Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
July 13, 2016
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 DUR Board Meeting – July 13, 2016

DATE: June 30, 2016

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 July 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

Action Item – Update on Medication Coverage Authorization Unit/Opioid Prescriptions in Pregnant Women – Appendix B

Action Item – Vote to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium-223 Dichloride), and Provenge® (Sipuleucel-T) – Appendix C

Action Item – Vote to Prior Authorize Dyanavel™ XR (Amphetamine Extended-Release), QuilliChew ER™ (Methylphenidate Extended-Release), and Adzenys XR-ODT™ (Amphetamine Extended-Release) – Appendix D

Action Item – Vote to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil) – Appendix E

Action Item – Vote to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole) – Appendix F

Action Item – Vote to Prior Authorize OsmoPrep® (Sodium Phosphate Monobasic/Sodium Phosphate Dibasic), Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid), Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/Sodium Chloride/Sodium Bicarbonate/Potassium Chloride), and SUPREP® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) – Appendix G

Action Item – Vote to Prior Authorize Nuvessa™ (Metronidazole Vaginal Gel 1.3%), Zyclara® (Imiquimod Cream), and Kristalose® (Lactulose Packets) – Appendix H

Action Item – Vote to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection) – Appendix I

Action Item – Vote to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution – Appendix J

30-Day Notice to Prior Authorize Ocaliva™ (Obeticholic Acid) – Appendix K

Annual Review of Opioid Analgesics and Buprenorphine Products & 30-Day Notice to Prior Authorize Belbuca™ (Buprenorphine Buccal Film), Dolophine® (Methadone), MorphaBond™ (Morphine Extended-Release), Xtampza™ ER (Oxycodone Extended-Release), & Probuphine® (Buprenorphine Implant) – Appendix L

Annual Review of Anti-Ulcer Medications and 30-Day Notice to Prior Authorize Dexilant™ SoluTab (Dexlansoprazole Delayed-Release Orally Disintegrating Tablets) – Appendix M

Annual Review of Antidepressants – Appendix N

Annual Review of Myalept® (Metreleptin) – Appendix O

FDA and DEA Updates – Appendix P

Future Business (Upcoming Product and Class Reviews)

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – July 13, 2016 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

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

A. June 8, 2016 DUR Minutes – Vote
B. June 8, 2016 DUR Recommendations Memorandum

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

4. Action Item – Update on Medication Coverage Authorization Unit/Opioid Prescriptions in Pregnant Women – See Appendix B

A. Medication Coverage Activity for June 2016
B. Pharmacy Help Desk Activity for June 2016
C. Opioid Prescriptions in Pregnant Women – Vote

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

5. Action Item – Vote to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium-223 Dichloride), and Provenge® (Sipuleucel-T) – See Appendix C

A. Introduction
B. Recommendations

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

6. Action Item – Vote to Prior Authorize Dyanavel™ XR (Amphetamine Extended-Release), QuilliChew ER™ (Methylphenidate Extended-Release), and Adzenys XR-ODT™ (Amphetamine Extended-Release) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil) – See Appendix E

A. Indication(s)
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole) – See Appendix F

A. Introduction
B. Regimen Comparison
C. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize OsmoPrep® (Sodium Phosphate Monobasic/Sodium Phosphate Dibasic), Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid), Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/Sodium Chloride/Sodium Bicarbonate/Potassium Chloride), and SUPREP® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) – See Appendix G

A. Cost Savings
B. Bowel Preparation Medications Summary
C. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Nuvessa™ (Metronidazole Vaginal Gel 1.3%), Zyclara® (Imiquimod Cream), and Kristalose® (Lactulose Packets) – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection) – See Appendix I

A. Introduction
B. College of Pharmacy Recommendations

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

12. Action Item – Vote to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution – See Appendix J

A. Introduction
B. College of Pharmacy Recommendations

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

13. 30-Day Notice to Prior Authorize Ocaliva™ (Obeticholic Acid) – See Appendix K

A. Primary Biliary Cholangitis (PBC) Background Information
B. Ocaliva™ (Obeticholic Acid) Product Summary
C. College of Pharmacy Recommendations

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

14. Annual Review of Opioid Analgesics and Buprenorphine Products & 30-Day Notice to Prior Authorize Belbuca™ (Buprenorphine Buccal Film), Dolophine® (Methadone), MorphaBond™ (Morphine Extended-Release), Xtampza™ ER (Oxycodone Extended-Release), & Probuphine® (Buprenorphine Implant) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Opioid Analgesics and Buprenorphine Products
C. Prior Authorization of Opioid Analgesics & Buprenorphine Products
D. Opioid Analgesic Utilization Trends
E. Market News and Updates
F. Belbuca™ (Buprenorphine Buccal Film) Product Summary
G. MorphaBond™ (Morphine Extended-Release) Product Summary
H. Xtampza™ ER (Oxycodone Extended-Release) Product Summary
I. Probuphine® (Buprenorphine Implant) Product Summary
J. College of Pharmacy Recommendations
K. Utilization Details of Opioid Analgesics
L. Utilization Details of Buprenorphine Products

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

15. Annual Review of Anti-Ulcer Medications and 30-Day Notice to Prior Authorize Dexilant™ SoluTab (Dexlansoprazole Delayed-Release Orally Disintegrating Tablets) – See Appendix M

A. Current Prior Authorization Criteria
B. Utilization of Anti-Ulcer Medications
C. Prior Authorization of Anti-Ulcer Medications

D. Market News and Updates
E. Dexilant™ SoluTab (Dexlansoprazole) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Anti-Ulcer Medications

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

16. Annual Review of Antidepressants – See Appendix N

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

Non-presentation; Questions only:

17. Annual Review of Myalept® (Metreleptin) – See Appendix O

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Myalept® (Metreleptin)
D. Prior Authorization of Myalept® (Metreleptin)
E. College of Pharmacy Recommendations

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

18. FDA and DEA Updates – See Appendix P

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

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

August 2016 not scheduled as a live meeting (packet only)

A. Ocular Anti-Infectives
B. Glaucoma Medications
C. Prednisolone Special Formulations
D. Alzheimer's Medications
E. Nasal Allergy Medications
F. Nonsteroidal Anti-Inflammatory Medications

*Future business subject to change.

20. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF JUNE 8, 2016

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
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	
Tammy Lambert, Ph.D.; Postdoctoral Research Fellow		x
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Graduate Students: Christina Bulkley, Pharm.D.		x
David George, Pharm.D.		x
Timothy Pham, Pharm.D.		x
Visiting Pharmacy Student(s): Sarah Anderson and Morgan Masterson	x	

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

OTHERS PRESENT:		
Gerard Buonpane, Tris Pharma	Dan Keeney, Tris Pharma	Sean Seago, Merck
David Freti, Impax	David Large, Supernus	Jason Lurk, Novo Nordisk
Kristin Pareja, Otsuka	Rose Mullen, Alkermes	Rose Juarez, St. Anthony
Jeff Knappen, Allergan	Jennifer Schukert, Allergan	Tyler Craddock, The Medicines Co.
Lee Stout, Chiesi USA	Dana Koehn, Baxalta	Terry McCurren, Otsuka
Ron Cain, Pfizer	Toby Thompson, Pfizer	Doug Wood, Viiv Healthcare
Bob Gustafson, Lundbeck	Aaron Shaw, Boehringer Ingelheim	Mai Duong, Novartis
Marc Parker, Sunovion	Richard Ponder, J & J	Sasha Cheatham, BioRx
Matthew Flores, BioRx	Scott Sorenson, BioRx	Jim Dunlap, PhRMA
Ann Halloran, Sunovion	Brent Hildebrand, Gilead	Jim Fowler, AstraZeneca
Maren Lehman, Merck	Brian Maves, Pfizer	Ron Schnare, Shire
Jason Scheier, Amgen		

PRESENT FOR PUBLIC COMMENT:	
Kristin Pareja	Otsuka
Rose Mullen	Alkermes
Jason Lurk	Novo Nordisk
Mai Duong	Novartis
Scott Sorenson	BioRx
Dan Keeney	Tris Pharma

AGENDA ITEM NO. 1: **CALL TO ORDER**

1A: ROLL CALL

Dr. Muchmore called the meeting to order. Roll call by Dr. Cothran established the presence of a quorum.

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

2A: AGENDA NO. 6 SCOTT SORENSON
2B: AGENDA NO. 8 JASON LURK
2C: AGENDA NO. 9 MAI DUONG
2D: AGENDA NO. 11 DAN KEENEY
2E: AGENDA NO. 13 KRISTIN PAREJA
2F: AGENDA NO. 13 ROSE MULLEN

ACTION: NONE REQUIRED

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

3A: APRIL 13, 2016 DUR MINUTES – VOTE
3B: APRIL 13, 2016 DUR RECOMMENDATIONS MEMORANDUM

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR APRIL 2016
4B: PHARMACY HELP DESK ACTIVITY FOR APRIL 2016
4C: MEDICATION COVERAGE ACTIVITY FOR MAY 2016
4D: PHARMACY HELP DESK ACTIVITY FOR MAY 2016
4E: SOONERPSYCH PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE ZEPATIER™ (ELBASVIR/GRAZOPREVIR)

5A: INTRODUCTION

5B: MARKET NEWS AND UPDATES

5C: REGIMEN COMPARISON

5D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE ELOCTATE™ [ANTIHEMOPHILIC FACTOR (RECOMBINANT), FC FUSION PROTEIN], ADYNOVATE® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), PEGYLATED], ALPROLIX® [COAGULATION FACTOR IX (RECOMBINANT), FC FUSION PROTEIN], IDELVION® [COAGULATION FACTOR IX (RECOMBINANT), ALBUMIN FUSION PROTEIN], OBIZUR® [ANTIHEMOPHILIC FACTOR (RECOMBINANT), PORCINE SEQUENCE], CORIFACT® [FACTOR XIII CONCENTRATE (HUMAN)], TRETTEN® [COAGULATION FACTOR XIII ASUBUNIT (RECOMBINANT)], AND COAGADEX® [COAGULATION FACTOR X (HUMAN)], AND ESTABLISH PHARMACY PROVIDER STANDARDS OF CARE

6A: INTRODUCTION

6B: RECOMMENDATIONS

6C: HEMOPHILIA FACTOR DISPENSING FORM

6D: HEMOPHILIA AND OTHER RARE BLEEDING DISORDERS PATIENT IN-HOME ASSESSMENT

Materials included in agenda packet; presented Dr. Ratterman

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE VAGINAL PROGESTERONE PRODUCTS (CRINONE® AND ENDOMETRIN®) AND UPDATE MAKENA® (HYDROXYPROGESTERONE CAPROATE) APPROVAL CRITERIA

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

7C: SOONERCARE COVERAGE OF MAKENA®, CRINONE®, AND ENDOMETRIN® - ALGORITHM

7D: SOONERCARE COVERAGE OF PROGESTERONE PRODUCTS - CHART

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE HUMALOG® KWIKPEN® U-200 (INSULIN LISPRO), TRESIBA® (INSULIN DEGLUDEC), RYZODEG® 70/30 (INSULIN DEGLUDEC/INSULIN ASPART), BASAGLAR® (INSULIN GLARGINE), AND SYNJARDY® (EMPAGLIFLOZIN/METFORMIN)

8A: INDICATION(S)

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE ENTRESTO™ (SACUBITRIL/VALSARTAN)

9A: INTRODUCTION

9B: MARKET NEWS AND UPDATES

9C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: **30-DAY NOTICE TO PRIOR AUTHORIZE ZYTIGA® (ABIRATERONE), JEVTANA® (CABAZITAXEL), XTANDI® (ENZALUTAMIDE), XOFIGO® (RADIUM-223 DICHLORIDE), AND PROVENGE® (SIPULEUCEL-T)**

10A: INTRODUCTION
10B: UTILIZATION OF PROSTATE CANCER MEDICATIONS
10C: MARKET NEWS AND UPDATES
10D: PRODUCT SUMMARIES
10E: COLLEGE OF PHARMACY RECOMMENDATIONS
10F: UTILIZATION DETAILS OF PROSTATE CANCER MEDICATIONS

Materials included in agenda packet; presented by Dr. Schmidt, Dr. Borders, Dr. Medina

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: **ANNUAL REVIEW OF ADHD & NARCOLEPSY MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE DYANAVEL™ XR (AMPHETAMINE EXTENDED-RELEASE), QUILLICHEW ER™ METHYLPHENIDATE EXTENDED-RELEASE), AND ADZENYS XR-ODT™ (AMPHETAMINE EXTENDED-RELEASE)**

11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF ADHD & NARCOLEPSY MEDICATIONS
11C: PRIOR AUTHORIZATION OF ADHD & NARCOLEPSY MEDICATIONS
11D: MARKET NEWS AND UPDATES
11E: DYANAVEL™ XR (AMPHETAMINE EXTENDED-RELEASE) PRODUCT SUMMARY
11F: QUILLICHEW ER™ (METHYLPHENIDATE EXTENDED-RELEASE) PRODUCT SUMMARY
11G: ADZENYS XR-ODT™ (AMPHETAMINE EXTENDED-RELEASE) PRODUCT SUMMARY
11H: COLLEGE OF PHARMACY RECOMMENDATIONS
11I: UTILIZATION DETAILS OF ADHD & NARCOLEPSY MEDICATIONS

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF CHOLBAM® (CHOLIC ACID)**

12A: INTRODUCTION
12B: CURRENT PRIOR AUTHORIZATION CRITERIA
12C: UTILIZATION OF CHOLBAM® (CHOLIC ACID)
12D: PRIOR AUTHORIZATION OF CHOLBAM® (CHOLIC ACID)
12E: MARKET NEWS AND UPDATES
12F: COLLEGE OF PHARMACY RECOMMENDATIONS

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF ATYPICAL ANTIPSYCHOTIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE REXULTI® (BREXPIPRAZOLE), VRAYLAR™ (CARIPRAZINE), AND ARISTADA™ (ARIPIPRAZOLE LAUROXIL)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ATYPICAL ANTIPSYCHOTIC MEDICATIONS
13C: PRIOR AUTHORIZATION OF ATYPICAL ANTIPSYCHOTIC MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: REXULTI® (BREXPIPRAZOLE) PRODUCT SUMMARY
13F: VRAYLAR™ (CARIPRAZINE) PRODUCT SUMMARY
13G: ARISTADA™ (ARIPIPRAZOLE LAUROXIL) PRODUCT SUMMARY
13H: COLLEGE OF PHARMACY RECOMMENDATIONS
13I: UTILIZATION DETAILS OF ATYPICAL ANTIPSYCHOTIC MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **ANNUAL REVIEW OF ANTHELMINTIC MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ALBENZA® (ALBENDAZOLE) AND EMVERM™ (MEBENDAZOLE)**

14A: BACKGROUND INFORMATION
14B: UTILIZATION OF ANTHELMINTIC MEDICATIONS
14C: MARKET NEWS AND UPDATES
14D: REGIMEN COMPARISON
14E: ALBENZA® (ALBENDAZOLE) PRODUCT SUMMARY
14F: EMVERM™ (MEBENDAZOLE) PRODUCT SUMMARY
14G: COLLEGE OF PHARMACY RECOMMENDATIONS
14H: UTILIZATION DETAILS OF ANTHELMINTIC MEDICATIONS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **30-DAY NOTICE TO PRIOR AUTHORIZE H.P. ACTHAR® GEL (CORTICOTROPIN INJECTION)**

