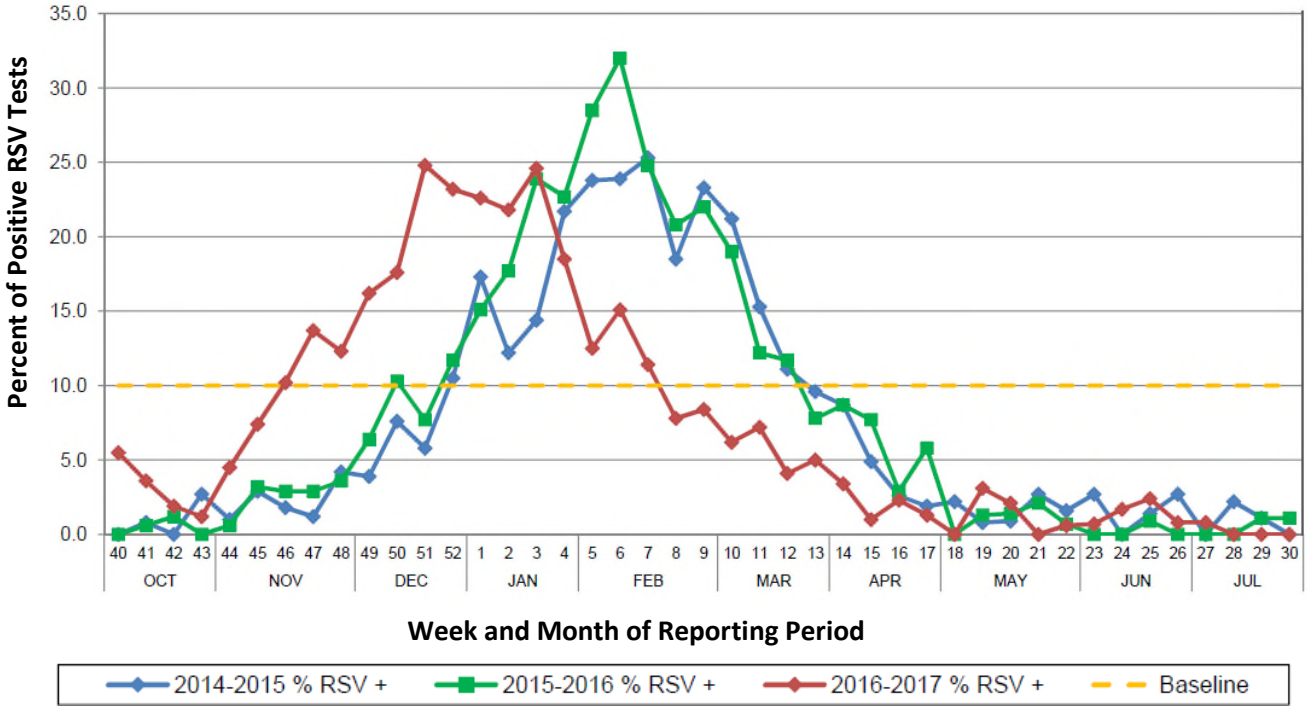
Criteria List:

1. Infants 0 to 24 months old at the start of RSV season born before 32 weeks, 0 days gestation and have CLD of prematurity.
2. Infants who have hemodynamically significant congenital heart disease and will require surgical procedures, or moderate-to-severe pulmonary hypertension.
3. Infants born before 29 weeks, 0 days gestation.
4. Infants with neuromuscular disease or congenital anomaly that impairs the ability to clear secretions from the upper airway because of ineffective cough.
5. Infants who undergo cardiac transplantation during RSV season.
6. Infants who are profoundly immunocompromised during RSV season.
7. Infants with cystic fibrosis with clinical evidence of CLD and/or nutritionally compromised.

Season Comparison[1,2,3]

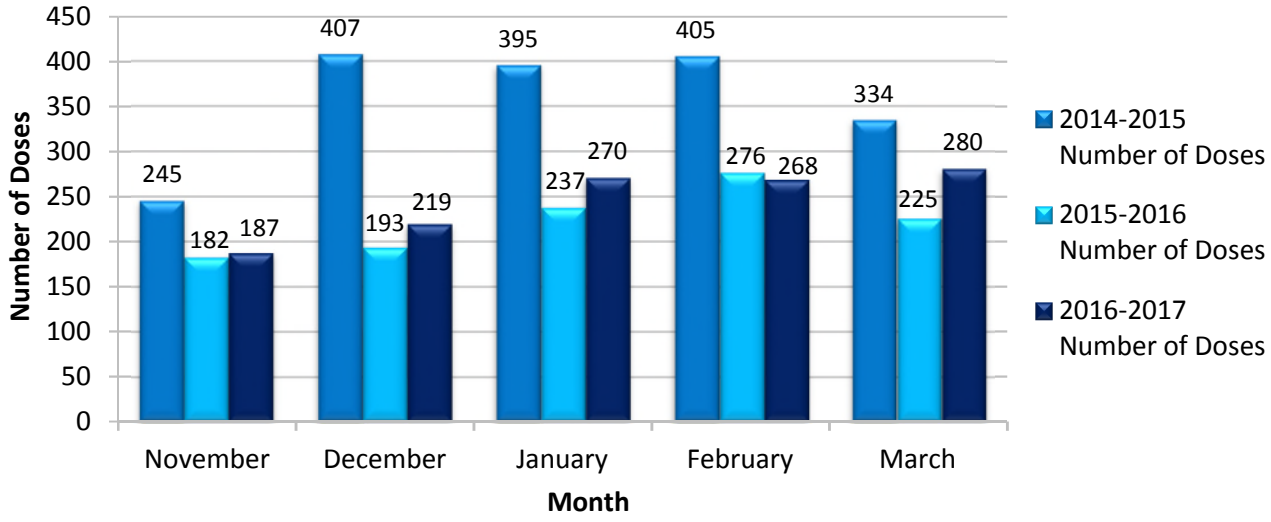
The following chart contains the weekly percent of laboratory positive RSV tests in Oklahoma as reported by the Oklahoma State Department of Health (OSDH) Viral Respiratory Illness Sentinel Surveillance System. The chart is included to compare RSV seasons since 2014. RSV is determined to be in season once the percent of positive tests is greater than 10% for two consecutive weeks. Similarly, the season is determined to be at an end when the percent of positive tests is below 10% for two consecutive weeks. RSV seasons appear to be similar with a peak typically in January or February and a season end by late March. Palivizumab prior authorization approvals are initiated with a start date of November 1st and continue to March 31st; this approval window corresponds to the following state monitoring graph as well as with state data reported by the Centers for Disease Control and Prevention (CDC). For the 2016-2017 RSV season for Oklahoma, the CDC determined the onset week was the week of December 3rd with a season offset the week of March 11th.

Weekly Percent of Sentinel Laboratory Positive RSV Tests 2014-2017



The following bar graph shows the number of palivizumab doses paid for by SoonerCare for each month during the last three seasons. In 2015, SoonerCare adopted the Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection released by the American Academy of Pediatrics (AAP). The guidance, which was released in 2014, urged more limited use than previously recommended in children born after 29 weeks gestation or those in the second year of life. Many hospitals across the state updated their protocols at that time resulting in fewer doses dispensed in the 2014 season as well as in the 2015 season when SoonerCare adopted the updated guidance.

Doses Dispensed Each Month



Market News and Updates[4,5]

Pipeline News:

- **September 2016:** Novavax announced that its RSV F-protein vaccine candidate failed to meet its primary endpoint of preventing moderate-to-severe RSV-associated lower respiratory tract disease and secondary endpoint of reducing the incidence of all symptomatic respiratory disease due to RSV in a Phase 3 trial of 11,856 adults 60 years of age and older.
- **August 2017:** Regeneron Pharmaceuticals announced it was stopping development of suptavumab, an investigational antibody, after it failed to reduce RSV infections in healthy pre-term infants in a Phase 3 trial.

Recent Publication(s):

- A compilation of recent palivizumab and RSV publications will be presented at the Drug Utilization Review (DUR) meeting.

Recommendations

The College of Pharmacy does not recommend any changes to the current Synagis® (palivizumab) criteria at this time.

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[1] Oklahoma State Department of Health. Weekly Percent of Sentinel Laboratory Positive RSV Tests, Oklahoma Viral Respiratory Illness Sentinel Surveillance System, 2014-2017: Week ending July 19, 2017. Available online at: https://www.ok.gov/health2/documents/RSV2011-12andPast2Seasons-10-06-2012.pdf. Last revised 08/03/2017. Last accessed 08/08/2017.

[2] Centers for Disease Control and Prevention (CDC). RSV State Trends. Available online at: https://www.cdc.gov/surveillance/nrevss/rsv/state.html#OK. Last accessed 08/08/2017.

[3] Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. RSV Policy Statement —Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics.* 2014; 134 (2):415–420.

[4] Genetic Engineering and Biotechnology News. Novavax RSV F Vaccine Fails Phase III Trial. *GEN.* Issued 09/16/2016. Last accessed 08/08/2017.

[5] Carroll J. In a rare misfire, Regeneron scraps its RSV drug after a PhIII failure. Available online at: https://endpts.com/in-a-rare-misfire-regeneron-scraps-its-rsv-drug-after-a-phiii-failure/. Issued 08/14/2017. Last accessed 08/16/2017.

Appendix O

30-Day Notice to Prior Authorize Endari™ (L-Glutamine)

Oklahoma Health Care Authority
September 2017

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

Sickle cell disease (SCD) is an inherited blood disorder that causes red blood cells (RBCs) to be abnormally shaped. It is one of the most common genetic disorders in the world. It is estimated that between 80,000 and 100,000 Americans are affected by SCD. This disorder mainly affects individuals of African, Mediterranean, and Asian descent. Patients with SCD have sickle-shaped RBCs which are not flexible and can stick to vessel walls, causing a blockage that can slow or stop the flow of blood and cause pain and organ damage.

SCD is inherited in an autosomal recessive pattern. If a person only inherits one copy of the sickle cell gene he or she will have sickle cell trait. People who have sickle cell trait do not have the disease; however, like people who have SCD, they can pass the gene on to their children. SCD is caused by mutations in the *HBB* gene. The *HBB* gene is responsible for providing instructions for making beta-globin. At least one of the beta-globin subunits in hemoglobin is replaced with hemoglobin S in patients with SCD. In a common form of SCD, sickle cell anemia, hemoglobin S replaces both beta-globin subunits in hemoglobin. In other types of SCD, hemoglobin S only replaces one beta-globin subunit in hemoglobin. The other beta-globin subunit is replaced with a different abnormal variant. *HBB* mutations can also cause unusually low levels of beta-globin and this abnormality is referred to as beta thalassemia.

At birth, high levels of fetal hemoglobin help to ward off symptoms. In the first few months after birth, fetal hemoglobin levels begin to decrease and sickle hemoglobin becomes the predominant hemoglobin present in RBCs. Patients with SCD are at risk for clots due to alterations in platelet function, RBCs, and the coagulation cascade. The acute and chronic complications of SCD are due to the blockage of small blood vessels, tissue damage, and organ impairment. Patients with SCD are at risk for complications such as stroke, myocardial infarction, acute and chronic pain, acute chest syndrome, chronic lung disease, infection, and renal impairment. Patients with sickle cell have poorly functioning spleens or are asplenic, and are considered immunocompromised. Patients with SCD are at an increased risk of bacterial infections and at high risk for sepsis and meningitis. In the United States, the average life expectancy for patients with SCD is approximately 40 to 60 years.

Hematopoietic cell transplantation is a potentially curative treatment for SCD; however, its use it limited by concerns for transplant-related toxicities and lack of donors. Disease-modifying therapies, such as hydroxyurea and blood transfusions, can reduce or prevent many of the complications of SCD. The current mainstay of SCD management is hydroxyurea which helps to improve blood flow, reduces the likelihood that RBCs will stick, and increases fetal hemoglobin. It can take up to six months to be effective and not all patients will respond to therapy with hydroxyurea. Long-term daily hydroxyurea can reduce the rate of stroke, acute pain episodes,

need for transfusions, and hospitalizations by as much as 40%. It may also help to reduce mortality and preserve spleen and kidney function in patients over nine months of age. Blood transfusions can be used as a source of normal hemoglobin for patients with SCD. Providing a source of normal hemoglobin helps to lower the percentage of circulating RBCs that are sickled and helps to reduce the vascular changes and clotting associated with sickled hemoglobin. Transfusions carry a greater risk than hydroxyurea as patients can develop hemolysis, iron overload, antibodies to donor blood, or blood that is too viscous. The success of future transfusions can be limited by developing antibodies. In patients who develop iron overload, chelation therapy such as deferoxamine or deferasirox may be necessary. It is recommended to consult a hematologist and SCD expert prior to beginning long-term transfusions. In July 2017, the U.S. Food and Drug Administration (FDA) approved Endari™ (L-glutamine oral powder) for the treatment of patients 5 years of age and older with SCD to reduce severe complications associated with the disease. This is the first new treatment for SCD approved by the FDA in nearly 20 years. The medication was granted orphan drug designation.

Market News and Updates[7,8]

Pipeline:

- **Crizanlizumab:** Results of the Phase 3 SUSTAIN trial were presented at the American Society of Hematology 58th Annual Meeting and were also published in *The New England Journal of Medicine*. Results of the trial show crizanlizumab, a humanized antibody against P-selectin, reduced the frequency of pain crises by nearly half compared to placebo. The median times to first and second crises were also 2 to 3 times as long compared with placebo. The trial included 198 patients with SCD randomized to 2.5 or 5mg/kg crizanlizumab or placebo and the primary endpoint was the annual rate of sickle cell related pain crises (SCPC) in the 5mg/kg group compared to placebo. The median rate of SCPC per year in the 5mg/kg arm was 1.63 (p=0.01) compared to 2.01 in the 2.5mg/kg arm (p=0.18) and 2.98 in the placebo group. The median time to first crisis was significantly longer for patients in the 5mg/kg arm than with placebo (4.1 vs 1.4 months [p=0.001]). The SUSTAIN trial was not designed to determine if there was a survival benefit and a longer-term follow-up is needed to establish that endpoint.

Other News:

- **March 2017:** According to a report published in *The New England Journal of Medicine*, gene therapy that delivered an antisickling variant of hemoglobin in an autologous hematopoietic stem cell transplant ameliorated symptoms of severe SCD in a 15-year-old boy. A lentiviral vector bearing an antisickling variant of hemoglobin A (HbA) was introduced into the patient when he was 13 years old. The researchers stated the patient “had complete clinical remission with correction of hemolysis and biologic hallmarks of the disease.” At 12 months posttransplant, the proportion of sickled cells in the patient and his oxygen saturation level were similar to those of his mother, a heterozygote.

Endari™ (L-Glutamine) Product Summary[9]

Indication(s): Endari™ (L-glutamine oral powder) is an amino acid indicated to reduce the acute complications of sickle cell disease (SCD) in adult and pediatric patients 5 years of age and older.

Dosing:

- Endari™ is supplied in paper-foil-plastic laminate packets containing 5 grams of L-glutamine powder.
- The recommended dose is 5 grams to 15 grams orally, twice daily based on body weight. Please refer to the full prescribing information for detailed information regarding recommended dosing.
- Each dose of Endari™ should be mixed in 8 oz. of cold or room temperature beverage or 4 oz. to 6 oz. of food before ingestion.

Mechanism of Action: The mechanism of action of the amino acid L-glutamine in treating SCD is not fully understood. Oxidative stress phenomena are involved in the pathophysiology of SCD. Sickle RBCs are more susceptible to oxidative damage than normal RBCs, which may contribute to the chronic hemolysis and vaso-occlusive events associated with SCD. The pyridine nucleotides, NAD^+ and its reduced form NADH, play roles in regulating and preventing oxidative damage in RBCs. L-glutamine may improve the NAD redox potential in sickle RBCs through increasing the availability of reduced glutathione.

Contraindication(s): None.

Adverse Reactions: The most common adverse reactions (incidence >10%) are constipation, nausea, headache, abdominal pain, cough, pain in extremity, back pain, and chest pain.

Use in Specific Populations:

- Pregnancy: There are no available data on Endari™ use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. Animal reproduction studies were not conducted with Endari™.
- Lactation: There are no data on the presence of Endari™ in human milk, the effect on the breastfed infant, or the effect on milk production.
- Pediatric Use: The safety and effectiveness of Endari™ have been established in pediatric patients 5 years and older. Use of Endari™ is supported by evidence from two placebo-controlled trials in adults and pediatric patients with SCD. The safety and effectiveness of Endari™ in pediatric patients with SCD younger than 5 years of age have not been established.
- Geriatric Use: Clinical studies of Endari™ did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Efficacy: The efficacy of Endari™ in SCD was evaluated in a randomized, double-blind, placebo-controlled, multi-center clinical trial.

- The trial evaluated the efficacy and safety of Endari™ in 230 patients, ranging in age from 5 to 58 years, with sickle cell anemia or sickle beta thalassemia who had two or more painful crises within the 12 months prior to enrollment. Patients stabilized on hydroxyurea for at least 3 months continued their therapy with hydroxyurea throughout the study. Patients who had received blood products within 3 weeks, had renal insufficiency or uncontrolled liver disease, or were pregnant, planning to become pregnant, or lactating were excluded from the trial. Patients enrolled in the study received Endari™ or placebo for a treatment duration of 48 weeks followed by 3 weeks of tapering.
- Efficacy was demonstrated by a reduction in the number of sickle cell crises through Week 48 and prior to the start of tapering among patients that received Endari™ compared to patients who received placebo. A sickle cell crisis was defined as a visit to an emergency room/medical facility for sickle cell disease-related pain which was treated with a parenterally administered narcotic or parenterally administered ketorolac. In addition, the occurrence of chest syndrome, priapism, and splenic sequestration were considered sickle cell crises.

Event	Endari™ (n = 152)	Placebo (n = 78)
Median number of sickle cell crises (min, max)	3 (0, 15)	4 (0, 15)
Median number of hospitalizations for sickle cell pain (min, max)	2 (0, 14)	3 (0, 13)
Median cumulative days in hospital (min, max)	6.5 (0, 94)	11 (0, 187)
Median time (days) to first sickle cell crises (95% CI)*	84 (62, 109)	54 (31, 73)
Patients with occurrences of acute chest syndrome (%)	13 (8.6%)	18 (23.1%)

*Hazard Ratio = 0.69 (95% CI = 0.52, 0.93), estimated based on unstratified Cox's proportional model. Median time and 95% CI were estimated based on the Kaplan Meier method.