15A: INTRODUCTION
15B: UTILIZATION OF H.P. ACTHAR® GEL (CORTICOTROPIN INJECTION)
15C: H.P. ACTHAR® GEL (CORTICOTROPIN INJECTION) PRODUCT SUMMARY
15D: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **ANNUAL REVIEW OF BOWEL PREPARATION MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE OSMOPREP® (SODIUM PHOSPHATE MONOBASIC/SODIUM PHOSPHATE DIBASIC), PREPOPIK® (SODIUM PICOSULFATE/MAGNESIUM OXIDE/CITRIC ACID), SUCLEAR® (SODIUM SULFATE/POTASSIUM SULFATE/MAGNESIUM SULFATE/PEG-3350/SODIUM CHLORIDE/SODIUM BICARBONATE/POTASSIUM CHLORIDE), AND SUPREP® (SODIUM SULFATE/POTASSIUM SULFATE/MAGNESIUM SULFATE)**

16A: INTRODUCTION
16B: UTILIZATION OF BOWEL PREPARATION MEDICATIONS
16C: MARKET NEWS AND UPDATES
16D: BOWEL PREPARATION MEDICATIONS SUMMARY
16E: OSMOPREP® (SODIUM PHOSPHATE MONOBASIC/SODIUM PHOSPHATE DIBASIC) PRODUCT SUMMARY
16F: PREPOPIK® (SODIUM PICOSULFATE/MAGNESIUM OXIDE/CITRIC ACID) PRODUCT SUMMARY
16G: SUCLEAR® (SODIUM SULFATE/POTASSIUM SULFATE/MAGNESIUM SULFATE/PEG-3350/ SODIUM CHLORIDE/SODIUM BICARBONATE/POTASSIUM CHLORIDE) PRODUCT SUMMARY
16H: SUPREP® (SODIUM SULFATE/POTASSIUM SULFATE/MAGNESIUM SULFATE) PRODUCT SUMMARY
16I: COLLEGE OF PHARMACY RECOMMENDATIONS
16J: UTILIZATION DETAILS OF BOWEL PREPARATION MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF VARIOUS SPECIAL FORMULATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NUVESSA™ (METRONIDAZOLE VAGINAL GEL 1.3%), ZYCLARA® (IMIQUIMOD CREAM), AND KRISTALOSE® (LACTULOSE PACKETS)**

17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF SPECIAL FORMULATIONS
17D: PRIOR AUTHORIZATION OF SPECIAL FORMULATIONS
17E: NUVESSA™ (METRONIDAZOLE VAGINAL GEL 1.3%) PRODUCT SUMMARY
17F: ZYCLARA® (IMIQUIMOD CREAM) PRODUCT SUMMARY
17G: KRISTALOSE® (LACTULOSE PACKETS) PRODUCT SUMMARY

17H: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ANNUAL REVIEW OF TOPICAL ANTIFUNGAL PRODUCTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ECONAZOLE NITRATE 1% CREAM AND CLOTRIMAZOLE 1% SOLUTION
18A: CURRENT PRIOR AUTHORIZATION CRITERIA
18B: UTILIZATION OF TOPICAL ANTIFUNGAL PRODUCTS
18C: PRIOR AUTHORIZATION OF TOPICAL ANTIFUNGAL PRODUCTS
18D: MARKET NEWS AND UPDATES
18E: COLLEGE OF PHARMACY RECOMMENDATIONS
18F: UTILIZATION DETAILS OF TOPICAL ANTIFUNGAL PRODUCTS
Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: ANNUAL REVIEW OF NATPARA® (PARATHYROID HORMONE INJECTION)
19A: INTRODUCTION
19B: CURRENT PRIOR AUTHORIZATION CRITERIA
19C: UTILIZATION OF NATPARA® (PARATHYROID HORMONE)
19D: PRIOR AUTHORIZATION OF NATPARA® (PARATHYROID HORMONE)
19E: MARKET NEWS AND UPDATES
19F: COLLEGE OF PHARMACY RECOMMENDATIONS
19G: UTILIZATION DETAILS OF NATPARA® (PARATHYROID HORMONE)
Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: FDA AND DEA UPDATES
Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 21: FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)
21A: OPIOID ANALGESICS AND BUPRENORPHINE PRODUCTS
21B: ANTIDEPRESSANT MEDICATIONS
21C: ALZHEIMER'S MEDICATIONS
21D: ANTI-ULCER MEDICATIONS
21E: NASAL ALLERGY MEDICATIONS
FUTURE BUSINESS SUBJECT TO CHANGE.
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 22: ADJOURNMENT
The meeting was adjourned at 5:40 pm

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

Memorandum

Date: June 09, 2016

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 June 08, 2016

Recommendation 1: SoonerPsych Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Zepatier™ (elbasvir/ grazoprevir) with criteria similar to the other prior authorized hepatitis C medications (see criteria noted in red). Additionally, the College of Pharmacy recommends the changes noted in red to the individual hepatitis C medications prior authorization criteria. The following table highlights the preferred regimens for each genotype in treatment-naïve and PEG-IFN and RBV-experienced members (listed in alphabetical order). Additional regimens other than those listed may be considered based on patient-specific clinical situations.

Genotype	Patient Factors	Preferred Regimen(s)
Genotype-1		
1	Treatment-naïve, non-cirrhotic	Harvoni® for 8 or 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-naïve, cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 24 weeks 1b: Viekira Pak™ +/- RBV for 12 weeks 1a: Zepatier™ for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-experienced, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 12 weeks 1b: Viekira Pak™ for 12 weeks 1a: Zepatier™ + RBV for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
1	Treatment-experienced, cirrhotic	Harvoni® + RBV for 12 weeks Harvoni® for 24 weeks Sovaldi® + RBV + PEG IFN for 12 weeks 1a: Viekira Pak™ + RBV for 24 weeks 1b: Viekira Pak™ +/- RBV for 12 weeks 1a: Zepatier™ + RBV for 12 weeks (without baseline RAVs) 1a: Zepatier™ + RBV for 16 weeks (with baseline RAVs) 1b: Zepatier™ for 12 weeks
Genotype-2		
2	Treatment-naïve, non-cirrhotic	Sovaldi® + RBV for 12 weeks Sovaldi® + Daklinza™ for 12 weeks (if RBV intolerant)
2	Treatment-naïve, cirrhotic	Sovaldi® + RBV for 12 or 16 weeks Sovaldi® + Daklinza™ for 16 weeks (if RBV intolerant)
2	Treatment-experienced, non-cirrhotic	Sovaldi® + RBV for 12 weeks Sovaldi® + Daklinza™ for 12 weeks
2	Treatment-experienced, cirrhotic	Sovaldi® + RBV for 12 or 16 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + Daklinza™ for 16 weeks
Genotype-3		
3	Treatment-naïve, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
3	Treatment-naïve, cirrhotic	Daklinza™ + Sovaldi® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks

Genotype	Patient Factors	Preferred Regimen(s)
3	Treatment-experienced, non-cirrhotic	Daklinza™ + Sovaldi® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
3	Treatment-experienced, cirrhotic	Daklinza™ + Sovaldi® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Sovaldi® + RBV for 24 weeks
Genotype-4		
4	Treatment-naïve, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-naïve, cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-experienced, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
4	Treatment-experienced, cirrhotic	Harvoni® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
Genotype-5 or Genotype-6		
5 or 6	Treatment-naïve or -experienced, non-cirrhotic or cirrhotic	Harvoni® for 12 weeks

Not all regimens included are FDA approved.
All regimens are either FDA approved or recommended in AASLD/IDSA treatment guidance.
If not specified, regimen applies to all genotypic subtypes.
RBV = ribavirin PEG IFN = peginterferon alfa RAV = resistance-associated polymorphisms

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

Zepatier™ (Elbasvir/Grazoprevir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1** or **genotype-4**; and

3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Zepatier™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. If the member has genotype-1a, testing results for the presence of virus with NS5A resistance-associated polymorphisms must be indicated on the prior authorization request; and
7. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
8. The following regimens and requirements based on genotype, polymorphisms, and prior treatment status will apply (all regimens apply to patients with and without cirrhosis, HIV/HCV co-infected patients, and patients with or without renal impairment):
    a. **Genotype-1a, treatment-naïve or peginterferon alfa + ribavirin experienced without baseline NS5A polymorphisms:**
        i. Zepatier™ for 12 weeks
    b. **Genotype-1a, treatment-naïve or peginterferon alfa + ribavirin experienced <u>with</u> baseline NS5A polymorphisms:**
        i. Zepatier™ with weight-based ribavirin for 16 weeks
    c. **Genotype-1b, treatment-naïve or peginterferon alfa + ribavirin experienced:**
        i. Zepatier™ for 12 weeks
    d. **Genotype-1a or -1b, peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor (e.g., boceprevir, simeprevir, teleprevir) experienced:**
        i. Zepatier™ with weight-based ribavirin for 12 weeks
    e. **Genotype-4, treatment-naïve:**
        i. Zepatier™ for 12 weeks
    f. **Genotype-4, treatment-experienced:**
        i. Zepatier™ with weight-based ribavirin for 16 weeks
    g. New regimens will apply as approved by the FDA
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and

15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
16. The prescriber must verify that the member's ALT levels will be monitored prior to treatment initiation, at treatment week eight, and as clinically indicated thereafter (patients receiving 16 weeks of therapy should receive additional ALT levels at treatment week 12); and
17. Member must not be taking the following medications: phenytoin, carbamazepine, rifampin, St. John's wort, efavirenz, atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine, nafcillin, ketoconazole, bosentan, etravirine, elvitegravir/cobicstat/ emtricitabine/tenofovir, or modafinil; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 or 16 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Daklinza™ (Daclatasvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-3**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Daklinza™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype and concomitant drug therapy will apply:
    a. **Genotype-1, treatment-naïve or treatment-experienced, without cirrhosis or with compensated cirrhosis:**
        i. Daklinza™ 60mg with Sovaldi® for 12 weeks
    b. **Genotype-1, treatment-naïve or treatment-experienced, with decompensated cirrhosis, or post-transplant:**
        i. Daklinza™ 60mg with Sovaldi® and weight-based ribavirin for 12 weeks

c. **Genotype-2, treatment-naïve or treatment-experienced, without cirrhosis, RBV intolerant:**
    i. Daklinza™ 60mg with Sovaldi® for 12 weeks
d. **Genotype-2, treatment-naïve or treatment-experienced, with cirrhosis, RBV intolerant:**
    i. Daklinza™ 60mg with Sovaldi® for 16 weeks
e. **Genotype-3, treatment-naïve or treatment-experienced, without cirrhosis:**
    i. Daklinza™ 60mg with Sovaldi® for 12 weeks
f. **Genotype-3, treatment-naïve or treatment-experienced, with compensated or decompensated cirrhosis, or post-transplant:**
    i. Daklinza™ 60mg with Sovaldi® and weight-based ribavirin for 12 weeks
g. **Concomitant use of moderate CYP3A inducer(s):**
    i. Daklinza™ 90mg (all other regimen criteria applies)
    ii. Moderate Inducers: bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, and rifapentine
h. **Concomitant use of strong CYP3A inhibitors:**
    i. Daklinza™ 30mg (all other regimen criteria applies)
    ii. Strong CYP3A inhibitors include the following: atazanavir/ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, and voriconazole
i. New regimens will apply as approved by the FDA

8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
~~13. Member must not have decompensated cirrhosis; and~~
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: carbamazepine, phenytoin, phenobarbital, rifampin, amiodarone, or St. John's wort; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and

18. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
19. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Technivie™ (Ombitasvir/Paritaprevir/Ritonavir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-4**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Technivie™ must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on genotype, cirrhosis status, and prior treatment status will apply:
    a. **Genotype-4, treatment-naïve or treatment-experienced, non-cirrhotic or compensated cirrhotic:**
        i. Technivie™ in combination with weight-based ribavirin for 12 weeks
    b. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have cirrhosis, decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
16. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and

17. Member must not be taking the following medications: alfuzosin, carbamazepine, phenytoin, phenobarbital, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol containing medications (combined oral contraceptives), St. John's wort, lovastatin, simvastatin, pimozide, efavirenz, sildenafil, triazolam, orally administered midazolam, atazanavir/ritonavir, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine, salmeterol, or voriconazole; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Harvoni® (Ledipasvir/Sofosbuvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) **genotype-1, genotype-4, genotype-5, or genotype-6**; and
3. Member must have a METAVIR fibrosis score of **F2** or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Harvoni® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, baseline viral load, and cirrhosis will apply:
    a. **Genotype-1:**
        i. **Treatment-naïve without cirrhosis who have a pre-treatment HCV-RNA less than 6 million IU/mL:**
            1. Harvoni® for 8 weeks
        ii. **Treatment-naïve with or without compensated cirrhosis:**
            1. Treatment-naïve patients who are cirrhotic or have a pre-treatment HCV-RNA greater than 6 million IU/mL
            2. Harvoni® for 12 weeks
        iii. **Treatment-experienced without cirrhosis:**
            1. Harvoni® for 12 weeks
        iv. **Treatment-experienced with compensated cirrhosis:**

1. Harvoni® for 24 weeks

v. Treatment-naïve or treatment-experienced with decompensated cirrhosis:

1. Harvoni® with weight-based ribavirin for 12 weeks

b. Genotype-1 or Genotype-4:

i. Treatment-naïve or treatment-experienced liver transplant recipients with or without compensated cirrhosis:

1. Harvoni® with weight-based ribavirin for 12 weeks

c. Genotype-4, Genotype-5, or Genotype-6:

i. Treatment-naïve or treatment-experienced with or without compensated cirrhosis:

1. Harvoni® for 12 weeks

d. New regimens will apply as approved by the FDA

8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Member must have no illicit IV drug use or alcohol abuse in the last six months and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. ~~Member must not have decompensated cirrhosis; and~~
14. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m^2); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
16. Member must not be taking the following medications: rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, simeprevir, rosuvastatin, St. John's wort, or elvitegravir/cobicistat/ emtricitabine in combination with tenofovir disoproxil fumarate; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Recommendation 3: Vote to Prior Authorize Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein], Adynovate® [Antihemophilic Factor (Recombinant), PEGylated], Alprolix® [Coagulation Factor IX (Recombinant), Fc Fusion Protein], Idelvion® [Coagulation Factor IX (Recombinant), Albumin Fusion Protein], Obizur® [Antihemophilic Factor (Recombinant), Porcine Sequence], Corifact® [Factor XIII Concentrate (Human)], Tretten® [Coagulation Factor XIII A-Subunit (Recombinant)], and Coagadex® [Coagulation Factor X (Human)], and Establish Pharmacy Provider Standards of Care

MOTION CARRIED by unanimous approval.

Prior authorize Eloctate™ [antihemophilic factor (recombinant), Fc fusion protein], Adynovate® [antihemophilic factor (recombinant), PEGylated], Alprolix® [coagulation factor IX (recombinant), Fc fusion protein], Idelvion® [coagulation factor IX (recombinant), albumin fusion protein], Obizur® [antihemophilic factor (recombinant), porcine sequence], Corifact® [factor XIII concentrate (human)], Tretten® [coagulation factor XIII A-subunit (recombinant)], and Coagadex® [coagulation factor X (human)] with the following 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.
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.
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.
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.
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.

Additionally, the following standards of care are recommended for pharmacies providing factor replacement products:

1. The Provider/Pharmacy shall 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 of providing a full range of factor products including all available vial sizes.
    b. The Provider/Pharmacy shall provide support services to patients on a "24/7" basis in order to assure availability of appropriate support in the event of an after-hours emergency.
    c. The Provider/Pharmacy staff shall deliver factor within 24 hours (with a delivery goal of four hours) of notification of a need due to a current bleeding episode. If the patient is not having an emergency/current bleeding episode, the Provider/Pharmacy shall deliver factor within three days of notification of need.
    d. The Provider/Pharmacy shall provide all necessary supplies for the appropriate preparation and administration of the factor product as well as appropriate sharps and bio-hazardous disposal unit (to include retrieval and destruction of the disposal unit). If the items are SoonerCare compensable, such items 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 for whom English is not their primary language. Interpreters must be available on a "24/7" basis, 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. An assessment must include, at a minimum:
            a. Verification of appropriate and adequate storage; and
            b. A current inventory of factor product and supplies; and
            c. Verification of access to a bio-hazardous waste disposal unit; and
            d. A review of current infusion/treatment records/logs; and
            e. A assessment of educational opportunities to be performed by appropriately trained staff (please refer to 3 b ii below); and
            f. Identification of any 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.
        3. The in-home assessment must be completed annually and must be documented and signed by patient or caregiver and pharmacy personnel acknowledging the availability of patient and/or caregiver training and the patient/caregiver's understanding of the items set forth in subparagraph 2(f)(ii)(1) above, together with any additional information discussed.
    iii. Regular follow up with the patient via telephone, video call, or in-person. This contact should be at least quarterly and must address, at a minimum:
        1. All recent bleeding episodes reported should be forwarded to the prescribing practitioner immediately.
        2. Current inventory:
            a. Number of factor doses on hand; and
            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 appropriately trained and knowledgeable about hemophilia and other bleeding disorders.
        ii. Two hours of Continuing Education (CE) on hemophilia or other related bleeding disorders must be completed annually. Licensed staff must use

accredited CE based on their license type. Non-licensed staff may use non-accredited CE provided by a licensed professional.

1. Staff members, whether employed or contracted by the pharmacy, who are required to complete CE include but are not limited to the following:
    a. Pharmacist in Charge; and
    b. Nurse manager; and
    c. Nurse performing direct patient care; and
    d. Social worker; and
    e. Case Manager (including customer service representatives).
2. Documentation of educational activity completed must be maintained by 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 shall encourage engagement with ~~the Oklahoma~~ a 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's or mid-level practitioner's recommendations. 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; and
        2. Proper disposal of bio-hazardous waste; and
        3. Preparation of factor and supplies; and
        4. Training on self-infusion; and
            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. Infusion/treatment record keeping; and
        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. If a prescription is written for prophylaxis with additional doses for breakthrough bleeding, then the monthly prophylaxis dispensing should not include further additional doses absent documented use of doses for breakthrough bleeding.

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, the vial/box should be labeled as such; and
    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 dispensed 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 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 ~~a copy of the prescription~~, 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 6 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 Oklahoma Health Care Authority these standards of care will be followed and must re-attest yearly.
6. Oklahoma Health Care Authority (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; and
        ii. Educational information and training provided; and
        iii. Adverse Event records including reports to other state and federal agencies; and
        iv. Sharps and bio-hazardous waste disposal units, delivery proof, and education on proper disposal in patient record; and
        v. Patient records, including:

1. Original Prescriptions; and
2. Dispensing records (including lot numbers and expiration dates).

b. The pharmacy will be excluded from providing blood factor products if OHCA finds that the pharmacy is out of compliance with the requirements as outlined.

Recommendation 4: Vote to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®) and Update Makena® (Hydroxyprogesterone Caproate) Approval Criteria

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Makena® (hydroxyprogesterone caproate injection) to expand the start window to a gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation.
2. The prior authorization of Crinone® (progesterone vaginal gel) with the criteria noted in red.
3. The prior authorization of Endometrin® (progesterone vaginal insert) with the criteria noted in red.

New proposed criteria specific to each medication is as follows:

Makena® (Hydroxyprogesterone Caproate) Approval Criteria:

1. Documented history of previous singleton spontaneous preterm delivery (SPTD) prior to 37 weeks gestation; and
2. Current singleton pregnancy; and
3. Gestational age between 16 weeks, 0 days and 26 weeks, 6 days of gestation.
4. Authorizations will be for once a week administration by a healthcare professional through 36 weeks, 6 days of gestation.

Crinone® (Progesterone Vaginal Gel) Approval Criteria:

1. Current singleton pregnancy; and
2. Member must not have history of previous singleton spontaneous preterm delivery (SPTD); and
3. Cervical length of ≤ 20mm; and
4. Gestational age between 20 weeks, 0 days and 26 weeks, 6 days of gestation; and
5. A patient-specific, clinically significant reason why the member cannot use Endometrin® (progesterone vaginal insert).
6. Authorizations will be given for treatment through 36 weeks, 6 days of gestation.
7. Crinone® will not be covered for use with assisted reproductive technology (ART) for female infertility.

Endometrin® (Progesterone Vaginal Insert) Approval Criteria:

1. Current singleton pregnancy; and
2. Member must not have history of previous singleton spontaneous preterm delivery (SPTD); and
3. Cervical length of ≤ 20mm; and

4. Gestational age between 20 weeks, 0 days and 26 weeks, 6 days of gestation.
5. Authorizations will be given for treatment through 36 weeks, 6 days of gestation.
6. Endometrin® will not be covered for use with assisted reproductive technology (ART) for female infertility.

Recommendation 5: Vote to Prior Authorize Humalog® KwikPen® U-200 (Insulin Lispro), Tresiba® (Insulin Degludec), Ryzodeg® 70/30 (Insulin Degludec/Insulin Aspart), Basaglar® (Insulin Glargine), and Synjardy® (Empagliflozin/Metformin)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Humalog® KwikPen® U-200 (insulin lispro 200 units/mL), Tresiba® (insulin degludec), Ryzodeg® (insulin degludec/insulin aspart), and Basaglar® (insulin glargine) with the following criteria:

Humalog® KwikPen® U-200 (Insulin Lispro 200 Units/mL) Approval Criteria:

1. A patient-specific, clinically significant reason the member cannot use the 100 unit/mL strength is required for authorization of the 200 unit/mL strength.

Tresiba® (Insulin Degludec) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir).

Ryzodeg® (Insulin Degludec/Insulin Aspart) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir) with Novolog® (insulin aspart).

Basaglar® (Insulin Glargine) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) or Levemir® (insulin detemir).

Additionally, the College of Pharmacy recommends the placement of Synjardy® (empagliflozin/metformin) into Tier-3 of the diabetes medications Product Based Prior Authorization (PBPA) category. The existing Tier-3 criteria for this category will apply.

Recommendation 6: Vote to Prior Authorize Entresto™ (Sacubitril/Valsartan)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Entresto™ (sacubitril/valsartan) with the following criteria:

Entresto™ (Sacubitril/Valsartan) Approval Criteria:

1. An FDA approved diagnosis of chronic heart failure (NYHA Class II, III, or IV); and
2. The prescriber must verify that the member has a left ventricular ejection fraction ≤40%; and

3. The member must be on a maximally tolerated dose of a beta-blocker or have a contraindication to beta-blocker therapy; and
4. The prescriber must verify the member has been on an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) for at least four weeks; and
5. The member must not take an ACE inhibitor while taking Entresto™ as concomitant use is contraindicated; and
6. Members with a diagnosis of diabetes must not be taking aliskiren while taking Entresto™ as concomitant use is contraindicated; and
7. A quantity limit of 60 tablets per 30 days will apply.

Additionally, the College of Pharmacy recommends the following changes to the Antihypertensive Medication Product Based Prior Authorization (PBPA) category:

1. Move Aceon® (perindopril) to Tier-1 of the ACE Inhibitor category based on state maximum allowable cost (SMAC).
2. Move Lotrel® (amlodipine/benazepril) to Tier-1 of the ACE Inhibitor/CCB combination category based on SMAC.
3. Remove Lexxel® (enalapril/felodipine) from the ACE Inhibitor/CCB combination category and remove Valturna® (aliskiren/valsartan) from the Direct Renin Inhibitors category due to product discontinuations.
4. Move Diovan® (valsartan) to Tier-1 of the ARBs/ARB combination category based on SMAC.
5. Move Micardis® (telmisartan) to Tier-2 of the ARBs/ARB combination category based on SMAC. Current Tier-2 criteria for this category will apply.

Angiotensin Converting Enzyme Inhibitors (ACEIs)		
Tier-1	**Tier-2**	**Special PA**
benazepril (Lotensin®)	Newly approved products	enalapril powder (Epaned®)
captopril (Capoten®)		
enalapril (Vasotec®)		
enalaprilat (Vasotec® IV)		
fosinopril (Monopril®)		
lisinopril (Prinivil®, Zestril®)		
moexipril (Univasc®)		
quinapril (Accupril®)		
perindopril erbumine (Aceon®)		
ramipril (Altace®)		
trandolapril (Mavik®)		

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

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

Direct Renin inhibitors		
Tier-1	**Tier-2**	**Tier-3**
Tier-1 ACE Inhibitor + Diuretic	ARB + Diuretic	aliskiren (Tekturna®)
		aliskiren/HCTZ (Tekturna HCT®)
		~~aliskiren/valsartan (Valturna®)~~
		aliskiren/amlodipine (Tekamlo®)

ARBs (Angiotensin Receptor Blockers) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
ACE Inhibitor:	amlodipine/olmesartan (Azor™)	amlodipine/valsartan/HCTZ (Exforge® HCT)
benazepril (Lotensin®)	amlodipine/valsartan (Exforge®)	azilsartan (Edarbi®)
captopril (Capoten®)	olmesartan (Benicar®)	azilsartan/chlorthalidone (Edarbyclor®)
enalapril (Vasotec®)	olmesartan/HCTZ (Benicar HCT®)	candesartan (Atacand®)
enalaprilat (Vasotec® IV)	olmesartan/ amlodipine/HCTZ (Tribenzor®)	candesartan/HCTZ (Atacand® HCT)
fosinopril (Monopril®)	**telmisartan (Micardis®)**	eprosartan (Teveten®)
lisinopril (Prinivil®, Zestril®)		eprosartan/HCTZ (Teveten® HCT)
moexipril (Univasc®)		telmisartan/HCTZ (Micardis® HCT)
quinapril (Accupril®)		telmisartan/amlodipine (Twynsta®)
perindopril erbumine (Aceon®)		
ramipril (Altace®)		
trandolapril (Mavik®)		
ARB:		
irbesartan (Avapro®)		
irbesartan/HCTZ (Avalide®)		
losartan (Cozaar®)		
losartan/HCTZ (Hyzaar®)		
valsartan/HCTZ (Diovan HCT®)		
valsartan (Diovan®)		

ACE = Angiotensin Converting Enzyme, HCTZ = Hydrochlorothiazide

Recommendation 7: 30-Day Notice to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium-223 Dichloride), and Provenge® (Sipuleucel-T)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of ADHD & Narcolepsy Medications and 30-Day Notice to Prior Authorize Dyanavel™ XR (Amphetamine Extended-Release), QuilliChew ER™ (Methylphenidate Extended-Release), and Adzenys XR-ODT™ (Amphetamine Extended-Release)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Cholbam® (Cholic Acid)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Anthelmintic Medications and 30-Day Notice to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole)

NO ACTION REQUIRED.

Recommendation 12: 30-Day Notice to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize OsmoPrep® (Sodium Phosphate Monobasic/ Sodium Phosphate Dibasic), Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid), Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/Sodium Chloride/Sodium Bicarbonate/Potassium Chloride), and SUPREP® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate)

NO ACTION REQUIRED.

Recommendation 14: Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Nuvessa™ (Metronidazole Vaginal Gel 1.3%), Zyclara® (Imiquimod Cream), and Kristalose® (Lactulose Packets)

NO ACTION REQUIRED.

Recommendation 15: Annual Review of Topical Antifungal Products and 30-Day Notice to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution

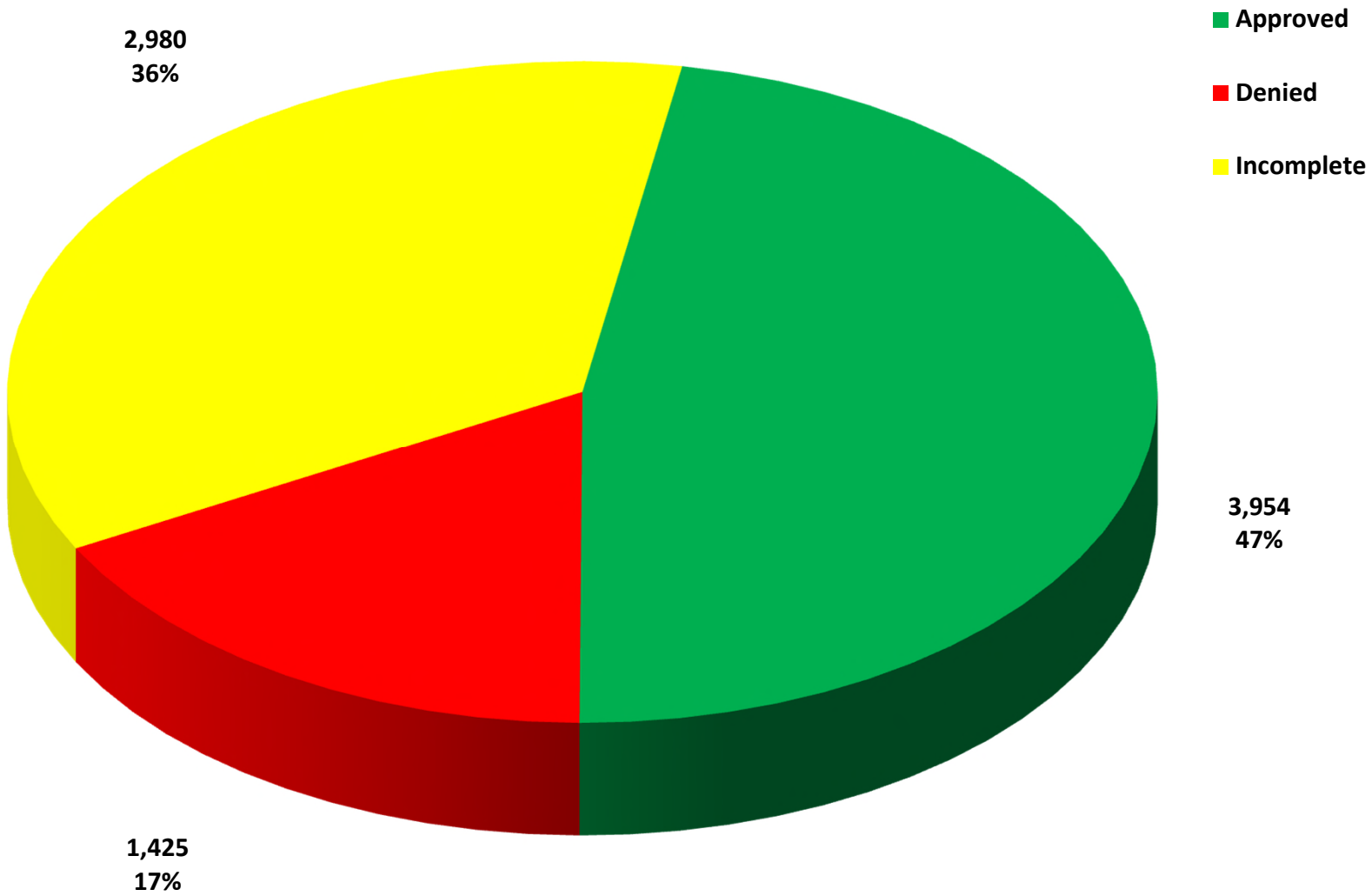
NO ACTION REQUIRED.