- The recurrent crisis event time yielded an intensity rate ratio (IRR) value of 0.75 with 95% confidence interval (CI)= (0.62, 0.90) and (0.55, 1.01) based on unstratified models using the Andersen-Gill and Lin, Wei, Yang and Ying methods, respectively, in favor of Endari™, suggesting that over the entire 48 week period, the average cumulative crisis count was reduced by 25% from the Endari™ group over the placebo group.

Cost: The wholesale acquisition cost (WAC) of Endari™ is currently unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Endari™ (L-glutamine) with the following criteria:

Endari™ (L-Glutamine) Approval Criteria:

1. An FDA approved diagnosis of sickle cell disease; and
2. Member must be at least 5 years of age or older; and

3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. Endari™ must be prescribed in consultation with a hematologist or a specialist with expertise in treatment of sickle cell disease (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating sickle cell disease); and
5. 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.
6. Initial approvals will be for a duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

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[9] Endari™ Prescribing Information. Emmaus Medical, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208587s000lbl.pdf. Last revised 07/2017. Last accessed 07/26/2017.

Appendix P

Fiscal Year 2017 Annual Review of Insomnia Medications

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

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

CR = controlled release; SL = sublingual
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Unique dosage formulations require a special reason for use in place of Tier-1 formulations.
+Individual criteria specific to tasimelteon.

- All medications have a quantity limit of 30 units per 30 days.

Insomnia Medications Tier-2 Approval Criteria:

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

Insomnia Medications Tier-3 Approval Criteria:

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

Hetlioz® (Tasimelteon) Approval Criteria:

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

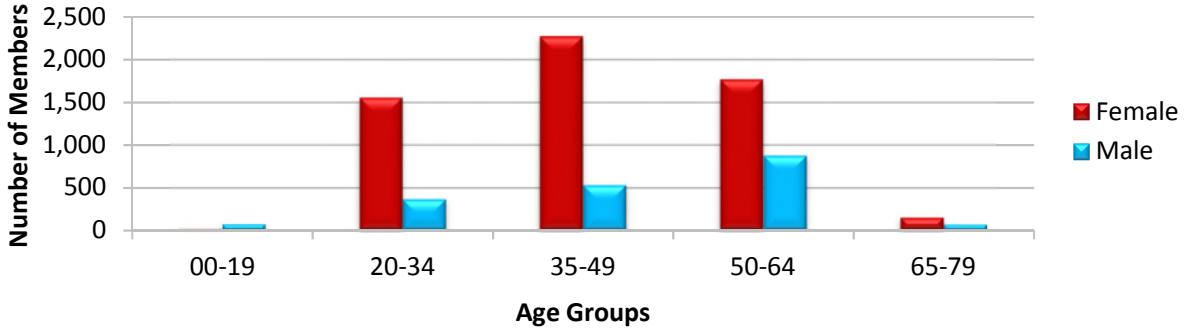
Utilization of Insomnia Medications: Fiscal Year 2017

Comparison of Fiscal Years

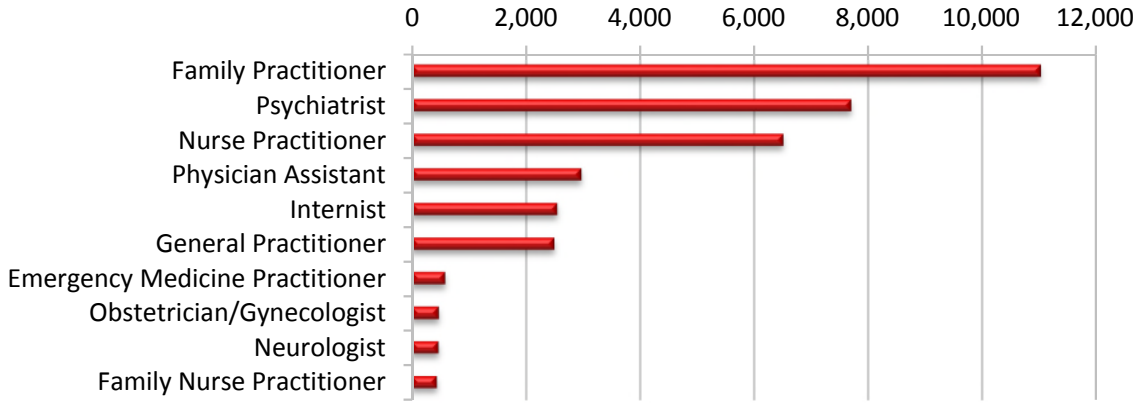
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	8,618	39,926	$362,618.16	$9.08	$0.31	1,168,604	1,166,646
2017	7,754	37,260	$587,195.70	$15.76	$0.54	1,091,326	1,089,400
% Change	**-10.00%**	**-6.70%**	**61.90%**	**73.60%**	**74.20%**	**-6.60%**	**-6.60%**
Change	**-864**	**-2,666**	**$224,577.54**	**$6.68**	**$0.23**	**-77,278**	**-77,246**

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

Demographics of Members Utilizing Insomnia Medications

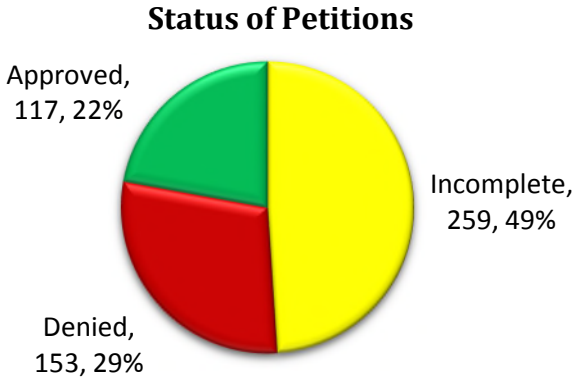


Top Prescriber Specialties of Insomnia Medications by Number of Claims



Prior Authorization of Insomnia Medications

There were 529 prior authorization requests submitted for insomnia medications during fiscal year 2017. The following chart shows the status of the submitted petitions for fiscal year 2017.



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

Anticipated Patent Expiration(s):

- Zolpimist® (zolpidem oral spray): October 2017
- Hetlioz® (tasimelteon capsules): December 2017
- Rozerem® (ramelteon tablets): July 2019
- Edluar® (zolpidem sublingual tablets): September 2019
- Silenor® (doxepin tablets): May 2020
- Intermezzo® (zolpidem sublingual tablets): February 2025
- Belsomra® (suvorexant tablets): November 2029

News:

- **July 2016:** The American College of Physicians (ACP) released a clinical guideline for management of chronic insomnia disorders in adults. The recommendations from this guideline include:
  - All adult patients should receive cognitive behavioral therapy for insomnia (CBT-I) as initial treatment for chronic insomnia; and
  - Clinicians should use a shared decision-making approach, including a discussion of the benefits, harms, and costs of short-term use of medications, to decide whether to add pharmacological therapy in adults with chronic insomnia in whom CBT-I alone was unsuccessful.
- **February 2017:** The American Academy of Sleep Medicine (AASM) released a clinical guideline for the pharmacologic treatment of chronic insomnia in adults. This guideline differs from other guidelines AASM has released in that it focuses on making recommendations on individual drugs commonly used to treat insomnia, instead of by insomnia disorders. This guideline did not review tasimelteon or provide any recommendations for this medication. The following table summarizes the recommendations.

Table 1. Summary of Recommendations for Pharmacological Treatment of Chronic Insomnia*

Recommended for Sleep Onset	Recommended for Sleep Maintenance
eszopiclone (Lunesta®)	doxepin (Sinequan®)
ramelteon (Rozerem®)	eszopiclone (Lunesta®)
temazepam (Restoril®)	suvorexant (Belsomra®)
triazolam (Halcion®)	temazepam (Restoril®)
zaleplon (Sonata®)	zolpidem (Ambien®)
zolpidem (Ambien®)	

*Table modified from American Academy of Sleep Medicine Pharmacologic Treatment of Chronic Insomnia Guidelines

- **June 2017:** A meta-analysis showed a 2.5-fold increased risk of Parkinson's disease among patients taking zolpidem. However, there were only two studies of high enough quality to be included in the review, which were both retrospective, observational studies from a health claims database from Taiwan. The first study reviewed 101,719 patients treated over five years where there were 42,171 zolpidem users and 809 Parkinson's cases and the second study reviewed 14,805 patients treated over 10 years with 2,961 zolpidem users and 157 Parkinson's cases. Both studies revealed a higher risk of developing Parkinson's among zolpidem users. Additional well-controlled studies are necessary in order to be able to generalize this perceived risk to other populations.

Pipeline Update(s):

- **Hetlioz® (tasimelteon):** Vanda Pharmaceuticals has begun Phase 3 trials for additional indications for the treatment of non-24-hour sleep-wake disorder (non-24) in pediatrics and Smith-Magenis syndrome (SMS), as well as Phase 2 trials for an indication of jetlag. Hetlioz® is currently only indicated for the treatment of non-24 in blind, adult patients.
- **Lemborexant:** Eisai and Purdue Pharma are jointly developing lemborexant, an orexin receptor antagonist. This product is currently in Phase 3 trials for an indication of insomnia disorder and Phase 2 trials for an indication of irregular sleep-wake rhythm disorder associated with Alzheimer's disease/insomnia disorder.
- **MIN-202:** Minerva Neurosciences is developing MIN-202, a selective orexin-2 receptor antagonist, jointly with Janssen Pharmaceuticals N.V. for the treatment of insomnia and major depressive disorder (MDD). This product has completed a Phase 2 trial for insomnia and a Phase 1b trial for MDD.
- **PedPRM:** In November 2016, Neurim Pharmaceuticals announced top-line results from its Phase 3 trial of PedPRM, pediatric prolonged-release melatonin, for sleep disturbances in children with Autism Spectrum Disorders (ASD). PedPRM is a specially formulated oral solid dosage form of prolonged-release melatonin, 3mm in diameter, for children who have difficulty swallowing. This randomized, double-blind, placebo-controlled, parallel group, multi-center (US and Europe) Phase 3 trial studied sleep disorders in 125 children with ASD or neurogenetic diseases. The trial met its primary endpoint of statistically improving total sleep time compared to placebo and demonstrated improvements in sleep initiation and maintenance. PedPRM has already been released throughout Europe and Neurim Pharmaceuticals plans to seek approval in the United States.

- **Piromelatine:** Neurim Pharmaceuticals is developing piromelatine, a melatonin MT1/2/3 and 5-HT-1A-1D receptor agonist, for primary insomnia and Alzheimer's disease. Piromelatine has completed a Phase 2 trial for primary insomnia and demonstrated efficacy and safety in patients 18 to 80 years of age. Based on the Phase 2 results, a Phase 2b trial has been initiated to study efficacy and safety in patients with mild Alzheimer's disease.
- **Zleepax™:** Blake Insomnia Therapeutics is currently in Phase 2 trials with their product Zleepax™, the first sleep aid with the beta blocker, nebivolol, as the major active ingredient. Zleepax™ is being studied specifically for stress-related insomnia.

Non-24-Hour Sleep-Wake Rhythm Disorder[11,12,13]

Non-24-Hour-Sleep-Wake Rhythm Disorder (N24SWD or Non-24) occurs when the hypothalamic circadian pacemaker fails to entrain to the 24-hour day. Patients with this condition exhibit sleep-wake patterns that show a progressive delay or advance, depending upon the period length (tau) of their endogenous circadian rhythms. As a result, patients can suffer from periodic nighttime insomnia and daytime somnolence as their circadian rhythms of sleep propensity and alertness drift in and out of synchrony with the 24-hour day. This condition primarily occurs in blind individuals, and at least 50% of the totally blind (i.e. those with no light perception) are thought to suffer from N24SWD. Due to N24SWD being often misdiagnosed as another sleep disorder or non-related psychiatric disorder, diagnosis by a sleep specialist is recommended.

Currently, tasimelteon is the only FDA-approved treatment for N24SWD; however, there two other medications currently on the market that could be used to treat N24SWD:

1. **Ramelteon (Rozerem®)** is a melatonin agonist that has affinity for melatonin receptors 1 and 2 (MT_1 and MT_2), and is currently FDA-approved for the treatment of insomnia characterized by difficulty with sleep onset. Although there are no published studies of ramelteon for N24SWD, the similarity in pharmacology between ramelteon and tasimelteon suggests that ramelteon would be an effective and lower cost treatment option for N24SWD.
2. **Melatonin** is a hormone normally secreted from the pineal gland at night and plays a pivotal role in the physiological regulation of circadian rhythms, including sleep. Melatonin is currently available as an over-the-counter (OTC) dietary supplement in a variety of strengths and formulations. Melatonin was given orphan drug designation for treatment of N24SWD in blind individuals without light perception by the FDA in 2004, and strategically timed melatonin is recommended for treatment of N24SWD in blind individuals by the AASM 2015 guidelines.

Cost Comparison:

Medication	Cost Per Unit	Cost for 30 Days of Therapy*
Hetlioz® (tasimelteon) tablets	**$444.60**	**$13,338.00**
Rozerem® (ramelteon) tablets	$11.40	$342.00[+]
melatonin 10mg quick dissolve tablet[◊]	$0.04	$1.20

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.
*30 days of therapy based on usual dose of medication
◊Cost based on Walgreens generic 240-count bottle from walgreens.com, last checked 07/20/2017
+FDA approved in 2005 and has a significant rebate.

Recommendations

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

1. Move ramelteon (Rozerem®) tablets into Tier-1 based on low net cost.
2. Add a previously failed trial of ramelteon (Rozerem®) and confirmation of Non-24-Hour Sleep-Wake Disorder (Non-24) diagnosis by a sleep specialist for authorization of Hetlioz® (tasimelteon).

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

Hetlioz® (Tasimelteon) Approval Criteria:

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

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

CR = controlled release; SL = sublingual

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

*Unique dosage formulations require a special reason for use in place of Tier-1 formulations.

+Individual criteria specific to tasimelteon.

Utilization Details of Insomnia Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
TIER-1 UTILIZATION					
TEMAZEPAM CAP 30MG	5,100	1,132	$38,798.99	4.51	$7.61
ZOLPIDEM TAB 5MG	3,877	1,380	$25,391.31	2.81	$6.55
TEMAZEPAM CAP 15MG	2,874	921	$21,682.61	3.12	$7.54
ESZOPICLONE TAB 3MG	1,734	412	$30,381.96	4.21	$17.52
TRIAZOLAM TAB 0.25MG	817	422	$20,011.85	1.94	$24.49
ESZOPICLONE TAB 2MG	666	249	$11,994.49	2.67	$18.01
ZALEPLON CAP 10MG	533	177	$7,923.86	3.01	$14.87
ESZOPICLONE TAB 1MG	301	138	$6,622.19	2.18	$22.00
FLURAZEPAM CAP 30MG	153	24	$3,041.15	6.38	$19.88
ZALEPLON CAP 5MG	137	72	$1,905.88	1.9	$13.91
ESTAZOLAM TAB 2MG	50	10	$1,122.83	5	$22.46
FLURAZEPAM CAP 15MG	22	8	$328.48	2.75	$14.93
TRIAZOLAM TAB 0.125MG	17	14	$396.69	1.21	$23.33
ESTAZOLAM TAB 1MG	6	2	$115.98	3	$19.33
TIER-1 SUBTOTAL	**16,287**	**4,339**	**$169,718.07**	**3.75**	**$10.42**
TIER-2 UTILIZATION					
ZOLPIDEM ER TAB 12.5MG	1,189	184	$51,893.99	6.46	$43.65
ROZEREM TAB 8MG	170	38	$56,968.97	4.47	$335.11
ZOLPIDEM ER TAB 6.25MG	113	35	$6,219.71	3.23	$55.04
AMBIEN CR TAB 12.5MG	20	2	$9,817.81	10	$490.89
TIER-2 SUBTOTAL	**1,492**	**248**	**$124,900.48**	**6.02**	**$83.71**
TIER-3 UTILIZATION					
BELSOMRA TAB 10MG	15	4	$4,526.68	3.75	$301.78
BELSOMRA TAB 15MG	15	3	$4,493.70	5	$299.58
BELSOMRA TAB 20MG	11	5	$2,891.28	2.2	$262.84
TIER-3 SUBTOTAL	**41**	**11**	**$11,911.66**	**3.73**	**$290.53**
SPECIAL PRIOR AUTHORIZATION (PA) UTILIZATION					
TEMAZEPAM CAP 7.5MG	16	6	$1,715.50	2.67	$107.22
HETLIOZ CAP 20MG	12	1	$158,313.00	12	$13,192.75
ZOLPIDEM TAR SUB 3.5MG	5	1	$1,200.00	5	$240.00
SILENOR TAB 6MG	1	1	$398.20	1	$398.20
SPECIAL PA SUBTOTAL	**34**	**9**	**$161,626.70**	**3.78**	**$4,753.73**
TOTAL	**37,260**	**7,754***	**$587,195.70**	**4.81**	**$15.76**

*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 06/2017. Last accessed 07/17/2017.
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Appendix Q

30-Day Notice to Prior Authorize Fabrazyme® (Agalsidase Beta)

Oklahoma Health Care Authority
September 2017

Introduction[1,2]

Fabry disease, also called Anderson-Fabry disease, is the second most prevalent lysosomal storage disorder after Gaucher disease. It is an X-linked inborn error of the glycosphingolipid metabolic pathway, caused by mutations in the galactosidase alpha (*GLA*) gene. The metabolic defect in Fabry disease causes deficiency of the lysosomal hydrolase, alpha-galactosidase A (alpha-Gal A), which catalyzes the hydrolytic cleavage of the terminal galactose from globotriaosyl-ceramide (GL-3). This results in accumulation of GL-3 within lysosomes throughout the body, particularly cells lining blood vessels in the skin and cells in the kidneys, heart, and nervous system. This leads to variable manifestations of the disease. *GLA* gene mutations that result in an absence of alpha-Gal A activity lead to the classic, severe form of Fabry disease. Mutations that decrease but do not eliminate the enzyme's activity usually cause the milder, late-onset forms of Fabry disease that affect only the heart or kidneys.

Although variability exists, the symptoms of Fabry disease tend to appear in a predictable order in classically affected males. Beginning in childhood or adolescence, characteristic features of Fabry disease include episodes of pain, particularly in the hands and feet (acroparesthesias); clusters of small, dark red spots on the skin called angiokeratomas; a decreased ability to sweat (hypohidrosis); cloudiness of the front part of the eye (corneal opacity); problems with the gastrointestinal system; ringing in the ears (tinnitus); and hearing loss. In adulthood, Fabry disease also involves potentially life-threatening complications such as progressive kidney damage, heart attack, and stroke. Cardiac manifestations occur in more than 80% of patients with Fabry disease, and transient ischemic attacks and strokes occur in approximately 25% of patients. Additionally, renal manifestations occur in at least 50% of male patients and about 20% of female patients.

Fabry disease affects an estimated 1 in 40,000 to 60,000 males. This disorder also occurs in females, although the prevalence is unknown. Milder, late-onset forms of the disorder are probably more common than the classic, severe form. The prevalence of Fabry disease is probably underestimated given incomplete ascertainment due, in part, to the nonspecific manifestations of the disease.

In the setting of clearly established family history and classic phenotype, the diagnosis can usually be confirmed in males by a low alpha-Gal A activity in leukocytes or plasma. Mutation analysis of the alpha-Gal A gene is required to make the diagnosis in female carriers unless the woman is an obligate heterozygote (i.e., the father is known to have Fabry), and in patients with atypical presentations or who have residual alpha-Gal A levels.

There is no cure for Fabry disease, and uniform recommendations for the use of enzyme replacement therapy (ERT) do not exist. The treatment of patients with Fabry disease primarily focuses upon replacing the missing or deficient enzyme (alpha-Gal A). All classically affected males (i.e., with very low or undetectable levels of alpha-Gal A) should receive ERT as soon as the diagnosis is made, regardless of whether or not clinical manifestations are present. Female carriers and atypically affected males (i.e., with marginal levels of alpha-Gal A) should receive ERT if clinical manifestations are present. It is recommended that patients with Fabry disease who have end-stage renal disease (ESRD) begin treatment with ERT, as this may reduce cardiovascular and neurologic complications of Fabry disease. Currently, Fabrazyme® (agalsidase beta) is the only U.S. Food and Drug Administration (FDA) approved ERT for Fabry disease.

Utilization of Fabrazyme® (Agalsidase Beta): Fiscal Year 2017

Fabrazyme® (Agalsidase Beta): Medical Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units
2017	1	12	$300,217.40	$25,018.12	1,820

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

Demographics of Members Utilizing Fabrazyme® (Agalsidase Beta)

- Due to the limited number of members utilizing Fabrazyme® (agalsidase beta), detailed member demographic information cannot be provided.

Top Prescriber Specialties of Fabrazyme® (Agalsidase Beta) by Number of Claims

- The only prescriber specialty listed on paid claims for Fabrazyme® (agalsidase beta) during fiscal year 2017 was hematology/oncology. However, upon further review treatment was started by a medical geneticist.

Market News & Updates[3,4,5,6]

News:

- **July 2017:** The FDA announced that it has accepted Amicus Therapeutics' submission of migalastat for review, a reversal from its decision under the Obama administration. Previously, the FDA told Amicus it would need to conduct further safety studies for migalastat, its drug candidate for Fabry disease. In December 2016, Amicus agreed to conduct a further study on Fabry patients with gastrointestinal symptoms. The FDA has since deemed the current data sufficient to support a New Drug Application (NDA) submission, saying the additional Phase 3 study would not be necessary.

Pipeline:

- **Migalastat:** As noted above, Amicus Therapeutics is developing migalastat. It is an oral, small molecule drug designed to bind to and stabilize the endogenous alpha-Gal A that

is made in the patient's own cells, with the intention of enabling effective delivery to lysosomes (designed to act as a "pharmacological chaperone"). Migalastat would provide monotherapy for Fabry disease patients with genetic mutations that are amenable to this chaperone therapy. That is, those patients who make some alpha-Gal A enzyme that is capable of degrading GL-3, but because of genetic mutation, the endogenously produced alpha-Gal A is not effectively delivered to lysosomes. It is estimated that 30% to 50% of the Fabry disease population have amenable mutations and may be eligible to receive migalastat monotherapy. Amicus is also working to develop an intravenous (IV) migalastat that is co-formulated with a novel ERT.

- **Pegunigalsidase Alfa (PRX-102):** Protalix BioTherapeutics announced in May 2017 that the FDA cleared an Investigational New Drug (IND) application for a clinical trial evaluating the safety and efficacy of administering 2mg/kg of pegunigalsidase alfa (PRX-102) once monthly in Fabry patients. The current dosing regimen using Fabrazyme® for Fabry disease is once every two weeks. Pegunigalsidase alfa is a PEGylated, chemically-modified version of the recombinant alpha-Gal A enzyme, resulting in a longer active and stable molecule compared to currently available ERTs. Pharmacokinetic analysis from clinical trials indicate that pegunigalsidase alfa levels the second week after infusion remain ten times higher than published Fabrazyme® levels at the day of infusion. Moreover, the amount of pegunigalsidase alfa in the circulation at weeks three and four are higher than those of Fabrazyme® during the two-week treatments.
- **AVR-RD-01:** AVROBIO currently has an ongoing Phase 1 trial to evaluate the safety and toxicity of AVR-RD-01, a clinical-stage gene therapy where the Fabry patient's blood stem cells are extracted and genetically modified by adding a new, fully functional copy of the faulty gene. The modified cells (which express the missing enzyme, alpha-Gal A) are then delivered back into the patient via a one-time infusion. An around the clock elevation of endogenous enzyme is expected, with the potential to significantly improve patient outcomes and eliminate burdensome and costly lifelong biweekly IV infusions of ERT.

Fabrazyme® (Agalsidase Beta) Product Summary[7]

Indication(s): Fabrazyme® (agalsidase beta) is a recombinant human alpha-Gal A enzyme with the same amino acid sequence as the native enzyme. It is indicated for use in patients with Fabry disease.

Dosing:

- Fabrazyme® (agalsidase beta) is supplied as 35mg or 5mg single-use vials of sterile, nonpyrogenic, lyophilized powder for reconstitution with sterile water for injection.
- The recommended dose is 1mg/kg of body weight given every two weeks as an IV infusion.
- It is recommended that patients receive antipyretics prior to infusion.

Mechanism of Action: Agalsidase beta is intended to provide an exogenous source alpha-Gal A in Fabry disease patients. Agalsidase beta reduces GL-3 deposition in capillary endothelium of the kidney and certain other cell types. Nonclinical and clinical studies evaluating a limited

number of cell types indicate that agalsidase beta will catalyze the hydrolysis of glycosphingolipids, including GL-3.

Contraindication(s): None.

Warnings and Precautions:

- Anaphylaxis and Allergic Reactions: Life-threatening anaphylactic and severe allergic reactions have been observed in patients during agalsidase beta infusions. Reactions have included localized angioedema, bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion. Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, epinephrine, and IV corticosteroids. In clinical trials and postmarketing safety experience with agalsidase beta, approximately 1% of patients developed anaphylactic or severe allergic reactions during infusion.
- Infusion Reactions: In clinical trials with agalsidase beta, approximately 50 to 55% of patients experienced infusion reactions during agalsidase beta administration, some of which were severe. Severe infusion reactions experienced by more than one patient in clinical studies included: chills, vomiting, hypotension, and paresthesia. Other infusion reactions included pyrexia, feeling hot or cold, dyspnea, nausea, flushing, headache, fatigue, pruritus, pain in extremity, hypertension, chest pain, throat tightness, abdominal pain, dizziness, tachycardia, nasal congestion, diarrhea, peripheral edema, myalgia, urticaria, bradycardia, and somnolence. In patients experiencing infusion reactions, pre-treatment with an antipyretic and antihistamine is recommended. Infusion reactions occurred in some patients after receiving pretreatment with antipyretics, antihistamines, and oral steroids. Infusion reactions tended to decline in frequency with continued use. However, infusion reactions may still occur despite extended duration of treatment.
- Immunogenicity and Re-challenge: In clinical trials with agalsidase beta, a few patients developed IgE antibodies or skin test reactivity specific to agalsidase beta. Two of six patients in the re-challenge study discontinued treatment prematurely due to recurrent infusion reactions. Four serious infusion reactions occurred in three patients during agalsidase beta infusions, including bronchospasm, urticaria, hypotension, and development of agalsidase beta-specific antibodies. Physicians should consider testing for IgE antibodies in patients who experience suspected allergic reactions and consider the risks and benefits of continued treatment in patients with anti-agalsidase beta IgE antibodies.

Adverse Reactions: Serious and/or frequently occurring (≥ 5% incidence) related adverse reactions consisted of one or more of the following:

- Chills
- Pyrexia
- Feeling Hot Or Cold
- Dyspnea
- Nausea
- Flushing
- Headache
- Vomiting
- Paresthesia
- Fatigue
- Pruritus
- Pain In Extremity
- Hypertension
- Chest Pain
- Throat Tightness

- Abdominal Pain
- Dizziness
- Tachycardia
- Nasal Congestion
- Diarrhea
- Peripheral Edema
- Myalgia
- Back Pain
- Pallor
- Bradycardia
- Urticaria
- Hypotension
- Face Edema
- Rash
- Somnolence

Use in Specific Populations:

- Pregnancy: Agalsidase beta is Pregnancy Category B. There are no adequate and well-controlled studies of agalsidase beta use in pregnant women. Reproduction studies performed in rats at doses up to 30 times the human dose have revealed no evidence of impaired fertility or negative effects on embryo fetal development due to agalsidase beta.
- Lactation: It is not known whether agalsidase beta is excreted in human milk.
- Pediatric Use: The safety and efficacy of agalsidase beta were assessed in a multi-national, multi-center, uncontrolled, open-label study in 16 pediatric patients with Fabry disease (14 males, 2 females), ages 8 to 16 years. Patients younger than 8 years of age were not included in clinical studies. The safety and efficacy in patients younger than 8 years of age have not been evaluated.
- Geriatric Use: Clinical studies of agalsidase beta did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects.
- Response in Women: Fabry disease is an X-linked genetic disorder. However, some heterozygous women will develop signs and symptoms of Fabry disease due to the variability of the X-chromosome inactivation within cells. Although the safety and efficacy data available in female patients in clinical studies are limited, there is no indication that female patients respond differently to agalsidase beta compared to males.

Efficacy: The safety and efficacy of agalsidase beta were assessed in four clinical studies in patients with Fabry disease.

- Study 1: The efficacy of agalsidase beta was evaluated in a randomized, double-blind, placebo-controlled study of 58 Fabry patients (56 males and 2 females), 16 to 61 years of age, all naïve to ERT. Patients received either 1mg/kg of agalsidase beta or placebo every two weeks for five months (20 weeks) for a total of 11 infusions. The primary efficacy endpoint of GL-3 inclusions in renal interstitial capillary endothelial cells was assessed by light microscopy and was graded on an inclusion severity score ranging from 0 (normal or near normal) to 3 (severe inclusions). A GL-3 inclusion score of 0 was achieved in 20 of 29 (69%) patients treated with agalsidase beta compared to 0 of 29 treated with placebo ($p<0.001$). Similar reductions in GL-3 inclusions were observed in the capillary endothelium of the heart and skin. No differences between groups in symptoms or renal function were observed during this five-month study. The reduction of GL-3 inclusions suggests that agalsidase beta may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.

- Study 2: The efficacy of agalsidase beta was evaluated in a randomized, double-blind, placebo-controlled study of 82 patients (72 males and 10 females), 20 to 72 years of age, all naïve to ERT. Patients received either 1mg/kg of agalsidase beta or placebo every two weeks for up to a maximum of 35 months (median 18.5 months). There was a significant difference in post-baseline plasma GL-3 levels in the agalsidase beta-treated patients compared to placebo. The reduction in plasma GL-3 levels in the agalsidase beta group compared to the placebo group was significant at one year ($p<0.0001$) and at two years ($p=0.0019$).
- Study 3 (Pediatric Study): Study 3 was an open-label, uncontrolled, multi-national, multi-center study to evaluate safety, pharmacokinetics, and pharmacodynamics of agalsidase beta treatment in 16 pediatric patients with Fabry disease (14 males, 2 females), who were 8 to 16 years of age at first treatment. All patients received agalsidase beta 1mg/kg every two weeks for up to 48 weeks. At weeks 24 and 48 of treatment, all 14 males had plasma GL-3 within the normal range. The two female patients' plasma GL-3 levels (found to be normal at baseline) remained normal through study week 48. No new safety concerns were identified in pediatric patients in this study, and the overall safety and efficacy profile of agalsidase beta treatment in pediatric patients was found to be consistent with that seen in adults. Immunologic responses in pediatric patients may differ from those in adults, as IgG seroconversion in pediatric patients was associated with prolonged half-life concentrations of agalsidase beta, a phenomenon rarely observed in adult patients.
- Study 4: Study 4 was an open-label, re-challenge study to evaluate the safety of agalsidase beta treatment in patients who had a positive skin test to agalsidase beta or who had tested positive for agalsidase beta-specific IgE antibodies. In this study, six adult male patients, who had experienced multiple or recurrent infusion reactions during previous clinical trials with agalsidase beta, were re-challenged with agalsidase beta administered as a graded infusion, for up to 52 weeks of treatment. The initial two re-challenge doses of agalsidase beta were administered as a 0.5mg/kg dose per week at an initial infusion rate of 0.01mg/min for the first 30 minutes ($1/25^{th}$ the usual recommended maximum infusion rate). The infusion rate was doubled every 30 minutes thereafter, as tolerated, for the remainder of the infusion up to a maximum rate of 0.25mg/min. If the patient tolerated the infusion, the dose was increased to 1mg/kg every two weeks (usual recommended dose), and the infusion rate was increased by slow titration upwards. Four of the six patients treated in this study received at least 26 weeks of study medication, and two patients discontinued prematurely due to recurrent infusion reactions.

Cost:

Medication	Cost Per Vial	Cost Per Treatment$^{\Delta}$	Cost Per Year$^{\Delta}$
Fabrazyme® (agalsidase beta) 35mg vial	**$5,663.00**	**$12,135.00**	**$291,240.00**
Fabrazyme® (agalsidase beta) 5mg vial	**$809.00**	**$12,135.00**	**$291,240.00**

Costs based on National Average Drug Acquisition Cost (NADAC), State Maximum Allowable Cost (SMAC), or Wholesale Acquisition Cost (WAC) if NADAC unavailable. Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

$^{\Delta}$Cost per treatment based on 75kg patient.

Coverage Information

Fabrazyme® (agalsidase beta) was FDA approved in 2003, and to date only of 20% of the state Medicaid plans reviewed currently require prior authorization for this medication. Of the states reviewed that do require prior authorization, criteria generally consists of diagnosis and certification of medical necessity. Medical necessity is determined by prescriber signature or submission of clinical notes to support the need. Additionally, upon reviewing various commercial plans, it was found that those plans requiring a prior authorization had criteria similar to the College of Pharmacy recommendations (below).

Recommendations[8,9,10]

The College of Pharmacy recommends the prior authorization of Fabrazyme® (agalsidase beta) with the following criteria:

Fabrazyme® (Agalsidase Beta) Approval Criteria:

1. An FDA approved diagnosis of Fabry disease. Diagnosis must be confirmed by one of the following:
    a. Genetic testing confirming positive *GLA* gene mutation; or
    b. Decreased plasma levels of alpha-galactosidase A (less than 5% of normal); and
2. Fabrazyme® (agalsidase beta) will initially be approved for six months. After that time, compliance will be required for continued authorization; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

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Appendix R

Fiscal Year 2017 Annual Review of Antihyperlipidemics and 30-Day Notice to Prior Authorize Zypitamag™ (Pitavastatin Magnesium) and Nikita™ (Pitavastatin Sodium)

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

Statin Medications and Ezetimibe Tier-2 Approval Criteria:

1. Member must have a documented trial with atorvastatin, consisting of at least 8 weeks of continuous therapy titrated to 40mg, which did not yield adequate LDL reduction. The minimum starting dose of the Tier-2 medication may only be at the moderate-to-high LDL lowering doses (20mg rosuvastatin or higher); or
2. A documented adverse effect or contraindication to all available lower tiered products; or
3. A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high-risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome, or for pediatric members with homozygous familial hypercholesterolemia (HoFH); and
4. Clinical exceptions for ezetimibe include the following:
    a. Documented active liver disease; or
    b. Documented unexplained, persistent elevations of serum transaminases; or
    c. Documented statin-related myopathy.

Statin Medications and Ezetimibe Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used.

Statin Medications and Ezetimibe*		
Tier-1	**Tier-2**	**Special PA**
atorvastatin (Lipitor®)	ezetimibe (Zetia®)	fluvastatin (Lescol® & Lescol® XL)
lovastatin (Mevacor®)	rosuvastatin (Crestor®)+	lovastatin (Altoprev®)
pravastatin (Pravachol®)		pitavastatin (Livalo®)
simvastatin (Zocor®)		simvastatin/ezetimibe (Vytorin®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
+Crestor® 5mg and Crestor® 10mg require special reason for use.

Omega-3 Fatty Acids Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL), and controlled diabetes (fasting glucose <150mg/dL at the time of triglycerides measurement and HgA1c <7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications; and

3. Use of Vascepa® or Epanova® requires a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®).

Juxtapid® (Lomitapide) and Kynamro® (Mipomersen) Approval Criteria:

1. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following criteria:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol >500mg/dL and triglycerides <300mg/dL and at least one of the following:
        i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
        ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; and
2. Documented failure of high dose statin therapy (LDL reduction capability equivalent to atorvastatin 80mg or higher); and
3. Prescriber must be certified with Juxtapid® or Kynamro® REMS program.