Recommendation 16: Annual Review of Natpara® (Parathyroid Hormone Injection)

NO ACTION REQUIRED.

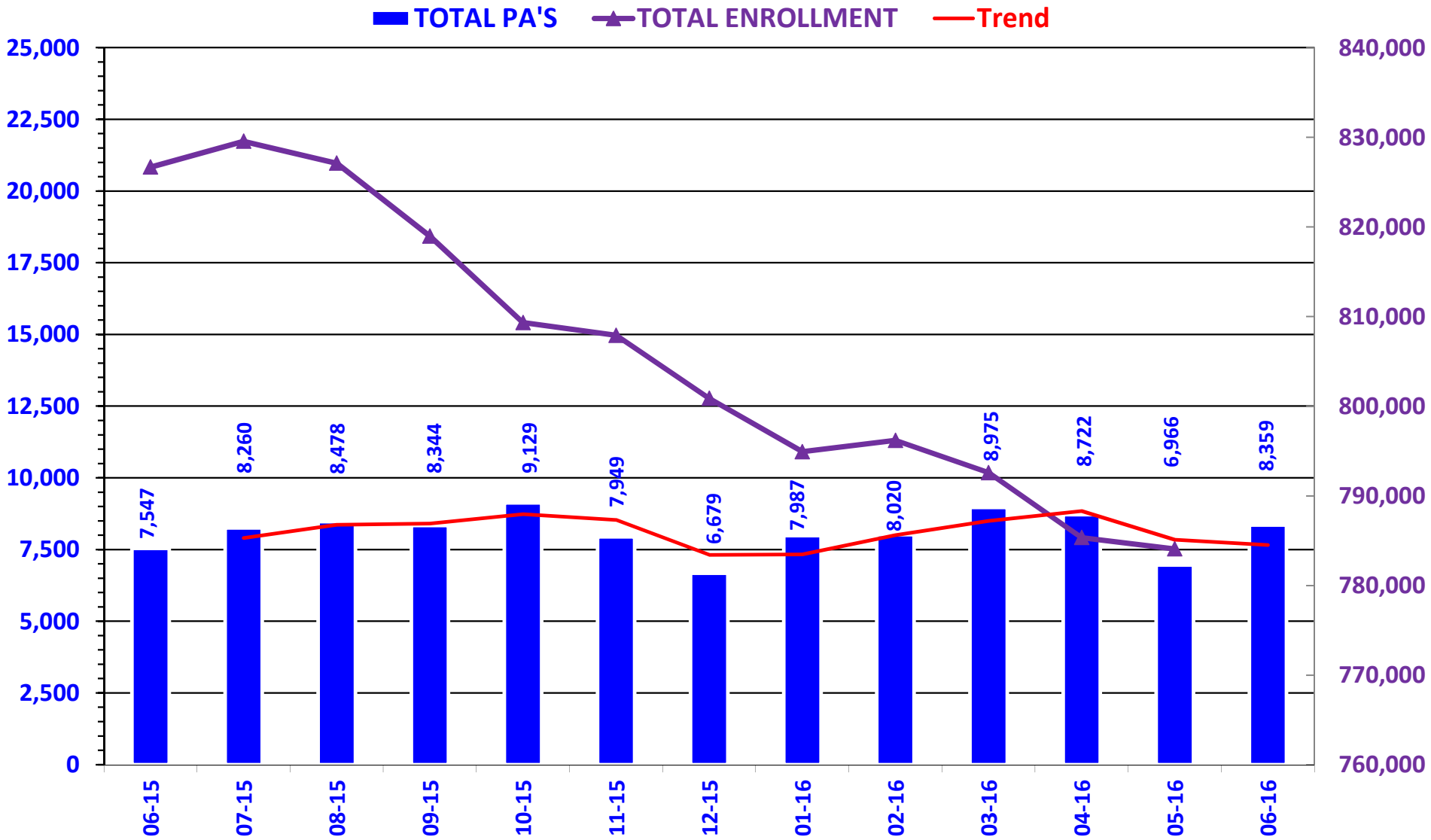
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: JUNE 2016



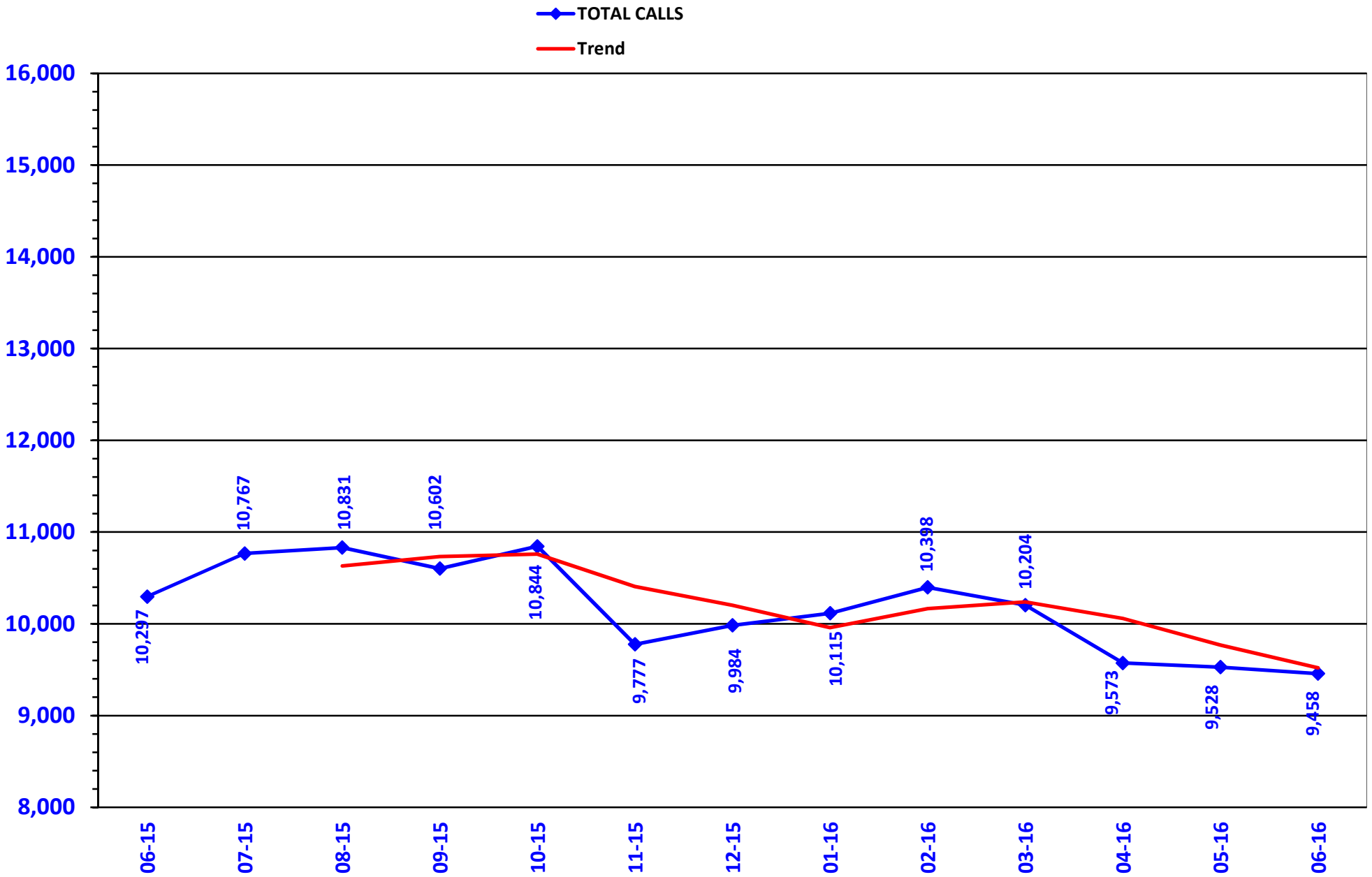
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: JUNE 2015 – JUNE 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
JUNE 2015 – JUNE 2016



Prior Authorization Activity

6/1/2016 Through 6/30/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	361	143	65	153	350
Analgesic - NonNarcotic	17	0	1	16	0
Analgesic - Narcotic	444	260	36	148	162
Angiotensin Receptor Antagonist	22	6	5	11	303
Antiasthma	79	24	22	33	324
Antibiotic	20	7	1	12	120
Anticonvulsant	103	46	13	44	326
Antidepressant	76	21	19	36	340
Antidiabetic	198	84	36	78	347
Antihistamine	208	170	8	30	358
Antimigraine	31	7	9	15	124
Antineoplastic	42	18	5	19	182
Antiplatelet	52	2	23	27	358
Antiulcers	159	32	50	77	179
Anxiolytic	58	43	3	12	247
Atypical Antipsychotics	417	228	38	151	340
Benign Prostatic Hypertrophy	12	1	6	5	358
Biologics	102	49	20	33	323
Bladder Control	67	21	15	31	345
Blood Thinners	183	111	13	59	326
Botox	23	16	5	2	335
Cardiovascular	96	30	26	40	304
Cephalosporins	14	6	2	6	7
Chronic Obstructive Pulmonary Disease	80	13	27	40	357
Contraceptive	26	18	1	7	337
Dermatological	112	20	70	22	115
Diabetic Supplies	528	278	24	226	196
Endocrine & Metabolic Drugs	74	54	2	18	124
Erythropoietin Stimulating Agents	25	18	3	4	89
Fibromyalgia	191	30	99	62	335
Fish Oils	14	0	6	8	0
Gastrointestinal Agents	139	37	45	57	158
Genitourinary Agents	15	8	3	4	105
Growth Hormones	71	52	8	11	137
Hematopoietic Agents	43	11	11	21	154
Hepatitis C	168	97	37	34	8
HFA Rescue Inhalers	56	19	12	25	344
Insomnia	58	10	25	23	185
Insulin	65	9	20	36	357
Linzess/Amitiza/Relistor	119	16	46	57	153
Miscellaneous Antibiotics	25	5	3	17	46
Multiple Sclerosis	40	14	13	13	242
Muscle Relaxant	69	13	25	31	75
Nasal Allergy	95	19	21	55	223
Neurological Agents	55	34	9	12	355
NSAIDs	192	30	41	121	233
Ocular Allergy	49	10	15	24	176
Ophthalmic Anti-infectives	20	4	6	10	23
Osteoporosis	32	12	8	12	327
Other*	299	53	79	167	181
Otic Antibiotic	61	1	11	49	25
Pediculicide	45	17	3	25	17
Statins	64	9	13	42	326
Stimulant	651	358	73	220	330
Suboxone/Subutex/Bunavail/Zubsolv	231	188	11	32	71

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Testosterone	69	12	20	37	289
Topical Antifungal	52	1	10	41	2
Topical Corticosteroids	150	2	59	89	220
Vitamins	104	23	57	24	285
Pharmacotherapy	80	68	0	12	318
Emergency PAs	1	1	0	0	
Total	**6,952**	**2,889**	**1,337**	**2,726**	
Overrides					
Brand	69	41	6	22	300
Cumulative Early Refill	5	4	1	0	98
Diabetic Supplies	1	1	0	0	51
Dosage Change	332	309	0	23	11
High Dose	5	3	1	1	166
Ingredient Duplication	22	17	0	5	10
Lost/Broken Rx	88	84	0	4	10
NDC vs Age	40	35	2	3	197
Nursing Home Issue	55	51	0	4	10
Opioid Quantity	14	13	1	0	165
Other*	40	25	8	7	12
Prescriber Temp Unlock	1	0	0	1	0
Quantity vs. Days Supply	680	453	64	163	264
STBS/STBSM	16	13	0	3	78
Stolen	19	11	0	8	8
Temporary Unlock	5	5	0	0	17
Third Brand Request	35	17	7	11	34
Wrong D.S. on Previous Rx	1	1	0	0	6
Overrides Total	**1,407**	**1,065**	**88**	**254**	
Total Regular PAs + Overrides	**8,359**	**3,954**	**1,425**	**2,980**	

Denial Reasons	
Unable to verify required trials.	2,529
Does not meet established criteria.	1,447
Lack required information to process request.	417
Ingredient Duplication Override	1

Other PA Activity	
Duplicate Requests	512
Letters	6,836
No Process	1
Changes to existing PAs	547
Helpdesk Initiated Prior Authorizations	720
PAs Missing Information	32

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

Opioid Prescriptions in Pregnant Women

Oklahoma Health Care Authority
July 2016
Data compiled by OHCA Reporting and Statistics: Sarah Walker

Introduction[1]

A study published in the *Journal of Obstetrics & Gynecology* in May 2014 evaluated the prevalence of prescription opioid use in a large national cohort of Medicaid-insured pregnant women from 2000 to 2007. The authors initiated the study in light of evidence indicating opioid analgesic use in the first trimester may be associated with neural tube defects, and the confirmed risk of neonatal abstinence syndrome (NAS) after persistent opioid exposure late in pregnancy.

More than 1.1 million Medicaid-enrolled women with completed pregnancies from 46 U.S. states and Washington, DC were analyzed. Overall study results found 21.6% of pregnant women received at least one prescription for an opioid during their pregnancy. The most common diagnoses of pregnant women receiving an opioid prescription were abdominal pain (48.4%), lower back pain (33.0%), headache syndromes (13.3%), joint pain (11.2%), or migraine (7.9%). When evaluated by trimester, the proportion with an opioid prescription was 10.5% in the first, 9.6% in the second, and 9.8% in the third. The median cumulative days of opioid availability during pregnancy was 5 (3 to 13) days, and the median number of prescriptions filled during pregnancy was one. The proportion of women with cumulative days of opioid availability greater than 30 was 2.5%. The most common opioid medications used were codeine (11.1%) and hydrocodone (10.0%).

The proportion of women with opioid prescriptions during pregnancy varied by state, ranging from 8.5% to 41.6%. The rate of opioid use in Oklahoma was found to be greater than 30%. Nationally, the proportion of women who filled an opioid prescription during pregnancy increased by 23.1% from 2000 to 2007; this trend was also seen during each trimester separately.

SoonerCare Claims Analysis

The following claims analysis for state fiscal year (SFY) 2014 and 2015 was conducted by Oklahoma Health Care Authority (OHCA) Reporting and Statistics. The results were compiled by loosely following the methodology of the study discussed in the introduction section of this report. Only completed pregnancies, or those with a paid claim for a delivery, were included in the analysis. SoonerCare paid claims for opioids were included except those opioid paid claims that fell after and up to three days prior to delivery. “Opioid pregnancies” are considered those deliveries where the mother had a paid opioid claim in the 39 weeks prior to delivery (excluding the three days before delivery).

Opioid Usage During Pregnancy: Overall Results

	SFY2014 Count of Members	% of Completed Pregnancy	SFY2015 Count of Members	% of Completed Pregnancy
Completed Pregnancy Members	32,148	100%	31,117	100%
Opioid Within 39 Weeks Prior to Delivery*	4,328	13%	4,963	16%
Count of Mothers With Opioid Prescriptions & Babies Born and Diagnosed With NAS	91	0.28%	116	0.37%

SFY = State fiscal year; NAS = Neonatal abstinence syndrome
*Minus prescriptions filled up to 3 days before delivery.

The national analysis estimated the rate of opioid usage among SoonerCare pregnant women to be greater than 30%, however OHCA found the rate to be 13% in SFY2014 and 16% in SFY2015.

Opioid Usage During Pregnancy SFY2014-2015: Claims Per Member

The following table shows the count of opioid claims by the number of members. Most members had only one paid claim for an opioid medication during pregnancy (SFY2014: 60.8%, SFY2015: 58.4%). A total of 32.9% of members in SFY2014 and 32.8% in SFY2015 had two to five paid pharmacy claims for an opioid medication during pregnancy. Members with 10 or more opioid claims accounted for 1.5% of members in SFY2014 and 2.8% of members in SFY2015. One member had a total of 36 opioid claims during pregnancy in SFY2015.

Count of Opioid Claims	SFY2014 Count of Members	SFY2015 Count of Members
1	2,630	2,898
2	798	923
3	337	388
4	172	210
5	117	105
6	69	96
7	69	79
8	45	53
9	25	70
10	23	39
11-15	38	74
16-20	3	23
21+	2	5
Total	**4,328**	**4,963**

*Claim numbers represent number of paid claims and do not account for days supply, strength, or units dispensed.

Opioid Usage During Pregnancy SFY2014-2015: Trimesters

Trimesters were calculated by subtracting 273 days from the delivery date and then dividing into 90 day increments. This method may allow for over-reporting of premature births and under-reporting of births that were longer than 39 weeks.

Trimester	SFY2014 Count of Members with Opioid Rx	SFY2014 Count of Opioid Claims (% of Total Claims)	SFY2015 Count of Members with Opioid Rx	SFY2015 Count of Opioid Claims (% of Total Claims)
1st	897	1,346 (15.3%)	1,895	3,150 (27.8%)
2nd	1,908	2,952 (33.5%)	2,448	4,103 (36.2%)
3rd	2,616	4,503 (51.2%)	2,288	4,062 (35.9%)
Total	**5,421**	**8,801**	**6,631**	**11,315**

Members are duplicated due to having opioids in more than one trimester.

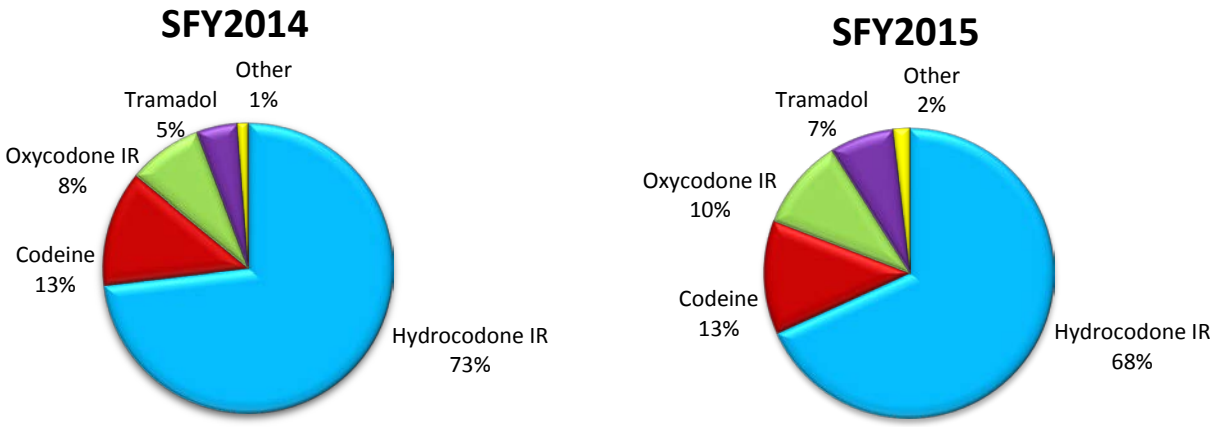
Opioid use during all three trimesters is associated with risk. The risk of birth defects associated with first trimester opioid use was found to be increased in a study by Broussard and colleagues. Results indicated that opioid use in the first trimester was statistically significantly associated with hypoplastic left heart syndrome (OR 2.4; 95% CI: 1.4, 4.1) and spina bifida (OR 2.0; 95% CI: 1.3, 3.2) in infants.[2] Desai and colleagues found the overall absolute risk of NAS in infants born to women who used opioids during pregnancy to be 5.9 per 1000 deliveries (95% CI: 5.6, 6.2). The authors also found long-term opioid use and late-pregnancy opioid use had greater risk of NAS [risk ratios 2.05 (95% CI: 1.81, 2.33) and 1.24 (95% CI: 1.12, 1.38)].[3] Results of these studies indicate careful consideration should be given before opioid use during any trimester.

OR = Odds ratio; CI = Confidence interval; NAS = Neonatal abstinence syndrome

	SFY2014 Deliveries				SFY2015 Deliveries			
Opioids	**1st Trimester Claims**	**2nd Trimester Claims**	**3rd Trimester Claims**	**Total Claims**	**1st Trimester Claims**	**2nd Trimester Claims**	**3rd Trimester Claims**	**Total Claims**
Hydrocodone IR	1,011	2,179	3,249	**6,439**	2,236	2,836	2,646	**7,718**
Codeine	132	399	607	**1,138**	244	574	617	**1,435**
Oxycodone IR	89	215	425	**729**	292	387	480	**1,159**
Tramadol	102	131	176	**409**	304	246	253	**803**
Oxycodone ER	2	4		**6**	16	19	19	**54**
Morphine ER	5	2	4	**11**	17	12	8	**37**
Methadone		4	9	**13**	10	12	10	**32**
Hydromorphone		3	5	**8**	4	5	13	**22**
Meperidine	1	4	10	**15**	10	4	9	**23**
Fentanyl	3	4	7	**14**	10		2	**12**
Oxymorphone ER		3	3	**6**	5	5	1	**11**
Morphine IR	1	3	4	**8**	1	1	3	**5**
Tapentadol		1	4	**5**				
Belladonna-Opium					1	2	1	**4**
Total	**1,346**	**2,952**	**4,503**	**8,801**	**3,150**	**4,103**	**4,062**	**11,315**

IR = Immediate-release; ER = Extended-release

The most commonly used opioid during any trimester for both SFY2014 and SFY2015 was immediate-release hydrocodone. Other opioids commonly used during pregnancy included codeine, oxycodone immediate-release, and tramadol.



Recommendations[1,2,3]

In light of the recent studies suggesting the teratogenic potential of opioid medications, and the known risks of neonatal withdrawal after in utero exposure, opioid use in pregnant women is a significant public health concern. Delays and inaccuracies in the SoonerCare claims database in obtaining pregnancy data limit options for implementation of edits that would stop payment for opioid claims in pregnant women alone. Additionally women who experience miscarriage or pre-term delivery may still be classified as pregnant in the claims database and hard-stop edits could limit appropriate treatment with opioid medications. Alternative methodologies for reducing rates of opioid use in pregnant women recommended by the College of Pharmacy in collaboration with the Oklahoma Health Care Authority include the following:

- Provider education targeted to obstetricians and gynecologists regarding the risk of opioid use during pregnancy and the SoonerCare rates of opioid use in pregnant women.
- A clinical edit at the pharmacy level for members with a pregnancy indicator in the SoonerCare claims database. The edit would recommend members be switched to buprenorphine when running a claim for an opioid medication but could be overridden without prior authorization submission if deemed appropriate.
- Removal of prior authorization for buprenorphine/naloxone for all female beneficiaries. Quantity limits and claim denials for concomitant opioid medications would still apply.

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[1] Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in Prescription Opioid Use During Pregnancy Among Medicaid-Enrolled Women. *Obstet Gynecol* 2014; 123:99-1002.

[2] Broussard CS, Rasmussen SA, Reefhuis J, et al. Maternal treatment with opioid analgesics and risk for birth defects. *Am J Obstet Gynecol* 2011; 204:314. e1-11.

[3] Desai RJ, Huybrechts KF, Hernandez-Diaz S, et al. Exposure to prescription opioid analgesics in utero and risk of neonatal abstinence syndrome: population based cohort study. *BMJ* 2015; 350:h2102.

Appendix C

Vote to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium-223 Dichloride), and Provenge® (Sipuleucel-T)

Oklahoma Health Care Authority
July 2016

Introduction[1]

Zytiga® (Abiraterone)

- Abiraterone is a pregnenolone derivative that is a selective, high-affinity, irreversible inhibitor of CYP17 that lowers serum testosterone concentrations to castrate levels without significantly affecting serum hydrocortisone levels indicated for the following:
    - Treatment of patients with metastatic, castration-resistant prostate cancer (CRPC) in combination with prednisone

Jevtana® (Cabazitaxel)

- Cabazitaxel is classified as a semi-synthetic taxane which works to inhibit microtubule formation indicated for the following:
    - Treatment of patients with hormone-refractory, metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen
- Cabazitaxel has reduced affinity for P-glycoprotein and thus is able to overcome resistance and maintain efficacy in docetaxel-resistant prostate cancers.

Xtandi® (Enzalutamide)

- Enzalutamide is distinct from the currently available antiandrogen agents in that it inhibits nuclear translocation of the androgen receptor, DNA binding, and coactivator recruitment. It also has a greater affinity for the receptor, induces tumor shrinkage in xenograft models (in which conventional agents only retard growth), and has no known agonistic effects. It is indicated in the following:
    - Treatment of patients with metastatic CRPC

Xofigo® (Radium-223 Dichloride)

- Radium-223 dichloride is an alpha-particle emitting radiotherapeutic drug. It mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases. The high linear energy transfer of alpha emitters leads to a high frequency of double-strand DNA breaks in adjacent cells, resulting in an anti-tumor effect on bone metastases. It is indicated for the following:
    - Treatment of patients with CRPC, symptomatic bone metastases, and no known visceral metastatic disease

Provenge® (Sipuleucel-T)

- Sipuleucel-T is a recombinant human protein, PAP-GM-CSF, consisting of prostatic acid phosphatase (PAP), an antigen expressed in prostate cancer tissue, linked to

granulocyte-macrophage colony stimulating factor (GM-CSF), an immune cell activator. It is designed to induce an immune response targeted against PAP. It is indicated for the following:

- Treatment of asymptomatic or minimally symptomatic metastatic CRPC (hormone-refractory)

Recommendations

Zytiga® (Abiraterone) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Abiraterone must be used in combination with a corticosteroid; and
3. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on abiraterone therapy.

Jevtana® (Cabazitaxel) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must have been previously treated with a docetaxel-containing regimen; and
3. Cabazitaxel should be used in combination with prednisone; and
4. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on cabazitaxel therapy.

Xtandi® (Enzalutamide) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on enzalutamide therapy.

Xofigo® (Radium-223 Dichloride) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must have symptomatic bone metastases; and
3. Member must not have known visceral metastatic disease; and
4. Prescriber must verify radium-223 is not to be used in combination with chemotherapy; and
5. Member must have an absolute neutrophil count ≥ 1.5 x 10^9/L, platelet count ≥ 100 x 10^9/L, and hemoglobin ≥10 g/dL; and
6. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents the following:
    a. The member has not shown evidence of progressive disease while on radium-223 dichloride therapy; and
    b. Member must have an absolute neutrophil count ≥ 1 x 10^9/L, platelet count ≥ 100 x 10^9/L (radium-223 dichloride should be delayed 6 to 8 weeks otherwise).

Provenge® (Sipuleucel-T) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Member must be asymptomatic or minimally symptomatic; and
3. Member must not have hepatic metastases; and
4. Member must have a life expectancy of greater than six months; and
5. Good performance status (ECOG 0 to 1); and
6. Approvals will be for the duration of three months at which time additional authorization may be granted if the prescriber documents that the member has not shown evidence of progressive disease while on sipuleucel-T therapy.

[1] National Comprehensive Cancer Network. "NCCN Clinical Practice Guidelines in Oncology (Prostate Cancer)." Available online at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed 05/16/2016.

Appendix D

Vote to Prior Authorize Dyanavel™ XR (Amphetamine Extended-Release), QuilliChew ER™ (Methylphenidate Extended-Release), and Adzenys XR-ODT™ (Amphetamine Extended-Release)

Oklahoma Health Care Authority
July 2016

Introduction[1,2,3]

- **Dyanavel™ XR (amphetamine extended-release)** is available as an extended-release, bubblegum-flavored oral suspension and is indicated for the treatment of ADHD in pediatric patients 6 to 17 years of age.
- **QuilliChew ER™ (methylphenidate extended-release)** is available as extended-release, cherry-flavored chewable tablets and is indicated for the treatment of ADHD. QuilliChew ER™ was studied in pediatric patients 6 to 12 years of age.
- **Adzenys XR-ODT™ (amphetamine extended-release)** is available as extended-release, orange-flavored orally disintegrating tablets (ODTs) and is indicated for the treatment of ADHD in patients 6 years of age and older.

Recommendations

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

1. Place Dyanavel™ XR (amphetamine ER) into the Special Prior Authorization (PA) category based on estimated acquisition cost (EAC).
    a. The existing criteria for special formulation products in the Special PA category will apply.
    b. A quantity limit of 240mL per 30 days will apply, based on the maximum dose of 20mg (or 8mL) per day.
    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.
2. Place QuilliChew ER™ (methylphenidate ER) into the Special PA category based on EAC.
    a. The existing criteria for special formulation products in the Special PA category will apply.
    b. A quantity limit of 30 chewable tablets per 30 days will apply on all strengths except for the 30mg strength, and a quantity limit of 60 chewable tablets per 30 days will apply on the 30mg strength, based on the maximum dose of 60mg per day.
        i. Members needing to titrate the dose of QuilliChew ER™ up or down should be instructed to break in half the functionally scored chewable

tablets to achieve the required dose, and the appropriate quantity of chewable tablets will be approved for dose titration purposes.