PCSK9 Inhibitors Approval Criteria:

1. An FDA approved diagnosis of heterozygous familial hypercholesterolemia (HeFH) defined by the presence of one of the following criteria:
    a. A documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or
    b. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or
2. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
    a. A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
    b. An untreated total cholesterol greater than 500mg/dL and at least one of the following:
        i. Documented evidence of definite HeFH in both parents; or
        ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
3. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
    a. High cardiovascular risk confirmed by Framingham risk score; and
        i. Supporting diagnoses/conditions signifying this risk level; or
    b. Documented history of Coronary Heart Disease (CHD); and
        i. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and
4. Member must be 18 years of age or older for the diagnosis of HeFH or clinical atherosclerotic cardiovascular disease, or must be 13 years of age or older for the diagnosis of HoFH; and
5. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and

a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
d. Tier structure rules still apply; and

6. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
7. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
8. A quantity limit of 2 syringes or pens per 28 days will apply for Praluent®. A quantity limit of 2 syringes or autoinjectors per 28 days will apply for Repatha® 140mg and a quantity limit of one autoinjector per 28 days for Repatha® 420mg. Patients requesting Repatha® 420mg strength will not be approved for multiple 140mg syringes but instead should use one 420mg autoinjector.
9. Initial approvals will be for the duration of three months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every six months thereafter for continued approval.

Utilization of Antihyperlipidemics: Fiscal Year 2017

Comparison of Fiscal Years: Statin Medications and Ezetimibe

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	15,055	59,176	$1,264,469.03	$21.37	$0.46	2,764,820	2,742,370
2017	15,577	61,171	$1,003,442.12	$16.40	$0.34	2,940,567	2,920,360
% Change	**3.50%**	**3.40%**	**-20.60%**	**-23.30%**	**-26.10%**	**6.40%**	**6.50%**
Change	**522**	**1,995**	**-$261,026.91**	**-$4.97**	**-$0.12**	**175,747**	**177,990**

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

Comparison of Fiscal Years: Omega-3 Fatty Acids

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	35	258	$36,783.80	$142.57	$4.67	26,440	7,883
2017	25	204	$20,871.57	$102.31	$3.33	22,086	6,266
% Change	**-28.60%**	**-20.90%**	**-43.30%**	**-28.20%**	**-28.70%**	**-16.50%**	**-20.50%**
Change	**-10**	**-54**	**-$15,912.23**	**-$40.26**	**-$1.34**	**-4,354**	**-1,617**

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

Fiscal Year 2016 Utilization: Juxtapid® (Lomitapide) and Kynamro® (Mipomersen)

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	1	11	$346,364.83	$31,487.71	$1,124.56	308	308

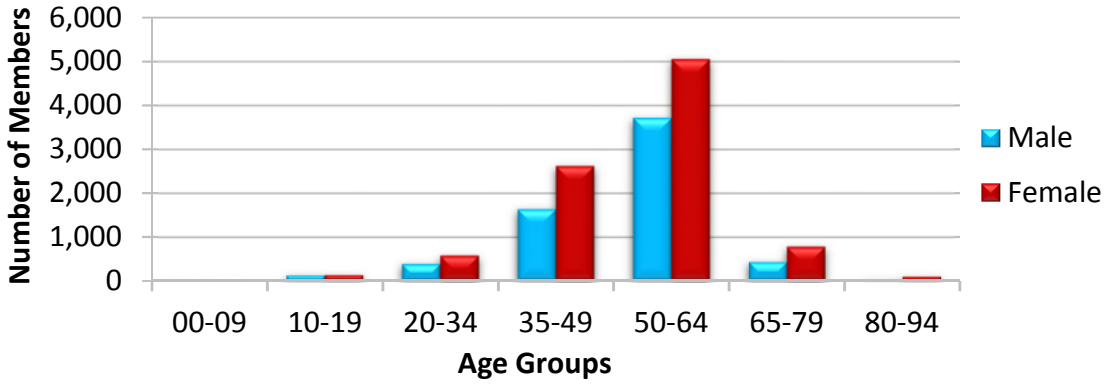
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
There was no utilization of Juxtapid® or Kynamro® during fiscal year 2017.

Comparison of Fiscal Years: PCSK9 Inhibitors

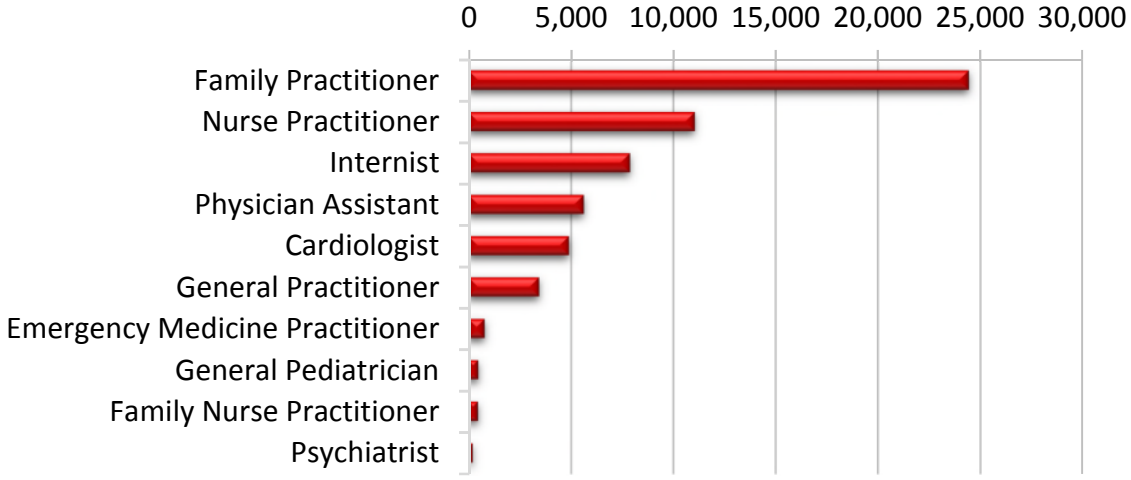
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	1	1	$1,186.32	$1,186.32	$39.54	2	30
2017	2	4	$4,634.26	$1,158.57	$41.38	8	112
% Change	**100.00%**	**300.00%**	**290.60%**	**-2.30%**	**4.70%**	**300.00%**	**273.30%**
Change	**1**	**3**	**$3,447.94**	**-$27.75**	**$1.84**	**6**	**82**

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

Demographics of Members Utilizing Antihyperlipidemics

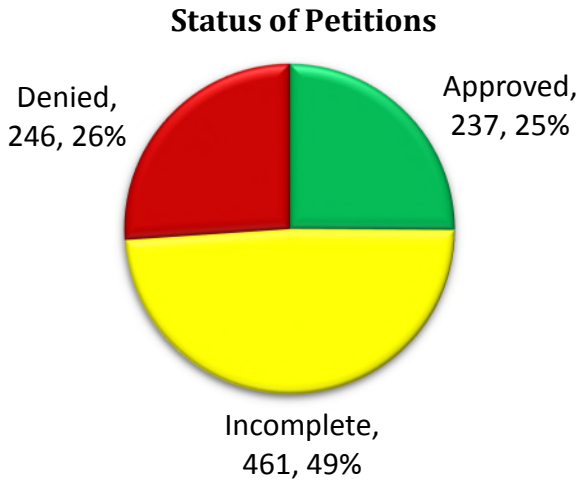


Top Prescriber Specialties of Antihyperlipidemics by Number of Claims



Prior Authorization of Antihyperlipidemics

There were 944 prior authorization requests submitted for antihyperlipidemics during fiscal year 2017. Computer edits are in place to detect Tier-1 statin medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24]

Anticipated Patent Expiration(s):

- Altoprev® (lovastatin): March 2018
- Kynamro® (mipomersen): January 2027
- Juxtapid® (lomitapide): August 2027
- Vascepa® (icosapent ethyl): April 2030
- Epanova® (omega-3-carboxylic acids): January 2033

New FDA Approval(s):

- **June 2015:** The U.S. Food and Drug Administration (FDA) approved an Abbreviated New Drug Application (ANDA) for the first generic version of Zetia® (ezetimibe). Seven additional pharmaceutical companies received FDA approval to market generic ezetimibe in June 2017. The College of Pharmacy will continue to monitor costs of generic ezetimibe in comparison to the lower tiered statin medications as more of the generic products become available.
- **December 2016:** The FDA approved an ANDA for the first generic version of Livalo® (pitavastatin calcium). Two additional pharmaceutical companies received FDA approval to market generic pitavastatin in February 2017, with one more following in August 2017. However, the anticipated release date and cost information for the new generic products are not currently available.
- **February 2017:** The FDA approved Vascepa® (icosapent ethyl) 0.5 gram capsules as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500mg/dL) hypertriglyceridemia. Vascepa® 1 gram capsules were first FDA approved in 2012 for the same indication. The recommended dose of Vascepa® is 4 grams per day, taken as

four 0.5 gram capsules or two 1 gram capsules twice daily with food. The wholesale acquisition cost (WAC) of Vascepa® 0.5 gram is $1.25 per capsule ($300.00 per month), compared to the national average drug acquisition cost (NADAC) of Vascepa® 1 gram at $2.05 per capsule ($246.00 per month).

- **April 2017:** The FDA approved a once-monthly (every four weeks) 300mg dose of Praluent® (alirocumab) as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-cholesterol (LDL-C). Praluent® 75mg and 150mg injections were first FDA approved in 2015 for the same indications. The recommended starting dose of Praluent® is 75mg subcutaneously once every two weeks, since the majority of patients achieve sufficient LDL-C reduction with this dosage. The newly approved alternative starting dosage for patients who prefer less frequent dosing is 300mg subcutaneously once every four weeks, which is administered as two 150mg injections at two different injection sites. If the LDL-C response is inadequate, the dosage may be adjusted to a maximum dosage of 150mg subcutaneously once every two weeks.
- **April 2017:** The FDA approved ANDAs for the first generic versions of Vytorin® (simvastatin/ezetimibe), with three pharmaceutical companies receiving FDA approval to market generic simvastatin/ezetimibe. The College of Pharmacy will continue to monitor costs of generic simvastatin/ezetimibe in comparison to the lower tiered statin medications as the generic products become available.
- **July 2017:** The FDA approved Zypitamag™ (pitavastatin magnesium) tablets for the treatment of patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), LDL-C, apolipoprotein B (Apo B), triglycerides (TG), and to increase HDL-cholesterol (HDL-C). The recommended dosing range is 1mg to 4mg once daily. Zypitamag™ tablets contain 1.026mg, 2.053mg, or 4.106mg of pitavastatin magnesium, which is equivalent to 1mg, 2mg, or 4mg, respectively, of free base. A different salt form, Livalo® (pitavastatin calcium), was FDA approved in 2009 for the same indications and is available as 1mg, 2mg, and 4mg tablets. The anticipated release date and cost information for Zypitamag™ are not currently available.
- **August 2017:** The FDA approved Nikita™ (pitavastatin sodium) tablets for the treatment of patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated TC, LDL-C, Apo B, TG, and to increase HDL-C. The recommended dosing range is 1mg to 4mg once daily. Nikita™ is available as 1mg, 2mg, and 4mg tablets. A different salt form, Livalo® (pitavastatin calcium), was FDA approved in 2009 for the same indications and is available as 1mg, 2mg, and 4mg tablets. The anticipated release date and cost information for Nikita™ are not currently available.

News:

- **November 2016:** Final recommendations were released by the U.S. Preventive Services Task Force (USPSTF) regarding the use of statins for the primary prevention of cardiovascular disease (CVD) in adults. Significant recommendations include:

- **Adults 40 to 75 years of age with no history of CVD, one or more CVD risk factor(s), and a calculated 10-year CVD event risk of 10% or greater:** use a low- to moderate-dose statin for the prevention of CVD events and mortality (recommendation grade B).
- **Adults 40 to 75 years of age with no history of CVD, one or more CVD risk factor(s), and a calculated 10-year CVD event risk of 7.5% to 10%:** clinicians may choose to offer a low- to moderate-dose statin to certain adults with the preceding criteria; however, the likelihood of benefit is smaller for this group of patients, because of a lower probability of disease and uncertainty in individual risk prediction (recommendation grade C).
- **Adults 76 years of age and older with no history of CVD:** the current evidence is insufficient to assess the balance of benefits and harms of initiating statin use for the primary prevention of CVD in this group of patients.

- **March 2017:** Results of the FOURIER (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) trial were presented during the first Late Breaking Clinical Trial session of the American College of Cardiology's (ACC) 66th Annual Scientific Session and Expo (ACC.17) and simultaneously published in *The New England Journal of Medicine*. The FOURIER trial was a randomized, double-blind, placebo-controlled, multinational clinical trial in which patients at 1,242 locations in 49 countries underwent randomization to receive subcutaneous injections of evolocumab or matching placebo. The primary efficacy endpoint was major cardiovascular events, defined as the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. Evolocumab significantly reduced the risk of the primary composite endpoint of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization (the primary endpoint occurred in 9.8% of patient in the evolocumab group compared to 11.3% in the placebo group; $p<0.001$).
- **April 2017:** The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) released updated guidelines for the management of dyslipidemia and prevention of CVD. Key updates compared to the previous guidelines include the following:
  - The 2017 atherosclerotic cardiovascular disease (ASCVD) risk factor modifications algorithm for patients with type 2 diabetes mellitus (T2DM) now includes an "extreme" risk category, defined as a diagnosis of T2DM plus a prior ASCVD event (i.e. established clinical CVD).
  - The new algorithm for T2DM focuses on lipid management goals for LDL-C, non-HDL-C, and Apo B, with treatment goals in the new "extreme" risk category including LDL-C < 55mg/dL, non-HDL-C < 80mg/dL, and Apo B < 70mg/dL.
  - Additional major independent risk factors for ASCVD listed in the updated guidelines include polycystic ovary syndrome (PCOS), chronic kidney disease (CKD) stages 3 and 4, and evidence of coronary artery calcification.
- **May 2017:** The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), a two-part study consisting of a double-blind, randomized, controlled trial followed by an open-label non-

randomized extension, found that patients taking statins were more likely to report side effects if they knew they were taking the drug. During the blinded phase, muscle-related adverse events were reported at a similar rate by patients randomly assigned to atorvastatin or placebo (2.03% vs. 2.00%; p=0.72). By contrast, during the non-blinded, non-randomized phase, muscle-related adverse events were reported at a significantly higher rate by patients taking statins than by those who were not (1.26% vs 1.00%; p=0.006). These analyses illustrate the so-called nocebo effect, with an excess rate of muscle-related adverse event reports only when patients and their physicians were aware that statin therapy was being used and not when its use was blinded. These results will help assure both physicians and patients that most adverse events associated with statins are not causally related to use of the drug and should help counter the adverse effect on public health by exaggerated claims about statin-related side effects.

- **August 2017:** A retrospective cohort study that included 28,266 patients with a presumed adverse reaction to a statin concluded that continued statin prescriptions after an adverse reaction were associated with a lower incidence of death and cardiovascular events. Information on adverse reactions to statins was obtained from structured electronic medical record data or natural-language processing of narrative provider notes. The primary composite outcome was time to a cardiovascular event (myocardial infarction or stroke) or death. Among the study patients, 70.7% continued receiving statin prescriptions after the adverse reaction. Four years after the presumed adverse reaction, the cumulative incidence of the composite primary outcome was 12.2% for patients with continued statin prescriptions, compared to 13.9% for those without them (p<0.001).
- **August 2017:** An updated cost-effectiveness analysis of PCSK9 inhibitors was completed based on the results of the FOURIER trial (see above) and current prices. A previous cost-effectiveness analysis of PCSK9 inhibitors, based on their lowering of LDL-C, demonstrated that the 2015 price of PCSK9 inhibitors would need to be reduced by more than two-thirds to meet generally accepted cost-effectiveness thresholds. Since that report, the FOURIER trial found that the PCSK9 inhibitor evolocumab reduced the risk of major adverse cardiovascular events. The updated analysis found that PCSK9 inhibitor use in patients with ASCVD was not cost effective at 2017 prices, and these updated analyses based on FOURIER estimates suggest that even greater price reductions than previously reported are required to meet cost-effectiveness thresholds (would require a 71% price reduction).

Pipeline:

- **November 2016:** Pfizer discontinued the clinical development of bococizumab, its investigational PCSK9 inhibitor, following the completion of six bococizumab lipid-lowering studies which included an unanticipated attenuation of LDL-C lowering over time, as well as a higher level of immunogenicity and a higher rate of injection-site reactions with bococizumab than shown with the other agents in this class of medications (PCSK9 inhibitors).

- **April 2017:** The Medicines Company and Alnylam Pharmaceuticals have agreed with the FDA on plans for the Phase 3 clinical program for inclisiran, which is designed to support the submission of a New Drug Application (NDA). The primary endpoint for all pivotal trials will be LDL-C change from baseline. Inclisiran is a long-acting, subcutaneous, N-acetylgalactosamine (GalNAc)-conjugated synthetic small interfering RNA (siRNA) molecule targeting PCSK9 – a genetically validated protein regulator of LDL receptor metabolism – being developed for the treatment of hypercholesterolemia. In contrast to anti-PCSK9 monoclonal antibodies (e.g., alirocumab, evolocumab) that bind to PCSK9 in the blood, inclisiran is a first-in-class investigational medication that acts by turning off PCSK9 synthesis in the liver.
- **April 2017:** Regeneron's evinacumab has received FDA breakthrough therapy designation for homozygous familial hypercholesterolemia (HoFH). Evinacumab is an investigational monoclonal antibody to angiopoietin-like protein 3 (ANGPTL3). ANGPTL3 acts as an inhibitor of lipoprotein lipase and endothelial lipase, and appears to play a role in lipoprotein metabolism. Regeneron previously reported positive interim Phase 2 results for evinacumab in HoFH patients and is currently planning a Phase 3 trial.
- **May 2017:** Esperion's bempedoic acid is currently in Phase 3 trials, with the reporting of top-line results expected in the second quarter of 2018 and NDA submission by the first half of 2019 for an LDL-C lowering indication. Bempedoic acid, a novel, non-statin, targeted therapy that works in the liver to block cholesterol biosynthesis, is an oral, once-daily LDL-C lowering drug. Bempedoic acid's mechanism of action is similar to statins, as it inhibits cholesterol synthesis, upregulates LDL receptors on liver cells, and lowers LDL-C. However, unlike statins, bempedoic acid does not inhibit the cholesterol biosynthesis pathway in skeletal muscle, nor promote the associated cytotoxicity believed to lead to muscle-related side effects. Bempedoic acid is differentiated in one key way: it remains inactive until it enters the liver where it is converted to its active form by the enzyme, ACSVL1, an enzyme not found in skeletal muscle. Esperion is also currently developing combination products with bempedoic acid, including a combination product with ezetimibe and a combination product with a PCSK9 inhibitor, both of which are currently in Phase 2 trials.