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.

3. Place Adzenys XR-ODT™ (amphetamine ER) into the Special PA category based on EAC.
   a. The existing criteria for special formulation products in the Special PA category will apply.
   b. A quantity limit of 30 ODTs per 30 days will apply.
   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.
4. Update the wording of the Tier-2, Tier-3, Kapvay®, and Xyrem® Approval Criteria to emphasize the requirement of previously failed trial(s) that resulted in an inadequate response, as requested by the Drug Utilization Review (DUR) Board at the previous DUR meeting in June 2016.

ADHD & Narcolepsy 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.

ADHD & Narcolepsy 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 capsule formulation.
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 & Narcolepsy Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo™, ProCentra® Solution, and Zenzedi® Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.
2. Adzenys XR-ODT™, 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.
3. Provigil®, Nuvigil®, and Xyrem® Criteria:
    a. An FDA approved diagnosis; and
    b. Use of Provigil® or Nuvigil® requires a patient-specific, clinically significant reason why the member cannot use stimulant medications to improve wakefulness during the daytime.
    c. Use of Xyrem® 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.
    d. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
    e. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0 to 4 years of age. All prior authorization requests for members younger than the age of 5 years must be reviewed by an OHCA-contracted psychiatrist.
3. Vyvanse® (Lisdexamfetamine) Approval Criteria: Binge Eating Disorder (BED)
    a. An FDA approved diagnosis of moderate-to-severe binge eating disorder; and
    b. Member must be 18 years or older; and
    c. Vyvanse® for the diagnosis of BED must be prescribed by a psychiatrist; and

d. Authorizations will not be granted for 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 per 30 days will apply; and
f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

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

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation.
+Unique criteria applies for the diagnosis of binge eating disorder (BED).
ER = Extended-Release, SR = Sustained-Release, ODT = Orally Disintegrating Tablet, Chew Tabs = Chewable Tablets, Soln = Solution, Susp = Suspension

[1] Dyanavel™ XR Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/dyanavel-xr-1/. Last revised 12/09/2015. Last accessed 06/16/2016.
[2] QuilliChew ER™ Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/quillichew-er/. Last revised 04/13/2016. Last accessed 06/16/2016.
[3] Adzenys XR-ODT™ Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/adzenys-xr-odt/. Last revised 02/18/2016. Last accessed 06/16/2016.

Appendix E

Vote to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil)

Oklahoma Health Care Authority
July 2016

Indication(s)[1,2,3]

- **Rexulti® (brexpiprazole)** is an atypical antipsychotic indicated for the use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) and indicated for the treatment of schizophrenia.
- **Vraylar™ (cariprazine)** is an atypical antipsychotic indicated for the treatment of schizophrenia and indicated for acute treatment of manic or mixed episodes associated with bipolar I disorder.
- **Aristada™ (aripiprazole lauroxil)** is an atypical antipsychotic indicated for the treatment of schizophrenia.

Recommendations

The College of Pharmacy recommends the following:

1. The addition of Rexulti® (brexpiprazole) to the current approval criteria for atypical antipsychotics as adjunctive treatment for major depression disorder.
2. The placement of Rexulti® (brexpiprazole), Vraylar™ (cariprazine), and Aristada® (aripiprazole lauroxil) into Tier-3 of the Atypical Antipsychotic Product Based Prior Authorization (PBPA) category. Current Tier-3 criteria for this category will apply.
    a. Aristada® (aripiprazole lauroxil) is currently rebated to Tier-2 but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.

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

ER = extended-release
*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Mandatory generic plan applies.
¥ Does not count towards a Tier-1 trial
∞ In addition to tier trials, use of Invega Trinza™ requires adequate treatment with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.

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

Atypical Antipsychotic Tier-2 Approval Criteria:

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

Atypical Antipsychotic Tier-3 Approval Criteria:

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

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

1. Authorization of Abilify® (aripiprazole), 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 (*pending aripiprazole move to Tier-1*) that did not yield adequate response. Tier structure applies.

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[1]Rexulti® Prescribing Information. Otsuka Pharmaceutical Co. Available online at: http://otsuka-us.com/products/Documents/Rexulti.PI.pdf. Last revised 08/2015. Last accessed 05/2016.
[2]Vraylar™ Prescribing Information. Actavis Pharma, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/204370lbl.pdf. Last revised 09/2015. Last accessed 05/2016.
[3]Aristada™ Prescribing Information. Alkermes, Inc. Available online at: http://aristada.com/hcp/ARISTADA-prescribing-information.pdf. Last revised 01/2016. Last accessed 05/2016.

Appendix F

Vote to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole)

Oklahoma Health Care Authority
July 2016

Introduction[1,2]

Albenza® (albendazole) is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium,* and treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus.* Albenza® (albendazole) is available as a 200mg tablet and the recommended dosing can be found in the table below.

Indication	Dose	Duration of Therapy
Hydatid disease	• Patients weighing 60kg or greater: 400mg twice a day • Patients weighing less than 60kg: 15mg/kg/day in divided doses twice daily (maximum total daily dose 800mg)	28-day cycle followed by 14-day albendazole-free interval for a total of 3 cycles
Neurocysticercosis	• Patients weighing 60kg or greater: 400mg twice a day • Patients weighing less than 60kg: 15mg/kg/day in divided doses twice daily (maximum total daily dose 800mg)	8 to 30 days

Emverm™ (mebendazole) is indicated for the treatment of *Enterobius vermicularis* (pinworm), *Trichuris trichiura* (whipworm), *Ascaris lumbricoides* (common roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections. Emverm™ (mebendazole) is available as a 100mg chewable tablet. The recommended dosing for mebendazole can be found in the table below.

	Pinworm (enterobiasis)	Whipworm (trichuriasis)	Common Roundworm (ascariasis)	Hookworm
Dose	1 tablet, once	1 tablet in the morning and evening for 3 consecutive days	1 tablet in the morning and evening for 3 consecutive days	1 tablet in the morning and evening for 3 consecutive days

Regimen Comparison[3,4,5,6,7,8,9,10]

The following table contains dosage regimens for the treatment of helminth infections based on current evidence-based recommendations and the Centers for Disease Control and Prevention (CDC).

	Medication	Usual Dose	Total Cost Per Initial Course	Cure Rates In Clinical Studies
Pinworm (Enterobiasis)	**Emverm™**	100mg orally once; repeat in three weeks if not cured^	$389.66◊	>90% after one dose; close to 100% if 2 doses are given 2 weeks apart
	Albenza®	400mg once; repeat in two weeks+ For children <20 kg: 200mg once; repeat in 2 weeks	$354.24◊	>90% after one dose; close to 100% if 2 doses are given 2 weeks apart
	Pyrantel Pamoate (OTC)	11mg/kg (maximum of 1g); repeat in two weeks	<$10¥	>90% after one dose; close to 100% if 2 doses are given 2 weeks apart
Whipworm (Trichuriasis)	**Emverm™**	100mg twice daily for three days	$2,337.96◊	70 to >90%
	Albenza®	400mg once daily for three days+*	$1,062.72◊	80% (considered 2nd line due to lower efficacy)
	Pyrantel Pamoate (OTC)	N/A	N/A	N/A
Common Roundworm (Ascariasis)	**Emverm™**	100mg twice daily for three days	$2,337.96◊	Approximately 95%
	Albenza®	400mg orally once+	$354.24◊	Approximately 100%
	Pyrantel Pamoate (OTC)	11mg/kg up to a maximum of 1g as a single dose+	<$10¥	Approximately 90%
Hookworm	**Emverm™**	100mg twice daily for three days	$2,337.96◊	54%
	Albenza®	400mg once or 400mg daily for 3 days+	$354.24 or $1,062.72◊	69% (single dose); 92% (triple-dose)
	Pyrantel Pamoate (OTC)	11mg/kg per day for three days, not to exceed 1g/day+	<$30¥	N/A

OTC = Over-the-Counter

+Not FDA approved for this indication

^Differs vs. CDC recommendations which recommend 100mg once; repeat in two weeks

*Considered second-line as its efficacy is lower

◊Cost based on estimated acquisition cost (EAC). Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

¥Cost based on over-the-counter (OTC) price of 1 ounce of medication (144mg/mL pyrantel pamoate) at walgreens.com

Recommendations

The College of Pharmacy recommends the prior authorization of Albenza® (albendazole) and Emverm™ (mebendazole) with the following criteria:

Albenza® (Albendazole) Approval Criteria:

1. A quantity of six tablets per 180 days will process without prior authorization. For infections requiring additional doses, a prior authorization will need to be submitted and the following criteria will apply:
    a. An FDA approved diagnosis of one of the following:
        i. Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*.
        ii. Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

Emverm™ (Mebendazole) Approval Criteria:

1. An FDA approved diagnosis of any of the following:
    a. Treatment of *Enterobius vermicularis* (pinworm); or
    b. Treatment of *Trichuris trichiura* (whipworm); or
    c. Treatment of *Ascaris lumbricoides* (common roundworm); or
    d. Treatment of *Ancylostoma duodenale* (common hookworm); or
    e. Treatment of *Necator americanus* (American hookworm); and
2. For the treatment of *Enterobius vermicularis* (pinworms), *Ascaris lumbricoides* (common roundworm), *Ancylostoma duodenale* (common hookworm), or *Necator americanus* (American hookworm), a patient-specific, clinically significant reason why a more cost-effective anthelmintic therapy, such as albendazole or pyrantel pamoate, cannot be used must be provided.
3. The following quantity limits will apply:
    a. *Enterobius vermicularis (*pinworms): 2 tablets per 30 days
    b. *Trichuris trichiura* (whipworm): 6 tablets per 30 days
    c. *Ascaris lumbricoides* (common roundworm): 6 tablets per 30 days
    d. *Ancylostoma duodenale* (common hookworm): 6 tablets per 30 days
    e. *Necator americanus* (American hookworm): 6 tablets per 30 days

[1] Albenza® Product Information. Amedra Pharmaceuticals LLC. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e8941166-b77d-45aa-a6e8-04f1c0afd845. Last revised 06/18/2015. Last accessed 05/2016.

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[5] Centers for Disease Control and Prevention. "Parasites-Enterobiasis (also known as Pinworm Infection)." Resources for Health Professionals. Available online at: http://www.cdc.gov/parasites/pinworm/health_professionals/index.html. Last revised 02/09/2016. Last accessed 05/2016.

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[8] Center for Disease Control and Prevention. "Parasites-Ascariasis." Available online at: http://www.cdc.gov/parasites/ascariasis/health_professionals/index.html. Last updated 01/10/2013. Last accessed 05/2016.

[9] Weller PF, Leder K. "Hookworm Infection". *Up-To-Date*. Available online at: http://www.uptodate.com/contents/hookworm-infection?source=search_result&search=ancylostoma&selectedTitle=1%7E23. Last updated 12/10/2014. Last accessed 05/2016.

[10] Center for Disease Control and Prevention. "Parasites-Hookworm." Available online at: http://www.cdc.gov/parasites/hookworm/health_professionals/index.html. Last updated 01/10/2013. Last accessed 05/2016.

Appendix G

Vote to Prior Authorize OsmoPrep® (Sodium Phosphate Monobasic/Sodium Phosphate Dibasic), Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid), Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/ Sodium Chloride/Sodium Bicarbonate/Potassium Chloride), and SUPREP® (Sodium Sulfate/Potassium Sulfate/ Magnesium Sulfate)

Oklahoma Health Care Authority
July 2016

Cost Savings

The estimated cost savings (based on the average cost per claim) over one year if all members switched to a lower cost bowel preparation medication including possible administrative costs is $70,281.09-$107,001.09.

Bowel Preparation Medications Summary[1,2,3,4]

Comparison of Bowel Preparation Medications

Class/Medication	Dosing*	Clinical Comments	Cost
Polyethylene Glycol (PEG) Electrolyte Solution Colyte®, Gavilyte®, Golytely®, and Trilyte®	**Split-Dose:** Ingest 2L or 3L the evening before colonoscopy and remaining 1L to 2L day of procedure **Single-Dose:** Ingest 8-oz (240mL) every 10 min. until 4L consumed or rectal effluent is clear	• Large volume required • Split-dose regimen not FDA approved but recommended in guidelines • 5% to 15% of patients do not finish • Poor tolerability due to taste • Preferred for patients at high risk of complications from electrolyte shifts • Administration via nasogastric tube is most effective method for colonic cleansing in infants and children • Does not alter colonic mucosa and may be used in patients with suspected IBD	$12.00 to $37.50[+]
Low-Volume Polyethylene Glycol (PEG) Electrolyte Solution MoviPrep®	**Split-Dose:** Ingest 1L the evening before colonoscopy and remaining 1L day of procedure **Single-Dose:** Ingest 2L evening before colonoscopy	• Large volume required, but smaller volume than 4L products • FDA approved split-dose regimen • Clinical comments are similar to 4L volume PEG electrolyte solution products	$91.56

Class/Medication	Dosing*	Clinical Comments	Cost
Low-Volume Polyethylene Glycol (PEG) Electrolyte Solution + Sodium Sulfate Suclear®	**Split-Dose:** Ingest 6-oz OSS with 10-oz water + 32-oz water evening before colonoscopy and 2L PEG-ELS day of procedure **Single-Dose:** Ingest 6-oz OSS with 10-oz water + 16-oz water followed by 2L PEG-ELS + 16-oz water evening before colonoscopy	• Large volume required, but smaller volume than 4L products • FDA approved split-dose regimen • Clinical comments are similar to 4L volume PEG electrolyte solution products	$74.40
Magnesium Citrate Citroma®, other OTC products	**Split-Dose:** Ingest 1-1.5 10-oz bottles day before and 1-1.5 10-oz bottles day of procedure	• Not FDA approved for use in colonoscopy procedures therefore limited efficacy data • Additional fluid supplementation required • May require use with bisacodyl to increase effectiveness • Risk of electrolyte abnormalities; magnesium primarily eliminated through the kidneys therefore avoid in elderly and kidney disease	$7.44[Δ]
Sodium Sulfate SUPREP®	**Split-Dose:** Ingest 6-oz OSS with 10-oz water + 32-oz water evening before colonoscopy and 6-oz OSS with 10-oz of water + 32-oz water day of procedure	• Low-volume osmotic laxative • FDA approved split-dose regimen • One study showed superior preparation administration and more frequent achievement of excellent preparation in comparison to PEG-ELS	$84.96
Sodium Picosulfate/ Magnesium Oxide/ Anhydrous Citric Acid Prepopik®	**Split-Dose:** Ingest 5-oz + 40-oz water evening before colonoscopy and 5-oz + 24-oz water day of procedure **Single-Dose:** Ingest 5-oz + 40-oz water followed by 5-oz + 24-oz water evening before colonoscopy	• Considered more tolerable than standard PEG regimens • FDA approved split-dose regimen • Risk of electrolyte abnormalities • Avoid in patients with renal insufficiency	$129.60
Sodium Phosphate Oral Products OsmoPrep®	**Split-Dose:** Ingest 4 tablets with 8-oz of water every 15 min. for a total of 20 tablets the evening before colonoscopy and 4 tablets with 8-oz of water every 15 min. for a total of 12 tablets the day of procedure	• Not recommended for routine use • Considered more tolerable than standard PEG regimens • FDA approved split-dose regimen • Risk of electrolyte abnormalities • Risk of acute phosphate nephropathy and renal failure in certain patients • Avoid in patients with renal insufficiency	$189.76

Table modified from American Society for Gastrointestinal Endoscopy guidelines and "Comparison of Bowel Preps" available in *Pharmacist's Letter*.