Recommendations

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

1. Move rosuvastatin into Tier-1 based on low net cost and add a required trial with rosuvastatin to current Tier-2 criteria, in addition to an atorvastatin trial, based on LDL lowering capability and low net cost.
2. Place Zypitamag™ (pitavastatin magnesium) and Nikita™ (pitavastatin sodium) into the Special Prior Authorization (PA) tier. Current Special PA criteria will apply.
3. Add criteria for Vascepa® 0.5 gram based on higher net cost compared to Vascepa® 1 gram. Use of Vascepa® 0.5 gram would require a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

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

Statin Medications and Ezetimibe Tier-2 Approval Criteria:

1. Member must have ~~a~~ documented trials with atorvastatin and rosuvastatin, consisting of at least 8 weeks of continuous therapy each, titrated to a dose of at least 40mg atorvastatin and 20mg rosuvastatin, which did not yield adequate LDL reduction. ~~The minimum starting dose of the Tier-2 medication may only be at the moderate-to-high LDL lowering doses (20mg rosuvastatin or higher)~~; or
2. A documented adverse effect or contraindication to all available lower tiered products; or
3. ~~A clinical exception will apply for Crestor® (rosuvastatin) 40mg for high-risk members hospitalized for recent acute myocardial infarction or acute coronary syndrome, or for pediatric members with homozygous familial hypercholesterolemia (HoFH); and~~
4. Clinical exceptions for ezetimibe include the following:
    a. Documented active liver disease; or
    b. Documented unexplained, persistent elevations of serum transaminases; or
    c. Documented statin-related myopathy.

Statin Medications and Ezetimibe Special Prior Authorization (PA) Approval Criteria:

1. Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used.

Statin Medications and Ezetimibe*		
Tier-1	**Tier-2**	**Special PA**
atorvastatin (Lipitor®)	ezetimibe (Zetia®)	fluvastatin (Lescol® & Lescol® XL)
lovastatin (Mevacor®)		lovastatin (Altoprev®)
pravastatin (Pravachol®)		pitavastatin **calcium** (Livalo®)
rosuvastatin (Crestor®)		**pitavastatin magnesium (Zypitamag™)**
simvastatin (Zocor®)		**pitavastatin sodium (Nikita™)**
		simvastatin/ezetimibe (Vytorin®)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
~~*Crestor® 5mg and Crestor® 10mg require special reason for use.~~

Omega-3 Fatty Acids Approval Criteria:

1. Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides ≥500mg/dL), and controlled diabetes (fasting glucose <150mg/dL at the time of triglycerides measurement and HgA1c <7.5%); and
2. Previous failure with both nicotinic acid and fibric acid medications; and
3. Use of Vascepa® or Epanova® requires a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®).
4. Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Utilization Details of Antihyperlipidemics: Fiscal Year 2017

Statin Medications and Ezetimibe

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ATORVASTATIN PRODUCTS						
ATORVASTATIN TAB 40MG	12,303	3,674	$147,935.61	$0.26	$12.02	14.74%
ATORVASTATIN TAB 20MG	9,576	2,875	$110,715.54	$0.25	$11.56	11.03%
ATORVASTATIN TAB 10MG	6,002	1,608	$61,782.87	$0.25	$10.29	6.16%
ATORVASTATIN TAB 80MG	4,177	1,268	$56,363.54	$0.27	$13.49	5.62%
SUBTOTAL	**32,058**	**9,425**	**$376,797.56**	**$0.26**	**$11.75**	**37.55%**
SIMVASTATIN PRODUCTS						
SIMVASTATIN TAB 20MG	6,232	1,698	$41,430.42	$0.14	$6.65	4.13%
SIMVASTATIN TAB 40MG	4,601	1,257	$33,271.41	$0.13	$7.23	3.32%
SIMVASTATIN TAB 10MG	2,062	558	$14,575.15	$0.16	$7.07	1.45%
SIMVASTATIN TAB 80MG	357	109	$3,214.10	$0.16	$9.00	0.32%
SIMVASTATIN TAB 5MG	116	32	$905.20	$0.21	$7.80	0.09%
SUBTOTAL	**13,368**	**3,654**	**$93,396.28**	**$0.14**	**$6.99**	**9.31%**
PRAVASTATIN PRODUCTS						
PRAVASTATIN TAB 40MG	5,560	1,474	$91,378.81	$0.33	$16.44	9.11%
PRAVASTATIN TAB 20MG	3,437	917	$46,993.57	$0.29	$13.67	4.68%
PRAVASTATIN TAB 80MG	1,017	255	$24,279.88	$0.47	$23.87	2.42%
PRAVASTATIN TAB 10MG	856	251	$12,883.13	$0.32	$15.05	1.28%
SUBTOTAL	**10,870**	**2,897**	**$175,535.39**	**$0.33**	**$16.15**	**17.49%**
LOVASTATIN PRODUCTS						
LOVASTATIN TAB 20MG	1,891	624	$13,911.64	$0.15	$7.36	1.39%
LOVASTATIN TAB 40MG	1,173	341	$10,989.98	$0.19	$9.37	1.10%
SUBTOTAL	**3,064**	**965**	**$24,901.62**	**$0.16**	**$8.13**	**2.48%**
TIER-1 SUBTOTAL	**59,360**	**15,323***	**$670,630.85**	**$0.24**	**$11.30**	**66.83%**
ROSUVASTATIN PRODUCTS						
ROSUVASTATIN TAB 20MG	539	143	$11,874.37	$0.44	$22.03	1.18%
ROSUVASTATIN TAB 40MG	454	116	$10,448.17	$0.47	$23.01	1.04%
ROSUVASTATIN TAB 10MG	67	21	$1,345.92	$0.40	$20.09	0.13%
ROSUVASTATIN TAB 5MG	36	12	$1,079.88	$0.65	$30.00	0.11%
CRESTOR TAB 20MG	32	32	$17,196.23	$8.91	$537.38	1.71%
CRESTOR TAB 40MG	28	28	$10,563.63	$8.19	$377.27	1.05%
CRESTOR TAB 10MG	3	3	$1,831.98	$8.72	$610.66	0.18%
CRESTOR TAB 5MG	2	2	$519.96	$8.67	$259.98	0.05%
SUBTOTAL	**1,161**	**357**	**$54,860.14**	**$0.95**	**$47.25**	**5.47%**
EZETIMIBE PRODUCTS						
ZETIA TAB 10MG	482	117	$207,048.67	$9.81	$429.56	20.63%
EZETIMIBE TAB 10MG	64	35	$21,147.60	$7.50	$330.43	2.11%
SUBTOTAL	**546**	**152**	**$228,196.27**	**$9.54**	**$417.94**	**22.74%**
TIER-2 SUBTOTAL	**1,707**	**393***	**$283,056.41**	**$3.46**	**$165.82**	**28.21%**
EZETIMIBE/SIMVASTATIN PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
VYTORIN TAB 10-40MG	52	11	$25,976.23	$9.41	$499.54	2.59%
VYTORIN TAB 10-20MG	4	1	$3,522.34	$9.78	$880.59	0.35%
VYTORIN TAB 10-80MG	4	1	$3,592.63	$9.98	$898.16	0.36%
EZETIM/SIMVA TAB 10-40MG	4	4	$1,145.02	$6.36	$286.26	0.11%
SUBTOTAL	**64**	**17**	**$34,236.22**	**$9.35**	**$534.94**	**3.41%**
PITAVASTATIN PRODUCTS						
LIVALO TAB 4MG	24	5	$9,382.62	$7.82	$390.94	0.94%
LIVALO TAB 2MG	16	4	$6,136.02	$7.87	$383.50	0.61%
SUBTOTAL	**40**	**9**	**$15,518.64**	**$7.84**	**$387.97**	**1.55%**
SPECIAL PA SUBTOTAL	**104**	**22***	**$49,754.86**	**$8.82**	**$478.41**	**4.96%**
TOTAL	**61,171**	**15,577***	**$1,003,442.12**	**$0.34**	**$16.40**	**100.00%**

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

Omega-3 Fatty Acids

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
OMEGA-3-ACID ETHYL ESTERS PRODUCTS						
OMEGA-3-ACID CAP 1GM	196	24	$18,830.63	$3.12	$96.07	90.22%
SUBTOTAL	**196**	**24**	**$18,830.63**	**$3.12**	**$96.07**	**90.22%**
ICOSAPENT ETHYL PRODUCTS						
VASCEPA CAP 1GM	8	1	$2,040.94	$8.50	$255.12	9.78%
SUBTOTAL	**8**	**1**	**$2,040.94**	**$8.50**	**$255.12**	**9.78%**
TOTAL	**204**	**25***	**$20,871.57**	**$3.33**	**$102.31**	**100.00%**

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

Juxtapid® (Lomitapide) and Kynamro® (Mipomersen)

There was no utilization of Juxtapid® or Kynamro® during fiscal year 2017.

PCSK9 Inhibitors

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ALIROCUMAB PRODUCTS						
PRALUENT INJ 75MG/ML	3	1	$3,546.96	$42.23	$1,182.32	76.54%
SUBTOTAL	**3**	**1**	**$3,546.96**	**$42.23**	**$1,182.32**	**76.54%**
EVOLOCUMAB PRODUCTS						
REPATHA SURE INJ 140MG/ML	1	1	$1,087.30	$38.83	$1,087.30	23.46%
SUBTOTAL	**1**	**1**	**$1,087.30**	**$38.83**	**$1,087.30**	**23.46%**
TOTAL	**4**	**2***	**$4,634.26**	**$41.38**	**$1,158.57**	**100.00%**

*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 06/2017. Last accessed 08/16/2017.

[2] U.S. Food and Drug Administration (FDA). ANDA Approval: Ezetimibe Tablets. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=078560. Issued 06/26/2015. Last accessed 08/16/2017.

[3] U.S. Food and Drug Administration (FDA). ANDA Approval: Pitavastatin Calcium Tablets. Available online at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=078560. Issued 12/20/2016. Last accessed 08/16/2017.

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Appendix S

Fiscal Year 2017 Annual Review of Alzheimer's Disease Medications and 30-Day Notice to Prior Authorize Namenda XR® (Memantine Extended-Release Capsules)

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

Alzheimer's Disease Medications Approval Criteria:

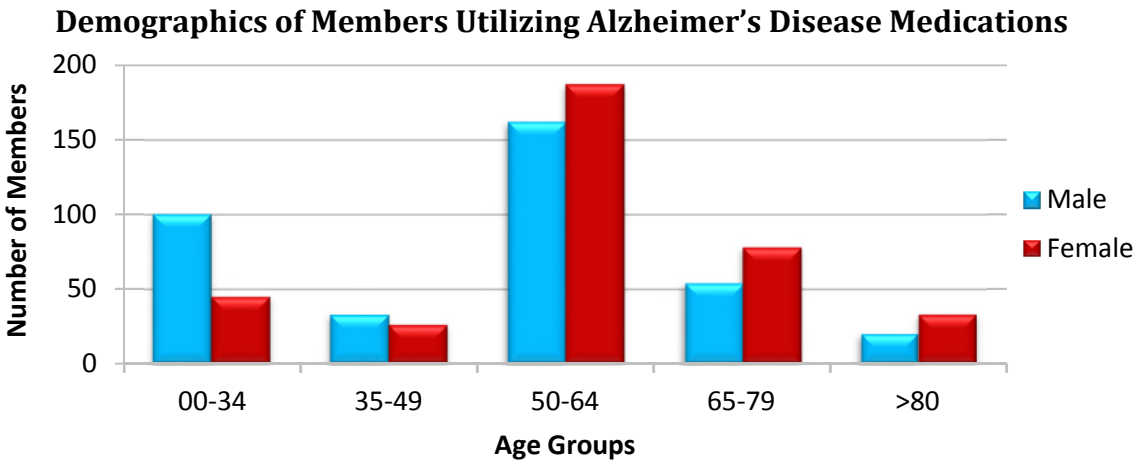
1. Special formulation products including oral solutions, transdermal patches, and other convenience formulations require prior authorization with the following approval criteria:
    a. A patient-specific, clinically significant reason why the special formulation is necessary in place of the standard formulation.
2. An age restriction for ages 0 to 50 years applies to all Alzheimer's disease medications. Members older than 50 years of age can receive regular formulations without prior authorization. Members younger than 50 years of age will require prior authorization with the following criteria:
    a. An FDA approved diagnosis; or
    b. Other patient-specific, clinically significant information supporting the use of the medication.
3. Namzaric™ (Memantine Extended-Release [ER]/Donepezil) Approval Criteria:
    a. Member must have a patient-specific, clinically significant reason why the separate products cannot be used over this combination product; and
    b. A quantity limit of 30 capsules per 30 days will apply.

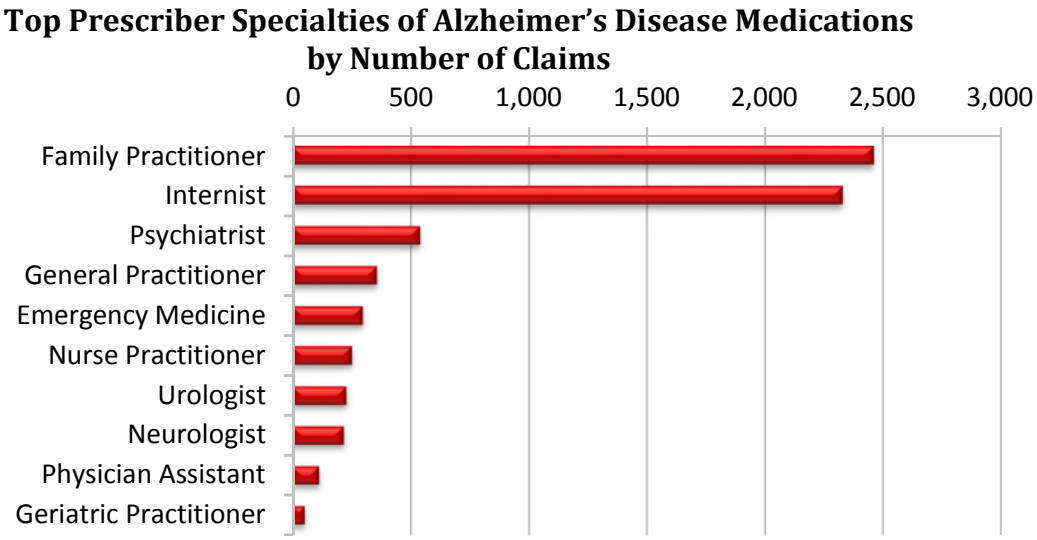
Utilization of Alzheimer's Disease Medications: Fiscal Year 2017

Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	764	7,401	$854,328.86	$115.43	$3.94	312,521	216,864
2017	738	7,010	$648,036.33	$92.44	$3.11	300,738	208,471
% Change	**-3.40%**	**-5.30%**	**-24.10%**	**-19.90%**	**-21.10%**	**-3.80%**	**-3.90%**
Change	**-26**	**-391**	**-$206,292.53**	**-$22.99**	**-$0.83**	**-11,783**	**-8,393**

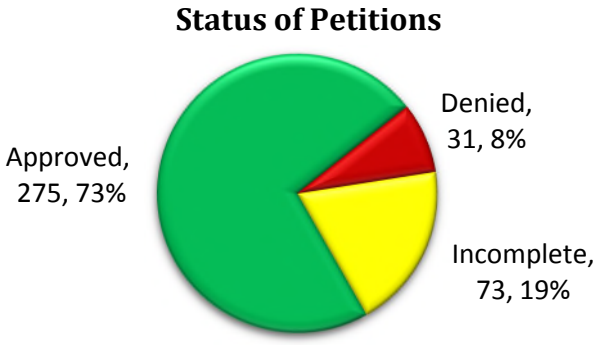
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.





Prior Authorization of Alzheimer's Disease Medications

There were 379 prior authorization requests submitted for Alzheimer's disease medications during fiscal year 2017. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expiration(s):

- Namenda XR® (memantine ER capsules): September 2029
- Namzaric™ (memantine ER/donepezil): December 2029

Pipeline:

- **August 2016:** Eli Lilly and Co. and AstraZeneca received U.S. Food and Drug Administration (FDA) fast track designation for their investigational treatment for early Alzheimer's disease (AD), AZD3293, an inhibitor of the beta-site amyloid precursor protein cleaving enzyme 1 (BACE1). The rationale of BACE inhibition is that it represents an upstream interference with the amyloid cascade. AZD3293 is one of several BACE1/2 inhibitors currently in development. In July 2016, a second Phase 3 trial, DAYBREAK-ALZ, began and is set to run until 2021.
- **November 2016:** Eli Lilly and Co. announced solanezumab did not meet the primary endpoint in the EXPEDITION3 clinical trial, a Phase 3 study of solanezumab in patients with mild dementia due to AD. Patients treated with solanezumab did not experience a statistically significant slowing in cognitive decline compared to patients treated with placebo ($p=0.095$), as measured by the ADAS-Cog_{14} (Alzheimer's Disease Assessment Scale-Cognitive subscale). While the study results, including many secondary clinical endpoints, directionally favored solanezumab, the magnitudes of treatment differences were small. There were no new safety signals identified in the study. Lilly will not pursue regulatory submissions for solanezumab for the treatment of mild dementia due to AD.
- **December 2016:** Biogen presented positive results from the Phase 1 (PRIME) study of aducanumab, an investigational treatment for early AD. Aducanumab is currently being evaluated in two global Phase 3 studies, ENGAGE and EMERGE, which are designed to evaluate its safety and efficacy in slowing cognitive impairment and the progression of disability in people with early AD. In September 2016, the FDA accepted aducanumab into its Fast Track program.
- **December 2016:** AstraZeneca and Eli Lilly and Co. announced a worldwide agreement to co-develop MEDI1814, an antibody selective for amyloid-beta 42 (Aβ42), currently in Phase 1 trials, as a potential disease-modifying treatment for AD. The build-up of plaques in the brain containing the peptide amyloid-beta (Aβ) is one of the characteristics of AD. MEDI1814 binds selectively to Aβ42, a form of Aβ which is particularly associated with the disease. MEDI1814 dose-dependently reduces levels of this peptide, potentially slowing the progression of AD.
- **February 2017:** Merck announced the discontinuation of the study known as EPOCH, a Phase 2/3 study evaluating verubecestat, an investigational small molecule inhibitor of BACE1, in people with mild-to-moderate AD. Merck stopped the study following recommendations from an external board which determined that there was "virtually no chance of finding a positive clinical effect." The committee noted that safety signals observed in the study "are not sufficient to warrant stopping the study" and recommended that study APECS, which is evaluating verubecestat in people with

prodromal AD, continue unchanged. Results from the APECS study are expected in February 2019.

- **February 2017:** AC Immune and Genetech announced the start of a second Phase 3 clinical trial of the Alzheimer's disease therapy crenezumab, an anti- Aβ antibody. CREAD2 will recruit 750 patients with prodromal or mild AD, and complements the current Phase 3 CREAD1 trial of 750 participants with prodromal or mild AD, expected to read out in 2020.
- **April 2017:** Biogen announced an agreement to exclusively license BMS-986168, a Phase-2-ready experimental medicine with potential in AD and progressive supranuclear palsy (PSP). BMS-986168 is a humanized IgG4 monoclonal antibody targeting extracellular tau, the protein that forms the deposits, or tangles, in the brain associated with AD and other neurodegenerative tauopathies such as PSP. PSP is a rare and devastating condition that affects movement, vision, speech, and cognitive function. Biogen plans to rapidly initiate Phase 2 studies for BMS-986168 in both PSP and AD. In 2015, both the European Medicines Agency (EMA) and the FDA assigned orphan drug status to BMS-986168.
- **July 2017:** Neurotrope presented clinical results from its recently completed 13-week, randomized, double-blind, placebo-controlled Phase 2 trial demonstrating that moderate-to-severe AD patients treated with 20mcg of bryostatin-1 showed preliminary evidence of sustained improvement in cognition compared to placebo, however, the results were not statistically significant. Byrostatin-1 40mcg was also studied but no therapeutic signal was observed. Bryostatin-1 is a protein kinase C epsilon (PKCε) activator that works through synaptic growth factors, as well as anti-amyloid and anti-tangle signaling pathways in the brain. It has been shown in preclinical efficacy studies to induce the growth of mature synapses in the brain and prevent neuronal death. Neurotrope plans to move forward with their clinical development program of bryostatin-1.
- **July 2017:** Axsome Therapeutics announced that the first patient has been enrolled in the ADVANCE-1 Phase 2/3 trial evaluating the safety and effectiveness of AXS-05 for the treatment of agitation in AD patients. AXS-05 is an investigational drug that combines dextromethorphan and bupropion and is being developed for the treatment of central nervous system disorders. Dextromethorphan is an N-methyl-d-aspartate (NMDA) receptor antagonist, sigma-1 receptor agonist, and serotonin and norepinephrine reuptake inhibitor. Bupropion is a norepinephrine and dopamine reuptake inhibitor and a nicotinic acetylcholine receptor antagonist used to increase the bioavailability of dextromethorphan. AXS-05 is currently in a Phase 3 trial for the treatment of treatment-resistant depression (TRD). AXS-05 was granted fast track status by the FDA in early 2017.

Namenda XR® (Memantine Extended-Release Capsules) Product Summary[13]

Indication(s): Namenda XR® (memantine extended-release [ER] capsules) is an NMDA receptor antagonist indicated for the treatment of moderate-to-severe dementia of the Alzheimer's type.

Dosing:

- Namenda XR® is supplied as an extended-release capsule in the following strengths: 7mg, 14mg, 21mg, and 28mg.
- The recommended starting dose of memantine ER is 7mg once daily.
- Memantine ER capsules can be taken intact or may be opened, sprinkled on applesauce, and then swallowed. The entire contents of memantine ER should be consumed; the dose should not be divided.
- The dose should be increased in 7mg increments to the recommended maintenance dose of 28mg once daily. The minimum recommended interval between dose increases is one week.
- The recommended maintenance dose for patients with severe renal impairment is 14mg once daily.
- In patients switching from memantine to memantine ER capsules, it is recommended that a patient who is on a regimen of 10mg twice daily of Namenda be switched to memantine ER 28mg once daily capsules the day following the last dose of 10mg memantine. There is no study addressing the comparative efficacy of these two regimens.

Mechanism of Action: Persistent activation of central nervous system NMDA receptors by the excitatory amino acid glutamate has been hypothesized to contribute to the symptomatology of AD. Memantine is postulated to exert its therapeutic effect through its action as a low-to-moderate affinity uncompetitive (open-channel) NMDA receptor antagonist which binds preferentially to the NMDA receptor-operated cation channels. There is no evidence that memantine prevents or slows neurodegeneration in patients with AD.

Contraindication(s):

- Memantine ER is contraindicated in patients with a known hypersensitivity to memantine hydrochloride or to any excipients used in the formulation.

Warnings and Precautions:

- Increased Plasma Levels of Memantine: Conditions that raise urine pH may decrease the urinary elimination of memantine resulting in increased plasma levels of memantine.

Adverse Reactions: The most common observed adverse reactions occurring at a frequency of at least 5% and greater than placebo with administration of memantine ER 28mg per day were headache, diarrhea, and dizziness.

Drug Interactions:

- Drugs That Make the Urine Alkaline: The clearance of memantine was reduced by about 80% under alkaline urine conditions at pH 8. Therefore, alterations of urine pH towards alkaline conditions may lead to an accumulation of the drug with a possible increase in adverse effects. 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 or severe infections of the urinary tract). Memantine should be used with caution under these conditions.

- Use with Other NMDA Antagonists: The combined use of memantine ER with other NMDA antagonists (e.g., amantadine, ketamine, dextromethorphan) has not been systematically evaluated and such use should be approached with caution.

Use in Specific Populations:

- Pregnancy Category B: There are no adequate and well-controlled studies of memantine in pregnant women. Memantine ER should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: It is not known whether memantine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when memantine ER is administered to a nursing mother.
- Pediatric Use: The safety and effectiveness of memantine ER have not been established in pediatric patients. Memantine failed to demonstrate efficacy in two 12-week controlled clinical studies of 578 pediatric patients 6 to 12 years of age with autism spectrum disorders (ASD), including autism, Asperger's disorder, and Pervasive Development Disorder-Not Otherwise Specified (PDD-NOS). Memantine has not been studied in pediatric patients under 6 years of age or over 12 years of age.
- Geriatric Use: The majority of people with AD are 65 years and older. In the clinical study of memantine ER, the mean age of patients was approximately 77 years; over 91% of patients were 65 years and older, 67% were 75 years and older, and 14% were at or above 85 years of age. There were no clinically meaningful differences in most adverse reactions reported by patients groups ≥65 years of age and <65 years of age.
- Renal Impairment: No dosage adjustment is needed in patients with mild or moderate renal impairment. A dosage reduction is recommended in patients with severe renal impairment. *See dosing section*.
- Hepatic Impairment: No dosage adjustment is needed in patients with mild or moderate hepatic impairment. Memantine ER was not studied in patients with severe hepatic impairment.

Efficacy:

- The effectiveness of memantine ER as a treatment for patients with moderate-to-severe AD was based on the results of a randomized double-blind, placebo-controlled, 24-week study. The study involved 677 outpatients with moderate-to-severe AD (diagnosed by Diagnostic and Statistical Manual of Mental Disorders 4th Edition [DSM-IV] criteria and National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association [NINCDS-ADRDA] criteria for AD with a Mini Mental State Examination [MMSE] score ≥3 and ≤14 at screening and baseline) receiving acetylcholinesterase inhibitor (AChEI) therapy at a stable dose for three months prior to screening.
- The co-primary efficacy parameters were Severe Impairment Battery (SIB) and the Clinician's Interview-Based Impression of Change (CIBIC-Plus). The SIB examines selected aspects of cognitive performance including elements of attention, orientation, language, memory, visuospatial ability, construction, praxis, and social interaction. The SIB scoring range is from 0 to 100, with lower scores indicating greater cognitive improvement. CIBIC-Plus required the use of caregiver information and is not a

standardized instrument like the SIB. CIBIC-Plus cannot be compared directly with the results of CIBIC-Plus evaluations from other clinical trials due to a variety of formats used. The CIBIC-Plus used in this trial was a structured instrument based on comprehensive evaluation at baseline and subsequent time-points of four domains: general (overall clinical status), functional (including activities of daily living), cognitive, and behavioral. The CIBIC-Plus is scored as a seven point categorical rating, ranging from a score of 1 indicating "marked improvement," a score of 4 indicating "no change," and a score of 7 indicating "marked worsening."

- At 24 weeks of treatment, the mean difference in SIB change scores for the memantine ER 28mg/AChEI-treated combination therapy patients compared to the patients on placebo/AChEI was 2.6 units. Memantine ER/AChEI treatment was statistically significantly superior to placebo/AChEI treatment. The mean difference in CIBIC-Plus scores at 24 weeks treatment for memantine ER 28mg/AChEI-treated patients compared to placebo/AChEI was 0.3 units making memantine ER combination treatment statistically significantly superior to placebo/AChEI treatment.

- **Cost Comparison:**

Medication	Cost Per Unit	Cost Per Month	Cost Per Year
Namenda XR® (memantine ER) 28mg capsule	**$12.42**	**$372.60**	**$4,471.20**
memantine 5mg tablet	$0.18	$10.80	$129.60
donepezil 23mg tablet	$1.71	$51.30	$615.60

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.
Unit = capsule or tablet

Recommendations

The College of Pharmacy recommends the prior authorization of Namenda XR® (memantine ER capsules) with the following criteria:

Namenda XR® (Memantine ER Capsules) Approval Criteria:

1. An FDA approved diagnosis for the treatment of moderate-to-severe Alzheimer's type dementia; and
2. A patient-specific, clinically significant reason why the member cannot use memantine immediate-release tablets.

Utilization Details of Alzheimer's Disease Medications: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MEMANTINE PRODUCTS						
MEMANTINE TAB HCL 10MG	2,713	317	$53,543.34	$0.68	$19.74	8.26%
NAMENDA XR CAP 28MG	1,507	144	$498,214.48	$12.48	$330.60	76.88%
MEMANTINE TAB HCL 5MG	370	85	$6,841.43	$0.64	$18.49	1.06%
NAMENDA XR CAP 14MG	75	11	$19,632.04	$12.72	$261.76	3.03%
NAMENDA XR CAP 21MG	20	8	$6,210.34	$12.62	$310.52	0.96%
NAMENDA XR CAP 7MG	16	8	$5,101.47	$13.60	$318.84	0.79%
MEMANTINE HC SOL 2MG/ML	12	2	$4,908.78	$13.64	$409.07	0.76%
NAMENDA XR CAP TITRATION	5	4	$1,740.69	$12.43	$348.14	0.27%
NAMENDA SOL 10MG/5ML	5	2	$2,935.55	$19.57	$587.11	0.45%
SUBTOTAL	**4,723**	**581**	**$599,128.12**	**$4.52**	**$126.85**	**92.46%**
DONEPEZIL PRODUCTS						
DONEPEZIL TAB 10MG	1,602	258	$14,069.43	$0.26	$8.78	2.17%
DONEPEZIL TAB 5MG	475	139	$4,034.41	$0.25	$8.49	0.62%
SUBTOTAL	**2,077**	**397**	**$18,103.84**	**$0.26**	**$8.72**	**2.79%**
RIVASTIGMINE PRODUCTS						
RIVASTIGMINE CAP 3MG	35	7	$2,579.90	$2.46	$73.71	0.40%
RIVASTIGMINE CAP 6MG	35	6	$2,948.87	$2.96	$84.25	0.46%
RIVASTIGMINE CAP 1.5MG	27	6	$2,003.04	$2.50	$74.19	0.31%
RIVASTIGMINE DIS 13.3MG/24	13	1	$2,637.69	$10.26	$202.90	0.41%
RIVASTIGMINE DIS 4.6MG/24	12	4	$3,658.08	$10.22	$304.84	0.56%
RIVASTIGMINE DIS 9.5MG/24	12	4	$4,347.92	$12.08	$362.33	0.67%
RIVASTIGMINE CAP 4.5MG	7	2	$618.79	$2.95	$88.40	0.10%
EXELON DIS 4.6MG/24	2	1	$1,149.56	$19.16	$574.78	0.18%
EXELON DIS 13.3MG/24	1	1	$271.79	$19.41	$271.79	0.04%
SUBTOTAL	**144**	**32**	**$20,215.64**	**$4.92**	**$140.39**	**3.13%**
GALANTAMINE PRODUCTS						
GALANTAMINE TAB 4MG	19	3	$906.10	$1.63	$47.69	0.14%
GALANTAMINE CAP 8MG	15	2	$1,159.73	$2.58	$77.32	0.18%
GALANTAMINE TAB 8MG	9	3	$549.93	$1.93	$61.10	0.08%
SUBTOTAL	**43**	**8**	**$2,615.76**	**$2.03**	**$60.83**	**0.40%**
MEMANTINE/DONEPEZIL PRODUCTS						
NAMZARIC CAP 28-10MG	23	5	$7,972.97	$11.56	$346.65	1.23%
SUBTOTAL	**23**	**5**	**$7,972.97**	**$11.56**	**$346.65**	**1.23%**
TOTAL	**7,010**	**738***	**$648,036.33**	**$3.11**	**$92.44**	**100%**

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

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Appendix T

Fiscal Year 2017 Annual Review of Anticoagulants and Platelet Aggregation Inhibitors

Oklahoma Health Care Authority
September 2017

Current Prior Authorization Criteria

Plavix® 300mg (Clopidogrel) Approval Criteria:

1. An FDA approved diagnosis of non-ST-segment elevated acute coronary syndrome or ST-segment elevated acute myocardial infarction; and
2. Approvals will be for one dose only of 300mg.

Brilinta® (Ticagrelor) Approval Criteria:

1. The first 365 days of therapy with Brilinta® 90mg twice daily does not require prior authorization.
2. After the first 365 days, a patient-specific, clinically significant reason for continuing the 90mg twice daily dosage will need to be provided or the member should be switched to the 60mg twice daily dosage.
3. Approvals will be for the duration of one year.

Zontivity® (Vorapaxar) Approval Criteria:

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

Pradaxa® (Dabigatran) Approval Criteria:

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

Xarelto® (Rivaroxaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), or to reduce the risk of recurrent DVT and PE; or
    c. Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery; and
2. Xarelto® (rivaroxaban) 15mg and 20mg:
    a. A diagnosis of non-valvular atrial fibrillation, DVT, PE, or prophylaxis of recurrent DVT or PE will be required; or
3. Xarelto® (rivaroxaban) 10mg:
    a. One prescription for up to 35 days of therapy is allowed without prior authorization every 6 months to allow for DVT prophylaxis use in patients following hip or knee replacement surgery.

Eliquis® (Apixaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Non-valvular atrial fibrillation; or
    b. Treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and PE following initial therapy; or
    c. PE or DVT prophylaxis in patients who have had hip or knee replacement surgery.

Savaysa® (Edoxaban) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. To reduce the risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation; or
    b. For the treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant; and
2. Requests for therapy for the treatment of DVT and PE must verify that the member has undergone 5 to 10 days of initial therapy with a parenteral anticoagulant; and
3. Member must not have a creatinine clearance (CrCl) greater than 95mL/min due to increased risk of ischemic stroke compared to warfarin at the highest dose studied (60mg); and
4. A quantity limit of 30 tablets per 30 days will apply.

Aggrenox® (Aspirin/Dipyridamole Extended-Release) Approval Criteria:

1. An FDA approved indication for the prophylaxis of recurrent thromboembolic stroke in patients who have had transient ischemia of the brain or completed ischemic stroke due to thrombosis; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use immediate-release dipyridamole and over-the-counter (OTC) aspirin in place of Aggrenox® must be provided.
4. A quantity limit of 60 capsules for a 30 day supply will apply.