Costs listed in the table do not take into account federal or supplemental rebate participation and do not reflect net costs.

* Split dosing regimen recommended whenever possible.

Costs based on estimated acquisition cost (EAC) unless otherwise noted.

[+] Cost based on state maximum allowable costs (SMAC).

[Δ] Cost based on estimated price from American Society for Gastrointestinal Endoscopy guidelines.

OTC: over-the-counter, OSS: oral sodium sulfate, PEG-ELS: polyethylene glycol electrolyte solution, IBD: inflammatory bowel disease, Min: minute

Recommendations

The College of Pharmacy recommends the prior authorization of OsmoPrep®, Prepopik®, Suclear®, and SUPREP® with the following criteria:

OsmoPrep®, Prepopik®, Suclear®, and SUPREP® Approval Criteria:

1. An FDA approved indication for use in cleansing of the colon as a preparation for colonoscopy; and
2. A patient-specific, clinically significant reason other than convenience the member cannot use other bowel preparation medications available without prior authorization.
3. If the member requires a low volume polyethylene glycol electrolyte lavage solution, Moviprep® is available without prior authorization. Other medications currently available without a prior authorization include: Colyte®, Gavilyte®, Golytely®, and Trilyte®.

Based on the low net cost of MoviPrep® the College of Pharmacy does not recommend the prior authorization of MoviPrep® at this time.

[1] American Gastroenterological Association, American College of Gastroenterology, and the American Society for Gastrointestinal Endoscopy. Optimizing Adequacy of Bowel Cleansing for Colonoscopy: Recommendations From the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2014; 147:903-924.

[2] American Society for Gastrointestinal Endoscopy. Bowel Preparation Before Colonoscopy. *Gastrointestinal Endoscopy* 2015; 81 (4):781-794.

[3] Pharmacist's Letter. "Comparison of Bowel Preps". Available online at: http://www.pharmacistletter.com. Issued 03/2014. Last accessed 05/2016.

[4] Chang D, Van K, Lie JD, Smith JP, Tu KN. Bowel Preparations: A Review for Community Pharmacists. *US Pharm*. 2013; 38(12):30-34.

Appendix H

Vote to Prior Authorize Nuvessa™ (Metronidazole Vaginal Gel 1.3%), Zyclara® (Imiquimod Cream), & Kristalose® (Lactulose Packets)

Oklahoma Health Care Authority
July 2016

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

- **Nuvessa™ (metronidazole vaginal gel 1.3%)** is indicated for the treatment of bacterial vaginosis in non-pregnant women.
  - Nuvessa™ is available as a vaginal gel containing 65mg of metronidazole in 5g of gel (1.3%) in a prefilled applicator. It should be administered as a single-dose via prefilled, disposable applicator intravaginally once at bedtime.
  - Other Formulations Available: metronidazole vaginal gel 0.75% and metronidazole 500mg oral tablet
- **Zyclara® (imiquimod 3.75% and 2.5% cream)** is indicated for the topical treatment of clinically typical, visible or palpable actinic keratosis (AK) of the full face or balding scalp in immunocompetent adults, or topical treatment of external genital and perianal warts/condyloma acuminata (EGW) in patients 12 years and older.
  - Zyclara® is available as 3.75% and 2.5% cream. Both strengths are available in a 30mL pump containing 28 actuations. The 3.75% strength is also available in single-use packets supplied in a box of 28.
    - Actinic Keratosis: Applied once daily to the skin of the affected area (either the entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no treatment period.
    - External Genital Warts: Applied once daily to the external genital/perianal warts until total clearance or up to eight weeks.
  - Other Formulations Available: imiquimod 5% cream
- **Kristalose® (lactulose packets for oral solution)** is indicated for the treatment of constipation.
  - Kristalose® is available in single-dose packets of 10g and single dose packets of 20g. The packets are supplied in cartons of 30. The usual adult dosage is 10g to 20g of lactulose daily. The dose may be increased to 40g daily if necessary.
  - Other Formulations Available: lactulose 10g/15mL oral solution

Recommendations

The College of Pharmacy recommends the prior authorization of Nuvessa™ (metronidazole vaginal gel 1.3%), Zyclara® (imiquimod), and Kristalose® (lactulose packets for oral solution) with the following criteria:

1. **Nuvessa™ (Metronidazole Vaginal Gel 1.3%) Approval Criteria:**
   a. An FDA approved diagnosis of bacterial vaginosis in non-pregnant women; and
   b. A patient-specific, clinically significant reason why the member cannot use MetroGel-Vaginal® 0.75% (metronidazole vaginal gel 0.75%) or the generic metronidazole oral tablet.

2. **Zyclara® (Imiquimod) 2.5% and 3.75% Cream Approval Criteria:**
   a. An FDA approved diagnosis of actinic keratosis (AK) of the full face or balding scalp in immunocompetent adults or topical treatment of external genital and perianal warts/condyloma acuminata (EGW) in patients 12 years and older; and
   b. Member must be 12 years or older; and
   c. Requests for a diagnosis of molluscum contagiosum in children 2 to 12 years of age will generally not be approved; and
   d. A patient-specific, clinically significant reason why the member cannot use generic imiquimod 5% cream in place of Zyclara® (imiquimod) 2.5% and 3.75%.

3. **Kristalose® (Lactulose Packets for Oral Solution) Approval Criteria:**
   a. A patient-specific, clinically significant reason why the member cannot use the liquid lactulose formulation.

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[1] Nuvessa™ Product Information. Allergan. Available online at: http://www.allergan.com/assets/pdf/nuvessa_pi. Last revised 01/2015. Last accessed 05/2016.
[2] Metrogel-Vaginal® Product Information. 3M Pharmaceuticals. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d36b7894-2152-452d-9bba-38067c52c79e. Last revised 12/2006. Last accessed 05/2016.
[3] Centers for Disease Control and Prevention (CDC). "2015 Sexually Transmitted Diseases Treatment Guidelines: Bacterial Vaginosis." Available online at: http://www.cdc.gov/std/tg2015/bv.htm. Last updated 06/2015. Last accessed 05/2016.
[4] Zyclara® Product Information. Valeant Pharmaceuticals. Available online at: http://valeant.com/Portals/25/Pdf/PI/Zyclara-PI.pdf. Last revised 08/2014. Last accessed 05/2016.
[5] Imiquimod Cream Product Information. Impax Generics. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=32175a84-c7ce-4e69-b6f1-8b645a13c2b4. Last revised 07/2015. Last accessed 05/2016.
[6] Kristalose® Product Information. Cumberland Pharmaceuticals. Available online at: http://www.kristalose.com/wp-content/themes/kristalose2015/pdf/Kristalose_-_Prescribing_Information_-_September_2012.pdf. Last revised 09/2012. Last accessed 05/2016.
[7] Lactulose Solution Product Information. Qualitest Pharmaceuticals. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=bd4d1c58-4b9b-47c1-a3c7-64f7a827d408. Last revised 02/2015. Last accessed 05/2016.
[8] Enulose® Product Information. Actavis Inc. Available online at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=00c42c5c-d19e-4130-aa08-a8bbd47d3e5b. Last revised 01/2011. Last accessed 05/2016.

Appendix I

Vote to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection)

Oklahoma Health Care Authority
July 2016

Introduction[1,2,3]

H.P. Acthar® Gel is an adrenocorticotropic hormone (ACTH) analogue, which stimulates the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and other weak androgenic substances. The elevated cortisol levels suppress ACTH release. H.P. Acthar® Gel was originally approved by the U.S. Food and Drug Administration (FDA) in 1952 and is FDA-approved to treat a variety of diseases and disorders. Examples of diseases for which ACTH may be used include infantile spasms, acute multiple sclerosis (MS) exacerbations, and nephrotic syndrome. In 2007, Questcor, the manufacturer of H.P. Acthar® Gel at the time, announced a new business model and strategy for the medication. The cost of the product increased from an average wholesale price (AWP) of $2,062.79 per vial to an estimated $23,000 per vial. The company stated that the price increase was necessary to continue manufacturing and distributing the medication to patients and to fund projects that could contribute to the company's growth. In 2012, Questcor announced that the Centers for Medicare and Medicaid Services (CMS) had informed the company that the mandatory state rebate that the company had been paying to state Medicaid programs for H.P. Acthar® Gel was eligible for a substantial reduction.

Cost Comparison:

Medication Name	Cost Per mL	Cost Per Vial	Cost Per Treatment
H.P. Acthar® Gel 80units/mL	**$7,157.10[+]**	**$35,785.50**	**$107,356.50[◊]**
Methylprednisolone 80mg/mL	$8.94*	$8.94	$558.75[¥]

[+]Estimated acquisition cost (EAC)
*State Maximum Allowable Cost (SMAC)
[◊]Dosing regimen based on 80 units for two weeks
[¥]Dosing regimen based on 1,000mg intravenously (IV) daily for five days.

Recommendations

H.P. Acthar® Gel (Corticotropin Injection) Approval Criteria:

1. An FDA approved diagnosis of infantile spasms; and
    a. Member must be two years of age or younger; and
    b. Must be prescribed by, or in consultation with, a neurologist or an advanced care practitioner with a supervising prescriber that is a neurologist; or
2. An FDA approved diagnosis of multiple sclerosis (MS); and
    a. Member is experiencing an acute exacerbation; and
    b. Must be prescribed by, or in consultation with, a neurologist or an advanced care practitioner with a supervising prescriber that is a neurologist or a physician that specializes in MS; and

    c. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy (e.g. IV methylprednisolone).
    d. Therapy will be limited to five weeks per approval (three weeks of treatment, followed by taper). Additional approval, beyond the initial five weeks, will require prescriber documentation of response to initial treatment and need for continued treatment; or
3. An FDA approved diagnosis of nephrotic syndrome without uremia of the idiopathic type or that is due to lupus erythematosus to induce a diuresis or a remission; and
    a. Must be prescribed by, or in consultation with, a nephrologist or an advanced care practitioner with a supervising prescriber that is a nephrologist; and
    b. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy (e.g., prednisone); or
4. An FDA approved diagnosis of the following disorders and diseases: rheumatic; collagen; dermatologic; allergic states; ophthalmic; respiratory; and edematous states; and
    a. A patient-specific, clinically significant reason why the member cannot use alternative corticosteroid therapy.

[1] H.P. Acthar® Gel Prescribing Information. Mallinckrodt Pharmaceuticals. Available online at: http://www.acthar.com/pdf/Acthar-PI.pdf. Last revised 01/2015. Last accessed 05/2016.
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Appendix J

Vote to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution

Oklahoma Health Care Authority
July 2016

Introduction[1,2,3]

Econazole nitrate 1% cream and clotrimazole 1% solution have increased in price by greater than 760% and greater than 600% respectively since August 2014. Both medications have been experiencing a price increase trend for the last several years.

- For econazole nitrate 1% cream, the state maximum allowable cost (SMAC) price update in February 2016 resulted in a cost of $3.38 per gram or $101.40 for a 30g tube. This is a significant increase in cost compared to August 2014, when a 30g tube cost $11.70.
- Clotrimazole 1% solution has undergone a similar change in pricing. The SMAC price update in February 2016, resulted in a cost of $2.04 per mL or $61.20 for a 30mL bottle. This, too, is a significant increase in cost compared to August 2014, when a 30mL bottle cost $8.70.

Tier-1 alternatives for econazole 1% nitrate cream include clotrimazole 1% cream and tolnaftate cream. Tier-1 alternatives for clotrimazole 1% solution include clotrimazole 1% cream and ketoconazole cream.

Recommendations

The College of Pharmacy recommends the following changes to the Topical Antifungal Product Based Prior Authoriation (PBPA) category:

1. Move econazole nitrate 1% cream and clotrimazole 1% solution from Tier-1 to Tier-2 based on increases in SMAC. The existing criteria for this category will apply.
2. Move ciclopirox suspension and clotrimazole/betamethasone cream from Tier-2 to Tier-1 based on decreases in SMAC.
3. Initiate pharmacy/prescriber education regarding these tier changes, which includes the option of using clotrimazole 1% cream as an alternative for econazole nitrate 1% cream and clotrimazole 1% cream or ketoconazole cream as an alternative for clotrimazole 1% solution.

Topical Antifungal Tier-2 Approval Criteria:

1. Documented, recent trials with at least two Tier-1 topical antifungal products for at least 90 days each; and
2. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for using a special dosage formulation of that medication in Tier-2 (foams, shampoos, sprays, kits, etc.).
3. Authorization of combination products nystatin/triamcinolone cream, nystatin/triamcinolone ointment, ~~or clotrimazole/betamethasone~~ or clotrimazole/betamethasone lotion requires a patient-specific, clinically significant

reason why the member cannot use the individual components separately, or in the case of clotrimazole/betamethasone lotion why Tier-1 cream cannot be used.

4. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).

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

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

[1] Econazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 02/2014. Last accessed 052016.
[2] Clotrimazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 04/2015. Last accessed 05/2016.
[3] Ketoconazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 01/2015. Last accessed 05/2016.

Appendix K

30-Day Notice to Prior Authorize Ocaliva™ (Obeticholic Acid)

Oklahoma Health Care Authority
July 2016

Primary Biliary Cholangitis (PBC) Background Information[1,2,3,4]

Primary Biliary Cholangitis (PBC) formerly known as primary biliary cirrhosis is a chronic, progressive disease of the liver. It is an ongoing immunological attack on the intralobular bile ducts that leads to cirrhosis and liver failure. Loss of bile ducts disrupts the normal flow of bile leading to retention of and deposition of toxic substances normally excreted in the bile. This causes further destruction of the bile ducts and hepatocytes. It occurs most frequently in women with the age of onset between 30 to 65 years. The prevalence of PBC is 65.4 cases for women and 12.1 cases for men (total of 40.2 cases) per 100,000 population. The etiology of PBC is thought to be due to both genetic predisposition and environmental triggers. Several larger studies have suggested an association with urinary tract infections, reproductive hormone replacement, nail polish, past cigarette smoking, and toxic waste sites. The serologic hallmark of PBC is the antimitochondrial antibody (AMA) which is found in 90% to 95% of patients.

The signs and symptoms of PBC include fatigue (65%), pruritus (55%) and right upper quadrant discomfort (8% to 17%). In those with PBC, 25% are diagnosed during routine blood evaluation. As the disease advances, signs and symptoms include: hepatomegaly, hyperpigmentation, splenomegaly, jaundice, xanthomas/xanthelasmas (due to hyperlipidemia), Sicca syndrome, metabolic bone disease, malabsorption, steatorrhea, and rarely Kayser-Fleischer rings. If patients become cirrhotic with advanced disease, they may experience spider nevi, palmer erythema, ascites, temporal and proximal muscle wasting, and peripheral edema. Additionally, those with cirrhosis are at increased risk of hepatocellular carcinoma.