Utilization of Anticoagulants and Platelet Aggregation Inhibitors: Fiscal Year 2017

Comparison of Fiscal Years: Anticoagulants

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,091	11,780	$1,462,344.27	$124.14	$3.73	473,463	391,884
2017	2,227	12,006	$2,091,723.07	$174.22	$5.26	509,083	397,730
% Change	**6.50%**	**1.90%**	**43.00%**	**40.30%**	**41.00%**	**7.50%**	**1.50%**
Change	**136**	**226**	**$629,378.80**	**$50.08**	**$1.53**	**35,620**	**5,846**

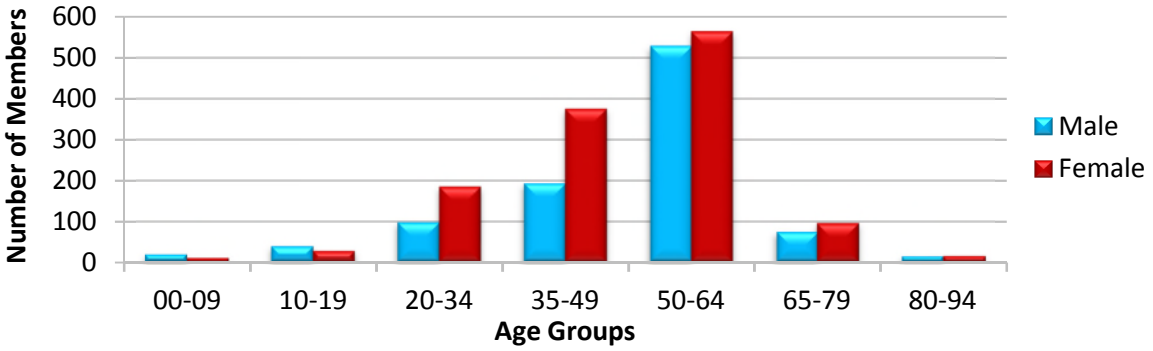
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Comparison of Fiscal Years: Platelet Aggregation Inhibitors

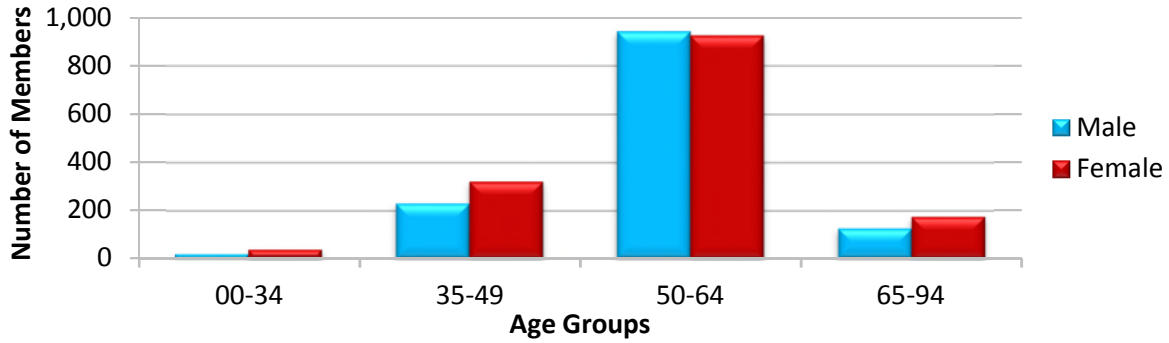
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	2,803	12,597	$741,758.51	$58.88	$1.39	560,831	532,083
2017	2,772	12,012	$675,276.32	$56.22	$1.29	549,136	524,358
% Change	**-1.10%**	**-4.60%**	**-9.00%**	**-4.50%**	**-7.20%**	**-2.10%**	**-1.50%**
Change	**-31**	**-585**	**-$66,482.19**	**-$2.66**	**-$0.10**	**-11,695**	**-7,725**

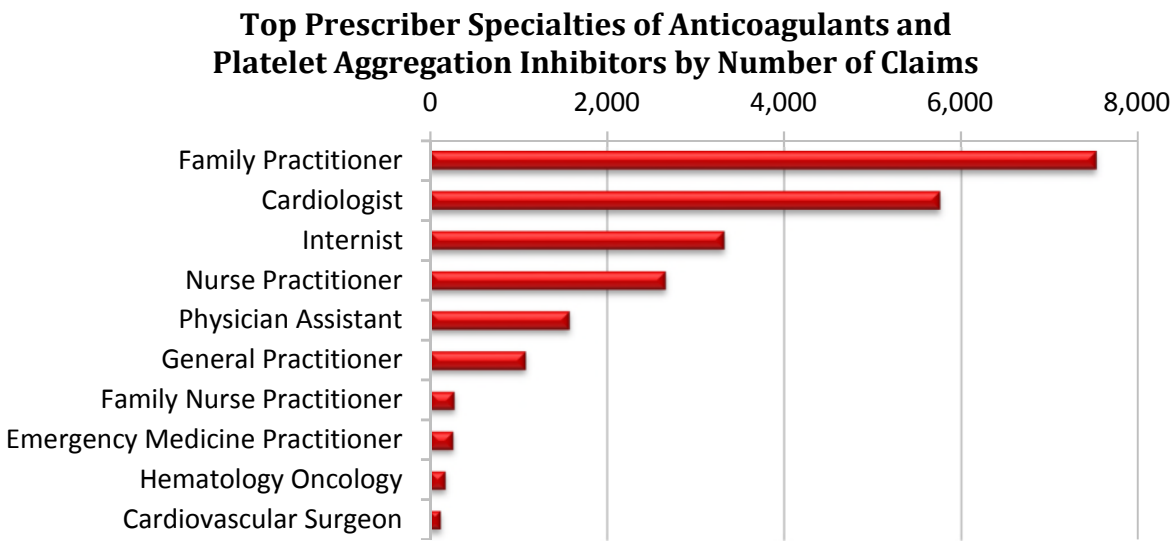
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Anticoagulants



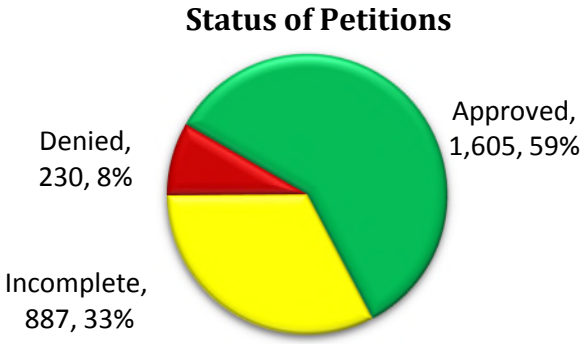
Demographics of Members Utilizing Platelet Aggregation Inhibitors





Prior Authorization of Anticoagulants and Platelet Aggregation Inhibitors

There were 2,722 prior authorization requests submitted for the anticoagulants and platelet aggregation inhibitors category during fiscal year 2017. The following chart shows the status of the submitted petitions.



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

Anticipated Patent/Exclusivity Expiration(s):

- Effient® (prasugrel): July 2023
- Zontivity® (vorapaxar): April 2024
- Savaysa® (edoxaban): March 2028
- Brilinta® (ticagrelor): April 2030
- Pradaxa® (dabigatran): January 2031
- Eliquis® (apixaban): February 2031
- Xarelto® (rivaroxaban): February 2034

News:

- **March 2017:** Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism was published in *The New England Journal of Medicine*. The randomized, double-blind, Phase 3 study assigned 3,396 patients with venous

thromboembolism (VTE) to receive either 20mg or 10mg rivaroxaban (Xarelto®) once-daily or 100mg of aspirin daily. The primary efficacy outcome was measured by symptomatic recurrent fatal or nonfatal VTE. The primary efficacy outcome occurred in 17 of 1,107 patients (1.5%) receiving 20mg of rivaroxaban and in 13 of 1,127 patients (1.2%) receiving 10mg of rivaroxaban, as compared with 50 of 1,131 patients (4.4%) receiving aspirin (hazard ratio [HR] for 20mg of rivaroxaban vs. aspirin, 0.34; 95% confidence interval [CI] [0.20, 0.59]; HR for 10mg of rivaroxaban vs. aspirin, 0.26; 95% CI [0.14, 0.47]; p<0.001 for both comparisons). The incidence of adverse events were similar in all three groups. The risk of a recurrent event was significantly lower with rivaroxaban at either a treatment dose (20mg) or a prophylactic dose (10mg) than with aspirin, without a significant increase in bleeding rates in patients with VTE needing continued anticoagulation treatment.

- **March 2017:** Results from GEMINI-ACS-1 were published in *The Lancet*. The GEMINI-ACS-1 trial is the first large attempt (n=3,037 patients from 371 sites in 21 countries) to replace the acute coronary syndrome therapy cornerstone of dual antiplatelet therapy consisting of aspirin and a P2Y12 inhibitor. A total of 1,518 patients were randomly assigned to receive aspirin 100mg daily and 1,519 patients were randomized to receive rivaroxaban 2.5mg twice daily within 10 days after admission for the index acute coronary syndromes. Patients also received a minimum of 180 days of treatment in conjunction with either clopidogrel or ticagrelor. The primary endpoint was thrombolysis in myocardial infarction (TIMI) or clinically significant bleeding not related to coronary artery bypass grafting (major, minor, or requiring medical attention). The primary endpoint was similar between groups and occurred in 80 (5%) patients in the rivaroxaban group and 74 (5%) patients in the aspirin group (HR 1.09; 95% CI [0.80, 1.50]; p=0.58) with no interaction between randomized treatment and P2Y12 inhibitor type. However, almost all bleeding metrics were non-significantly lower with aspirin and a 50% increased bleed rate with rivaroxaban cannot be excluded. The primary endpoint was non-significantly higher with ticagrelor versus clopidogrel, irrespective of aspirin or rivaroxaban therapy. The totality of the evidence of GEMINI-ACS-1 favors aspirin.
- **May 2017:** Influence of Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation was published in the *Journal of the American College of Cardiology*. Researchers reviewed data from the National Cardiovascular Data Registry, PINNACLE, focusing on 655,000 patients who were treated at cardiologists' offices for atrial fibrillation. Results indicated that, over the nearly 7-year study period, use of oral anticoagulants (OACs) didn't increase as much as anticipated, considering the new availability of direct oral anticoagulants (DOACs). In fact, prescriptions rose only from 52.4% to 60.7% for patients who met the criteria to use OACs for stroke prevention. The upshot: 40% of atrial fibrillation patients with elevated stroke risk still weren't receiving therapy. Furthermore, the review uncovered significant variations in prescribing practices of OACs and DOACs with variances in prescribing from 10% to 70%.
- **June 2017:** The Agency for Healthcare Research and Quality (AHRQ) released an updated systematic review that assessed the efficacy and safety of various venous thromboembolism (VTE) prevention methods following major orthopedic surgery

including total knee replacement, total hip replacement, and hip fracture surgery. The review found there are few head-to-head treatment comparisons that have sufficient evidence and most studies evaluated low molecular weight heparin (LMWH) versus low-risk interventions such as aspirin and mechanical devices.

- **July 2017:** The full cohort analysis of the Reversal Effects of Idarucizumab in Patients on Active Dabigatran (RE-VERSE AD) study results were published in *The New England Journal of Medicine* in July 2017. Idarucizumab is a humanized antibody-binding fragment (Fab) that essentially irreversibly binds free and thrombin-bound dabigatran with high affinity. Idarucizumab is specific for dabigatran and does not reverse the effects of heparin or other anticoagulants. After intravenous administration, it has a rapid onset of action and is short-lived in the circulation, with a half-life of about 45 minutes. The results of the RE-VERSE AD study validate the interim analysis as well as supports the U.S. Food and Drug Administration (FDA) approval of Praxbind® (idarucizumab) in October of 2015.

Guideline Update(s):

- **October 2016:** The 2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation was published in *The Canadian Journal of Cardiology*. An important change involves patients who suffer from coronary artery disease in addition to atrial fibrillation. Non-vitamin K antagonist oral anticoagulants are the preferred treatment over warfarin in those patients. The update also makes specific recommendations based on a patient's stroke risk.
- **February 2017:** The 2017 American College of Cardiology (ACC) Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation was published in the *Journal of American College of Cardiology*. The evidence-based recommendations address how and when to temporarily stop anticoagulants before scheduled surgeries.
- **March 2017:** The 2016 American Heart Association (AHA)/ACC Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease: Executive Summary was published in *Circulation*. Antiplatelet therapy with aspirin alone (range, 75 to 325mg/day) or clopidogrel alone (75mg/day) is recommended to reduce myocardial infarction (MI), stroke, and vascular death in patients with symptomatic peripheral artery disease.

Recommendations

The College of Pharmacy does not recommend any changes to the anticoagulants and platelet aggregation inhibitors prior authorization criteria at this time.

Utilization Details of Anticoagulants: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
WARFARIN PRODUCTS					
WARFARIN TAB 5MG	2,188	602	$21,899.12	$0.27	$10.01

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
WARFARIN TAB 1MG	734	206	$8,382.92	$0.33	$11.42
WARFARIN TAB 4MG	634	180	$6,897.52	$0.31	$10.88
WARFARIN TAB 3MG	577	169	$6,400.02	$0.31	$11.09
WARFARIN TAB 6MG	530	128	$6,157.59	$0.33	$11.62
WARFARIN TAB 10MG	479	144	$5,495.45	$0.28	$11.47
WARFARIN TAB 2MG	431	138	$4,305.16	$0.28	$9.99
WARFARIN TAB 7.5MG	426	129	$4,442.46	$0.24	$10.43
WARFARIN TAB 2.5MG	291	100	$3,109.25	$0.29	$10.68
JANTOVEN TAB 5MG	34	6	$361.47	$0.27	$10.63
COUMADIN TAB 10MG	13	1	$1,341.59	$3.80	$103.20
COUMADIN TAB 1MG	12	2	$3,031.26	$8.42	$252.61
JANTOVEN TAB 4MG	9	2	$77.17	$0.29	$8.57
COUMADIN TAB 5MG	9	2	$1,372.45	$4.30	$152.49
JANTOVEN TAB 1MG	8	5	$90.92	$0.38	$11.37
JANTOVEN TAB 2MG	7	1	$41.59	$0.12	$5.94
COUMADIN TAB 4MG	6	1	$418.93	$2.33	$69.82
JANTOVEN TAB 6MG	5	3	$68.89	$0.38	$13.78
JANTOVEN TAB 7.5MG	4	1	$40.79	$0.34	$10.20
COUMADIN TAB 7.5MG	2	2	$372.18	$3.10	$186.09
JANTOVEN TAB 10MG	1	1	$20.52	$0.23	$20.52
SUBTOTAL	**6,400**	**1,823**	**$74,327.25**	**$0.31**	**$11.61**
DABIGATRAN PRODUCTS					
PRADAXA CAP 150MG	222	32	$77,342.68	$11.94	$348.39
PRADAXA CAP 75MG	23	2	$8,475.60	$12.28	$368.50
SUBTOTAL	**245**	**34**	**$85,818.28**	**$11.97**	**$350.28**
RIVAROXABAN PRODUCTS					
XARELTO TAB 20MG	2,293	434	$840,151.03	$12.56	$366.40
XARELTO TAB 15MG	232	77	$93,451.78	$15.19	$402.81
XARELTO TAB 10MG	219	129	$62,479.00	$12.48	$285.29
XARELTO STAR TAB 15/20MG	12	12	$7,389.35	$20.47	$615.78
SUBTOTAL	**2,756**	**652**	**$1,003,471.16**	**$12.80**	**$364.10**
APIXABAN PRODUCTS					
ELIQUIS TAB 2.5MG	253	66	$82,709.57	$12.48	$326.92
ELIQUIS TAB 5MG	2,346	540	$843,564.75	$12.36	$359.58
SUBTOTAL	**2,599**	**606**	**$926,274.32**	**$12.37**	**$359.40**
EDOXABAN PRODUCTS					
SAVAYSA TAB 60MG	6	1	$1,832.06	$10.18	$305.34
SUBTOTAL	**6**	**1**	**$1,832.06**	**$10.18**	**$305.34**
TOTAL	**12,006**	**2,227***	**$2,091,723.07**	**$5.26**	**$174.22**

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Utilization Details of Platelet Aggregation Inhibitors: Fiscal Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
CLOPIDOGREL PRODUCTS					
CLOPIDOGREL TAB 75MG	10,404	2,491	$95,135.31	$0.20	$9.14
SUBTOTAL	**10,404**	**2,491**	**$95,135.31**	**$0.20**	**$9.14**
PRASUGREL PRODUCTS					
EFFIENT TAB 10MG	703	154	$293,616.73	$13.86	$417.66
EFFIENT TAB 5MG	15	6	$6,270.07	$13.93	$418.00
SUBTOTAL	**718**	**160**	**$299,886.80**	**$13.76**	**$417.67**
TICAGRELOR PRODUCTS					
BRILINTA TAB 90MG	791	199	$249,087.36	$10.79	$314.90
BRILINTA TAB 60MG	53	13	$17,120.07	$10.77	$323.02
SUBTOTAL	**844**	**212**	**$266,207.43**	**$10.79**	**$315.41**
VORAPAXAR PRODUCTS					
ZONTIVITY TAB 2.08MG	19	3	$5,656.47	$9.92	$297.71
SUBTOTAL	**19**	**3**	**$5,656.47**	**$9.92**	**$297.71**
ASPIRIN-DIPYRIDAMOLE PRODUCTS					
ASA/DIPYRIDA CAP 25-200MG	24	4	$6,947.99	$9.65	$289.50
AGGRENOX CAP 25-200MG	3	1	$1,442.32	$16.03	$480.77
SUBTOTAL	**27**	**5**	**$8,390.31**	**$10.36**	**$310.75**
TOTAL	**12,012**	**2,772***	**$675,276.32**	**$1.29**	**$56.22**

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

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Appendix U

Industry News and Updates

Oklahoma Health Care Authority
September 2017

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:

- **Oxycodone Extended-Release (ER):** A U.S. Food and Drug Administration (FDA) advisory committee voted against the approval of an abuse-deterrent formulation of oxycodone ER that releases blue dye when crushed or chewed. The viscous product also turns into a gel upon contact with water making it difficult to put into a syringe. The advisory committee noted that the sponsor of the medication, Intellipharmaceuticals, only provided category 1 studies (physical-manipulation and chemical-extraction) and not category 2 or 3 (oral and intranasal human abuse-potential studies). The 2015 FDA guidance for industry recommends the submission of studies in three categories: physical-manipulation and chemical-extraction studies, oral, and intranasal human abuse-potential studies. Some committee members worried the medication could possibly become more of an attraction than a deterrent and questioned whether it could potentially be a sort of status symbol among people. Many committee members stated that "shaming" people in an effort to reduce abuse is not helpful as addiction is a mental illness.
- **Gaucher Disease:** The FDA and the European Medicines Agency released a draft joint plan to support the development of pediatric treatments for Gaucher disease. The agencies state that the approach can apply to rare diseases in general. The draft plan proposes using data extrapolation to avoid unnecessary studies and encourages sponsors to make better use of clinical data modelling and simulation techniques to predict how a medication will work in the pediatric population. In the draft plan, the agencies propose safety and efficacy testing be done by different companies in a single clinical study using a single control to reduce the total number of children enrolled.
- **Generic Approvals:** According to a report by the FDA, the agency approved the most generic drugs during May and June 2017 than it has since it began counting approvals. During the two months, the FDA approved 165 generic drugs, making the total generic approvals for the year 565.
- **Influenza Vaccine:** A study published online in *The Lancet* found an experimental patch can safely deliver the influenza vaccine. The study was led by a team at the Georgia Institute of Technology and Emory University and funded by the National Institutes of Health. The dime-sized patch of microneedles is water-soluble and the microneedles are

just long enough to penetrate the skin. The influenza vaccine is encapsulated in the needles and released as the needle tips dissolve within minutes. An adhesive helps the patch stay on the skin and the patch is discarded afterwards. The study enrolled 100 adult participants. Antibody responses generated by the vaccine were similar in the groups vaccinated using patches and those receiving an intramuscular injection. The antibodies were still present after six months. The vaccines remained potent in the patches for at least one year without refrigeration. Researchers suggest the prospective vaccine technology would cost approximately the same to manufacture and would be less expensive to administer as it could be self-administered and healthcare professionals would not need to be involved.

- **Hepatitis C:** Rebekah Gee, Louisiana's health secretary, is looking for ways to lower the cost of hepatitis C virus (HCV) medications. She said the medications are so expensive that only 320 of the 35,000 individuals with HCV who rely on the state for care were able to receive treatment last year. Gee is considering the use of an obscure 1910 federal patent law that would allow the federal government to circumvent patents and use inventions while "reasonably compensating" the inventor. She stated this option would hopefully allow the federal government to substantially reduce the price of HCV medications. Pharmaceutical groups argue that forcing them to charge lower prices would discourage companies from future innovation. Another option she is considering involves the state and its insurance providers paying for a subscription to get access to a drug for a short period and treat as many people as possible during that time, she has dubbed this idea the "Netflix pricing methodology." The state will continue to restrict HCV medications to the most severe cases in the meantime.

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[1] Anderson, Pauline. FDA Committee Nixes Opioid with Blue Dye Deterrent. *Medscape*. Available online at: http://www.medscape.com/viewarticle/883485?nlid=117016_745&src=WNL_mdplsfeat_170801_mscpedit_phar&uac=255225HG&spon=30&impID=1401666&faf=1#vp_1. Issued 07/27/2017. Last accessed 08/02/2017.

[2] FDA and EMA Collaborate on Expandable Model for Rare Pediatric Drug Development. *FDANews*. Available online at: http://www.fdanews.com/articles/182468-fda-and-ema-collaborate-on-expandable-model-for-rare-pediatric-drug-development?utm_campaign=Drug%20Daily%20Bulletin&utm_source=hs_email&utm_medium=email&utm_content=53919164&_hsenc=p2ANqtz--VF14kLI8xnIPKwhHc38xvg93kkOZVCcCZ1fRsUUQMZ9X6--UkJQW0qvlOQk6wj4r2uSgkRKj-cVR_oFqaSdgdHPyajZqcWAQys2JYTgxHVqASLT0&_hsmi=53919164. Issued 07/06/2017. Last accessed 07/06/2017.

[3] Generic Approvals Continue to Speed Forward. *FDANews*. Available online at: http://www.fdanews.com/articles/182566-generic-approvals-continue-to-speed-forward?utm_campaign=Drug%20Daily%20Bulletin&utm_source=hs_email&utm_medium=email&utm_content=54128525&_hsenc=p2ANqtz-_ba4nUNVnBfDdBQcamZWXkqMZfPyXBLmZXgL2IKZqC5XHmIbnkJjbWcIe2-2A99gRwx1RvC6aMLtO_Lraw70fJqbpxhC_CNts8FFW0b4r0RFCL_SQ&_hsmi=54128525. Issued 07/12/2017. Last accessed 07/25/2017.

[4] Are the Flu Shot's Days Numbered? Vaccine Patch Tested. *U.S. Pharmacist*. Available online at: https://www.uspharmacist.com/article/are-the-flu-shots-days-numbered-vaccine-patch-tested/. Issued 07/12/2017. Last accessed 07/25/2017.

[5] American Pharmacists Association. Louisiana Studies Ways to Force Down HCV Drug Costs. Available online at: https://www.pharmacist.com/article/louisiana-studies-ways-force-down-hcv-drug-costs. Issued 07/14/2017. Last accessed 07/25/2017.

Appendix V

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: July 7th, 2017

FDA approves new treatment for sickle cell disease

First approval for this rare blood disorder in nearly 20 years

The U.S. Food and Drug Administration (FDA) approved Endari (L-glutamine oral powder) for patients age five years and older with sickle cell disease to reduce severe complications associated with the blood disorder. Sickle cell disease is an inherited blood disorder in which the red blood cells are abnormally shaped (in a crescent, or "sickle," shape). This restricts the flow in blood vessels and limits oxygen delivery to the body's tissues, leading to severe pain and organ damage. According to the National Institutes of Health, approximately 100,000 people in the United States have sickle cell disease. The disease occurs most often in African-Americans, Latinos and other minority groups. The average life expectancy for patients with sickle cell disease in the United States is approximately 40 to 60 years.

The safety and efficacy of Endari were studied in a randomized trial of patients ages five to 58 years old with sickle cell disease who had two or more painful crises within the 12 months prior to enrollment in the trial. Patients were assigned randomly to treatment with Endari or placebo, and the effect of treatment was evaluated over 48 weeks. Patients who were treated with Endari experienced fewer hospital visits for pain treated with a parenterally administered narcotic or ketorolac (sickle cell crises), on average, compared to patients who received a placebo, fewer hospitalizations for sickle cell pain, and fewer days in the hospital. Patients who received Endari also had fewer occurrences of acute chest syndrome (a life-threatening complication of sickle cell disease) compared with patients who received a placebo (8.6 percent vs. 23.1 percent).

Common side effects of Endari include constipation, nausea, headache, abdominal pain, cough, pain in the extremities, back pain, and chest pain.

Endari received Orphan Drug designation for this use, which provides incentives to assist and encourage the development of drugs for rare diseases. In addition, development of this drug was in part supported by the FDA Orphan Products Grants Program, which provides grants for clinical studies on safety and/or effectiveness of products for use in rare diseases or conditions.

The FDA granted the approval of Endari to Emmaus Medical Inc.

FDA NEWS RELEASE

For Immediate Release: July 18th, 2017

FDA approves Vosevi for Hepatitis C

The FDA approved Vosevi to treat adults with chronic hepatitis C virus (HCV) genotypes 1-6 without cirrhosis or with mild cirrhosis. Vosevi is a fixed-dose, combination tablet containing two previously approved drugs – sofosbuvir and velpatasvir – and a new drug, voxilaprevir. Vosevi is the first treatment approved for patients who have been previously treated with the direct-acting antiviral drug sofosbuvir or other drugs for HCV that inhibit a protein called NS5A.

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. According to the Centers for Disease Control and Prevention, an estimated 2.7 to 3.9 million people in the United States have chronic HCV. Some patients who suffer from chronic HCV infection over many years may have jaundice and develop complications, such as bleeding, fluid accumulation in the abdomen, infections, liver cancer, and death.

There are at least six distinct HCV genotypes, or strains, which are genetically distinct groups of the virus. Knowing the strain of the virus can help inform treatment recommendations. Approximately 75 percent of Americans with HCV have genotype 1; 20-25 percent have genotypes 2 or 3; and a small number of patients are infected with genotypes 4, 5, or 6.

The safety and efficacy of Vosevi was evaluated in two Phase 3 clinical trials that enrolled approximately 750 adults without cirrhosis or with mild cirrhosis.
The first trial compared 12 weeks of Vosevi treatment with placebo in adults with genotype 1 who had previously failed treatment with an NS5A inhibitor drug. Patients with genotypes 2, 3, 4, 5, or 6 all received Vosevi.
The second trial compared 12 weeks of Vosevi with the previously approved drugs sofosbuvir and velpatasvir in adults with genotypes 1, 2, or 3 who had previously failed treatment with sofosbuvir but not an NS5A inhibitor drug.
Results of both trials demonstrated that 96-97 percent of patients who received Vosevi had no virus detected in the blood 12 weeks after finishing treatment, suggesting that patients' infection had been cured.
Treatment recommendations for Vosevi are different depending on viral genotype and prior treatment history.
The most common adverse reactions in patients taking Vosevi were headache, fatigue, diarrhea, and nausea.
Vosevi is contraindicated in patients taking the drug rifampin.
Hepatitis B virus (HBV) reactivation has been reported in HCV/HBV coinfected adult patients who were undergoing or had completed treatment with HCV direct-acting antivirals, and who were not receiving HBV antiviral therapy. HBV reactivation in patients treated with direct-acting antiviral medicines can result in serious liver problems or death in some patients. Health care professionals should screen all patients for evidence of current or prior HBV infection before starting treatment with Vosevi.
The FDA granted this application Priority Review and Breakthrough Therapy designations.
The FDA granted approval of Vosevi to Gilead Sciences Inc.

FDA NEWS RELEASE

For Immediate Release: July 17th, 2017
FDA approves new treatment to reduce the risk of breast cancer returning

The FDA approved Nerlynx (neratinib) for the extended adjuvant treatment of early-stage, HER2-positive breast cancer. For patients with this type of cancer, Nerlynx is the first extended adjuvant therapy, a form of therapy that is taken after an initial treatment to further lower the risk of the cancer coming back. Nerlynx is indicated for adult patients who have been previously treated with a regimen that includes the drug trastuzumab.
Breast cancer is the most common form of cancer in the United States. The National Cancer Institute (NCI) estimates approximately 252,710 women will be diagnosed with breast cancer this year, and 40,610 will die of the disease. According to the NCI, approximately 15 percent of patients with breast cancer have tumors that are HER2-positive.
Nerlynx is a kinase inhibitor that works by blocking several enzymes that promote cell growth.
The safety and efficacy of Nerlynx were studied in a randomized trial of 2,840 patients with early-stage, HER2-positive breast cancer who completed treatment with trastuzumab within the previous two years. The study measured the amount of time after the start of the trial that it took for the cancer to come back or for death to occur from any cause (invasive, disease-free survival). After two years, 94.2 percent of patients treated with Nerlynx had not experienced cancer recurrence or death compared with 91.9 percent of patients receiving placebo.
Common side effects of Nerlynx include diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, swollen and sore mouth, decreased appetite, muscle spasms, indigestion, liver damage (AST or ALT enzyme increase), nail disorder, dry skin, abdominal swelling, weight loss, and urinary tract infection.
Patients should be given loperamide for the first 56 days of treatment with Nerlynx and as needed thereafter to help manage diarrhea. Additional antidiarrheals, fluids and electrolytes should also be given as clinically indicated to help manage diarrhea. Patients who experience severe side effects, including diarrhea or liver damage, should stop taking Nerlynx. Women who are pregnant or breastfeeding should not take Nerlynx because it may cause harm to a developing fetus or a newborn baby.
The FDA granted the approval of Nerlynx to Puma Biotechnology Inc.

FDA NEWS RELEASE

For Immediate Release: August 1st, 2017

FDA approves new targeted treatment for relapsed or refractory acute myeloid leukemia

The FDA approved Idhifa (enasidenib) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) who have a specific genetic mutation. The drug is approved for use with a companion diagnostic, the RealTime IDH2 Assay, which is used to detect specific mutations in the IDH2 gene in patients with AML.

AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. The National Cancer Institute at the National Institutes of Health estimates that approximately 21,380 people will be diagnosed with AML this year; approximately 10,590 patients with AML will die of the disease in 2017.

Idhifa is an isocitrate dehydrogenase-2 inhibitor that works by blocking several enzymes that promote cell growth. If the IDH2 mutation is detected in blood or bone marrow samples using the RealTime IDH2 Assay, the patient may be eligible for treatment with Idhifa.

The efficacy of Idhifa was studied in a single-arm trial of 199 patients with relapsed or refractory AML who had IDH2 mutations as detected by the RealTime IDH2 Assay. The trial measured the percentage of patients with no evidence of disease and full recovery of blood counts after treatment (complete remission or CR), as well as patients with no evidence of disease and partial recovery of blood counts after treatment (complete remission with partial hematologic recovery or CRh). With a minimum of six months of treatment, 19 percent of patients experienced CR for a median 8.2 months, and 4 percent of patients experienced CRh for a median 9.6 months. Of the 157 patients who required transfusions of blood or platelets due to AML at the start of the study, 34 percent no longer required transfusions after treatment with Idhifa.

Common side effects of Idhifa include nausea, vomiting, diarrhea, increased levels of bilirubin, and decreased appetite. Women who are pregnant or breastfeeding should not take Idhifa because it may cause harm to a developing fetus or a newborn baby.

The prescribing information for Idhifa includes a boxed warning that an adverse reaction known as differentiation syndrome can occur and can be fatal if not treated. Sign and symptoms of differentiation syndrome may include fever, difficulty breathing, acute respiratory distress, inflammation in the lungs, fluid around the lungs or heart, rapid weight gain, peripheral edema, or liver, kidney, or multi-organ dysfunction. At first suspicion of symptoms, doctors should treat patients with corticosteroids and monitor patients closely until symptoms go away.

Idhifa was granted Priority Review designation, 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. Idhifa also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Idhifa to Celgene Corporation. The FDA granted the approval of the RealTime IDH2 Assay to Abbott Laboratories.

FDA NEWS RELEASE

For Immediate Release: August 2nd, 2017

FDA approves treatment for chronic graft versus host disease

The FDA expanded the approval of Imbruvica (ibrutinib) for the treatment of adult patients with chronic graft versus host disease (cGVHD) after failure of one or more treatments. This is the first FDA-approved therapy for the treatment of cGVHD.

cGVHD is a life-threatening condition that can occur in patients after they receive a stem cell transplant from blood or bone marrow, called hematopoietic stem cell transplantation (HSCT), to treat certain blood or bone marrow cancers. cGVHD occurs when cells from the stem cell transplant attack healthy cells in a patient's tissues. Symptoms of cGVHD can occur in the skin, eyes, mouth, gut, liver, and lungs. The condition is estimated to occur in 30-70 percent of all patients who receive HSCT.

The efficacy and safety of Imbruvica for the treatment of cGVHD were studied in a single-arm trial of 42 patients with cGVHD whose symptoms persisted despite standard treatment with corticosteroids. Most patients' symptoms included mouth ulcers and skin rashes, and more than 50 percent of patients had two or more organs affected by cGVHD. In the trial, 67 percent of patients experienced improvements in their cGVHD

symptoms. In 48 percent of patients in the trial, the improvement of symptoms lasted for up to five months or longer.
Common side effects of Imbruvica in patients with cGVHD include fatigue, bruising, diarrhea, low levels of blood platelets (thrombocytopenia), muscle spasms, swelling and sores in the mouth, nausea, severe bleeding (hemorrhage), low levels of red blood cells, and lung infection.
Serious side effects of Imbruvica include severe bleeding (hemorrhage), infections, low levels of blood cells (cytopenias), irregular heartbeat (atrial fibrillation), hypertension, new cancers (second primary malignancies), and metabolic abnormalities (tumor lysis syndrome). Women who are pregnant or breastfeeding should not take Imbruvica because it may cause harm to a developing fetus or a newborn baby.
Imbruvica, a kinase inhibitor, was previously approved for certain indications in treating chronic lymphocytic leukemia, Waldenström's macroglobulinemia and marginal zone lymphoma, as well as under accelerated approval status for mantle cell lymphoma.
The FDA granted this application Priority Review and Breakthrough Therapy designations. Imbruvica also received Orphan Drug designation for this indication, which provides incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted the approval of Imbruvica to Pharmacyclics LLC.

FDA NEWS RELEASE

For Immediate Release: August 3rd, 2017
FDA approves first treatment for certain types of poor-prognosis acute myeloid leukemia

The FDA approved Vyxeos for the treatment of adults with two types of acute myeloid leukemia (AML): newly diagnosed therapy-related AML (t-AML) or AML with myelodysplasia-related changes (AML-MRC). Vyxeos is a fixed-combination of chemotherapy drugs daunorubicin and cytarabine.
AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of white blood cells in the bloodstream. The National Cancer Institute at the National Institutes of Health estimates that approximately 21,380 people will be diagnosed with AML this year; approximately 10,590 patients with AML will die of the disease in 2017. T-AML occurs as a complication of chemotherapy or radiation in approximately 8 to10 percent of all patients treated for cancer within an average of five years after treatment. AML-MRC is characterized by a history of certain blood disorders and other significant mutations within cancer cells. Patients with t-AML or AML-MRC have very low life expectancies.
The safety and efficacy of Vyxeos were studied in 309 patients with newly diagnosed t-AML or AML-MRC who were randomized to receive Vyxeos or separately administered treatments of daunorubicin and cytarabine. The trial measured how long patients lived from the date they started the trial (overall survival). Patients who received Vyxeos lived longer than patients who received separate treatments of daunorubicin and cytarabine (median overall survival 9.56 months vs. 5.95 months).
Common side effects of Vyxeos include bleeding events (hemorrhage), fever with low white blood cell count (febrile neutropenia), rash, edema, nausea, inflammation of the mucous membranes, diarrhea, constipation, musculoskeletal pain, fatigue, abdominal pain, shortness of breath (dyspnea), headache, cough, decreased appetite, arrhythmia, pneumonia, blood infection (bacteremia), chills, sleep disorders, and vomiting.
Patients who have a history of serious hypersensitivity to daunorubicin, cytarabine or any component of the formulation should not use Vyxeos. Patients taking Vyxeos should be monitored for hypersensitivity reactions and decreased cardiac function. Vyxeos has been associated with serious or fatal bleeding events. Daunorubicin has been associated with severe damage (necrosis) where the drug leaks into the skin and subcutaneous tissue from the intravenous infusion (extravasation). Women who are pregnant or breastfeeding should not take Vyxeos, because it may cause harm to a developing fetus or a newborn baby.
The prescribing information for Vyxeos includes a boxed warning not to interchange Vyxeos with other daunorubicin- and/or cytarabine-containing products.
The FDA granted this application Priority Review and Breakthrough Therapy designations. Vyxeos also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.
The FDA granted the approval of Vyxeos to Jazz Pharmaceuticals.

Safety Announcements

Update: FDA announces Leader Brand, Major Pharmaceuticals, and Rugby Laboratories recall of all liquid products manufactured by PharmaTech due to *B. cepacia* contamination risk

[8/10/17] The FDA announced a voluntary recall of all liquid products manufactured by PharmaTech, and distributed by Leader Brand, Major Pharmaceuticals, and Rugby Laboratories, due to possible *Burkholderia cepacia* contamination. These products, including various drugs and dietary supplements intended for use in infants and children, were distributed nationwide.
Patients, pharmacies, and healthcare facilities that have the recalled product on hand should stop using and dispensing them immediately.
Consumers with questions regarding this recall can contact the companies at the numbers below:

- Leader Customer Support: at 1-800-200-6313, option #1, Monday through Thursday 8 a.m.– 7p.m. and Friday 8 a.m.– 5 p.m. EST
- Rugby Laboratories/Major Pharmaceuticals Customer Support: 1-800-645-2158, Monday through Friday 8 a.m.– 8 p.m. EST

Current Drug Shortages Index (as of August 25th, 2017):

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

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***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Dihydroergotamine Mesylate Injection	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigotindisulfonate Sodium (Indigo Carmine) Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***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***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***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***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Scopolamine (Transderm Scop) Transdermal System Patch	***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***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tolmetin Sodium Tablets, USP	***Currently in Shortage***