PBC is staged based on liver biopsy, as follows:

- Stage 1 or portal stage of Ludwig: portal inflammation, bile duct abnormalities, or both
- Stage 2 or periportal stage: periportal fibrosis with or without periportal inflammation or prominent enlargement of the portal tracts with seemingly intact, newly forming limiting plates
- Stage 3 or septal stage: septal fibrosis with active inflammation, passive paucicellular septa, or both
- Stage 4 or cirrhosis: nodules with various degrees of inflammation are present

The first-line therapy for treatment of PBC is ursodeoxycholic acid (UDCA). UDCA delays disease progression, enhances survival, and is well tolerated. The response to UDCA during the first year of therapy is a useful marker of long-term prognosis. Patients taking UDCA are monitored with liver biochemical tests and typically show improvement in six to nine months. After two years of treatment, 20% of patients will have normal biochemical liver tests. An additional 15% to 35% will have normal liver tests after five years. About 35% of patients will have a

suboptimal response to UDCA. Colchicine, methotrexate and mycophenolate mofetil have been used in combination with UDCA, but none have proven to be consistently effective. Corticosteroids may alleviate symptoms and improve biochemical and histologic findings, but osteoporosis is a major concern. In May 2016, the U.S. Food and Drug Administration (FDA) approved Ocaliva™ (obeticholic acid), a farnesoid X receptor (FXR) agonist, indicated for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

Ocaliva™ (Obeticholic Acid) Product Summary[5]

FDA Approved: May 2016

Indications: Ocaliva™ (obeticholic acid), an FXR agonist, is indicated for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

Dosing:

- Ocaliva™ is available in 5mg and 10mg oral tablets.
- The recommended starting dose is 5mg by mouth once daily.
- Dosing should be titrated to 10mg daily if adequate reduction in alkaline phosphatase (ALP) and/or total bilirubin has not been achieved after three months of obeticholic acid at 5mg daily.
- The maximum recommended dose is 10mg once daily.

Mechanism of Action: Obeticholic acid is an agonist for FXR, a nuclear receptor expressed in the liver and intestine. FXR is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. FXR activation decreases the intracellular hepatocyte concentrations of bile acids by suppressing new synthesis from cholesterol as well as by increased transport of bile acids out of the hepatocytes. These mechanisms limit the overall size of the circulating bile acid pool while promoting secretion of bile by the liver, thus reducing hepatic exposure to bile acids.

Contraindications:

- Complete biliary obstruction

Warnings and Precautions:

- Liver-Related Adverse Reactions: Monitoring of patients during treatment for elevations in liver biochemical tests and for development of liver-related adverse reactions (jaundice, worsening ascites, and primary biliary cholangitis flare) is recommended. The potential risks should be weighed against the benefits of continuing treatment in patients who have experienced clinically significant liver-related adverse reactions. Adjusting the dosage for patients with moderate or severe hepatic impairment and discontinuing obeticholic acid in patients with complete biliary obstruction is recommended.
- Severe Pruritus: In patients with severe pruritus, the addition of bile acid resins or antihistamines, dose reduction of obeticholic acid, and/or temporary interruption of obeticholic acid dosing is recommended. Severe pruritus is defined as intense or

widespread itching, interfering with activities of daily living, or causing severe sleep disturbance, or intolerable discomfort, and typically requiring medical interventions.

- Reduction in High-Density Lipoprotein Cholesterol (HDL-C): Monitoring patients for changes is serum lipid levels during treatment with obeticholic acid is recommended. For patients who do not respond after one year at the highest recommended dosage that can be tolerated (maximum of 10mg once daily), and who experience a reduction in HDL-C, weighing the potential risks against the benefits of continuing treatment is recommended.

Adverse Reactions: The most common adverse reactions during clinical trials (>5% and greater than placebo) include the following:

- Pruritus
- Fatigue
- Abdominal pain and discomfort
- Rash
- Oropharyngeal pain
- Dizziness
- Constipation
- Arthralgia
- Thyroid function abnormality
- Eczema

Drug Interactions:

- Bile Acid Binding Resins: Cholestyramine, colestipol, or colesevelam adsorb and reduce bile acid absorption and may reduce the absorption, systemic exposure, and efficacy of obeticholic acid. Taking obeticholic acid at least four hours before or four hours after taking the bile acid binding resin, or at as great an interval as possible is recommended.
- Warfarin: Monitoring International Normalized Ratio (INR) and dose adjustment of warfarin, as needed, is recommended to maintain the target INR when taking obeticholic acid and warfarin. INR was shown to decrease following co-administration of warfarin and obeticholic acid.
- CYP1A2 Substrates with Narrow Therapeutic Index: Obeticholic acid may increase the exposure to concomitant drugs that are CYP1A2 substrates. Therapeutic monitoring of CYP1A2 substrates with a narrow therapeutic index (e.g., theophylline and tizanidine) is recommended when co-administered with obeticholic acid.

Use in Special Populations:

- Pregnancy: The limited available human data on the use of obeticholic acid during pregnancy are not sufficient to inform a drug-associated risk. In animal reproduction studies, no developmental abnormalities or fetal harm were observed when pregnant rats or rabbits were administered obeticholic acid during the period of organogenesis at exposures approximately 13 times and 6 times human exposures.
- Lactation: There is no information on the presence of obeticholic acid in human milk, the effects on the breast-fed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for obeticholic acid and any potential adverse effects on the breastfed infant from obeticholic acid or from the underlying maternal condition.
- Pediatric Use: The safety and effectiveness of obeticholic acid in pediatric patients have not been established.

- Geriatric Use: Of the 201 patients in clinical trials of obeticholic acid who received the recommended dosage (5mg or 10mg once daily), 41 (20%) were 65 years of age and older, while 9 (4%) were 75 years of age and older. No overall differences in safety or effectiveness were observed between these subjects and subjects less than 65 years of age, but greater sensitivity of some older individuals cannot be ruled out.
- Hepatic Impairment: Plasma exposure to obeticholic acid and its active conjugates, increases significantly in patients with moderate-to-severe hepatic impairment (Child-Pugh Classes B and C). Monitoring patients during treatment with obeticholic acid for elevations in liver biochemical tests and for the development of liver-related adverse reactions is recommended. Dosage adjustment is recommended for patients with moderate and severe hepatic impairment.

Efficacy: The efficacy and safety of obeticholic acid was studied in a randomized, double-blind, placebo-controlled, 12-month trial of 216 patients with PBC who were taking UDCA for at least 12 months (on a stable dosage for at least 3 months), or who were unable to tolerate UDCA and did not receive UDCA for at least 3 months. Inclusion criteria were ALP 1.67 times upper limit of normal (ULN) or greater and/or total bilirubin greater than 1-times ULN but less than 2-times ULN. Exclusion criteria included other liver disease, presence of clinically significant hepatic decompensation events (i.e., portal hypertension and its complications, cirrhosis with complications, or hepato-renal syndrome), severe pruritus, or a Model for End Stage Liver Disease (MELD) score of 15 or greater. The primary endpoint was a responder analysis at Month 12, where response was defined as a composite of three criteria: ALP less than 1.67-times the ULN, total bilirubin less than or equal to ULN, and an ALP decrease of at least 15%. The ULN for ALP was defined as 118 U/L for females and 124 U/L for males. The ULN for total bilirubin was defined as 1.1 mg/dL for females and 1.5 mg/dL for males. Patients were randomized to receive either obeticholic acid 10mg once daily for the entire 12 months of the trial, (n=73); obeticholic acid titration (5mg once daily for the initial 6 months, with the option to increase to 10mg once daily for the last 6 months if the patient was tolerating obeticholic acid but had ALP 1.67-times ULN or greater, and/or total bilirubin greater than ULN, or less than 15% ALP reduction) (n=70); or placebo (n=73). Obeticholic acid or placebo was administered in combination with UDCA in 93% of patients during the trial and as monotherapy in 7% of patients who were unable to tolerate UDCA.

- Obeticholic Acid 10mg Treatment Arm: The responder rate for the primary endpoint was 48%. Of those patients with Month 12 values, 55% had ALP less than 1.67 times ULN, 78% had a decrease in ALP of at least 15%, and 82% had a total bilirubin less than or equal to ULN.
- Obeticholic Acid Titration Treatment Arm: The responder rate for the primary endpoint was 46%. Of those patients with Month 12 values, 47% had ALP less than 1.67 times ULN, 77% had a decrease in ALP of at least 15%, and 89% had a total bilirubin less than or equal to ULN.
- Placebo Treatment Arm: The responder rate for the primary endpoint was 10%. Of those patients with Month 12 values, 16% had ALP less than 1.67 times ULN, 29% had a decrease in ALP of at least 15%, and 78% had a total bilirubin less than or equal to ULN.

Cost Comparison:

Medication	EAC Per Tablet	EAC for 30 Days of Therapy
Ocaliva™ (obeticholic acid) 5mg, 10mg	**$200.64**	**$6,019.20**
Ursodiol* 500mg (UDCA)	$4.02	$241.20

EAC = estimated acquisition cost; costs do not reflect rebated prices or net costs.
*Dosing 1g per day based on 13-15mg/kg/day for 68kg patient.

Recommendations

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

Ocaliva™ (Obeticholic Acid) Approval Criteria:

1. An FDA approved diagnosis of primary biliary cholangitis (PBC); and
2. Member must have taken ursodeoxycholic acid (UDCA) at an appropriate dose for at least one year and prescriber must confirm a lack of improvement in liver function tests, lack of superimposed liver disease, proper timing of bile sequestrants if co-administered with UDCA (4 hours before or 4 hours after), and patient compliance with UDCA; and
3. Ocaliva™ must be taken in combination with UDCA. For Ocaliva™ monotherapy consideration, the prescriber must document a patient-specific, clinically significant reason why the member is unable to take UDCA; and
4. A quantity limit of one tablet daily will apply.

[1] Pyrsopoulos, Nikolaos T. "Primary Biliary Cholangitis (Primary Biliary Cirrhosis)." *Medscape*. Available online at: http://emedicine.medscape.com/article/171117-overview. Last updated 06/03/2016. Last Accessed 06/08/2016.
[2] American Association for the Study of Liver Diseases (AASLD) Practice Guidelines. Primary Biliary Cirrhosis. *Hepatology*, July 2009; 50(1):291-308 Available online at: http://www.aasld.org/sites/default/files/guideline_documents/PrimaryBillaryCirrhosis2009.pdf. Issued 07/2009. Last accessed 06/14/2016.
[3] Poupon, Raoul. "Overview of the treatment of primary biliary cholangitis (primary biliary cirrhosis)." *Up-To-Date*. Available online at: http://www.uptodate.com/contents/overview-of-the-treatment-of-primary-biliary-cholangitis-primary-biliary-cirrhosis?source=search_result&search=primary+biliary+cholangitis&selectedTitle=1%7E142#H1. Last updated 12/18/2015. Last accessed 06/08/2016.
[4] U.S. Food and Drug Administration. "FDA approves Ocaliva for rare, chronic liver disease." Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm503964.htm. Issued 05/31/2016. Last accessed 06/27/2016.
[5] Ocaliva™ Prescribing Information. Intercept Pharmaceuticals, Inc. Available online at: https://ocaliva.com/ocaliva_pi.pdf. Last revised 05/2016. Last accessed 06/14/2016.

Appendix L

Calendar Year 2015 Annual Review of Opioid Analgesics and Buprenorphine Products & 30-Day Notice to Prior Authorize Belbuca™ (Buprenorphine Buccal Film), Dolophine® (Methadone), MorphaBond™ (Morphine Extended-Release), Xtampza™ ER (Oxycodone Extended-Release), & Probuphine® (Buprenorphine Implant)

Oklahoma Health Care Authority
July 2016

Current Prior Authorization Criteria

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting: methadone (Dolophine®) oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®)◊ **Short-Acting:** ASA/butalbital/caffeine/codeine (Fiorinal with Codeine®) codeine codeine/APAP hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) morphine IR (MSIR®) oxycodone IR (Oxy IR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone/ibuprofen (Combunox™) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** buprenorphine (Butrans®) fentanyl patches (Duragesic®) hydrocodone bitartrate ER (Hysingla™ ER) morphine ER tablets (MS Contin®) oxycodone ER (Oxycontin®)◊ **Short-Acting:** tapentadol IR (Nucynta®) oxymorphone IR (Opana®)	**Long-Acting:** hydrocodone bitartrate ER (Zohydro™ ER) hydromorphone ER (Exalgo®) morphine sulfate ER (Avinza®) morphine sulfate ER (Kadian®) morphine/naltrexone (Embeda®) oxymorphone (Opana® ER)+ tapentadol ER (Nucynta® ER) tramadol ER (Ultram ER®, Ryzolt®) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) oxycodone (Oxecta®)	**Long-Acting:** oxycodone/APAP ER (Xartemis™ XR) **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
*Tier Structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications subject to move to Tier-3.
◊Brand name preferred.
+Brand name Opana® ER preferred. Generic oxymorphone extended-release tablets require special authorization. The generic formulation is not abuse-deterrent.

- Tier-1 products are covered with no prior authorization necessary.
- Members with an oncology-related diagnosis are exempt from the prior authorization process, and do not require pain contracts.
- Only one long-acting and one-short acting agent can be used concurrently.

- Short-acting, solid dosage formulation products are limited to a quantity of four units per day or a quantity of 120 units per 30 days.
- An age restriction applies on oral liquid narcotic analgesic products for all members older than 12 years of age and oral solid dosage forms for all members younger than 10 years of age.

Opioid Analgesics Tier-2 Approval Criteria:

1. A documented 30-day trial/titration period with at least one Tier-1 medication within the last 90 days is required for a Tier-2 long-acting medication; or
2. A documented 30-day trial with at least two Tier-1 short-acting medications within the last 90 days is required for a Tier-2 short-acting medication; or
3. A chronic pain diagnosis requiring time-released medication (for long-acting medications).

Opioid Analgesics Tier-3 Approval Criteria:

1. A documented 30-day trial with at least two Tier-2 long-acting medications within the last 90 days is required for approval of a long-acting Tier-3 medication; or
2. A documented 30-day trial with at least two Tier-2 short-acting medications within the last 90 days is required for approval of a Tier-3 short-acting medication; or
3. A documented allergy or contraindication to all available Tier-2 medications.

Special PA Approval Criteria:

1. Actiq®, Fentora®, Onsolis®, Abstral®, Lazanda®, and Subsys™ are approved for oncology-related diagnoses only.
2. Authorization of unique strengths of hydrocodone/acetaminophen require a patient-specific, clinically significant reason the member cannot use generic Norco® (hydrocodone/APAP 5/325mg, 7.5/325mg, or 10/325mg).

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

1. An acute pain condition requiring around-the-clock opioid treatment; and
2. A patient-specific, clinically significant reason for the following:
    a. Why the member cannot use any other opioid medication for treatment of acute pain; and
    b. Why the member requires a long-acting medication for an acute pain condition; and
    c. Why the member cannot use Oxycontin® (oxycodone extended-release) and over-the-counter (OTC) acetaminophen individual products in place of this combination product.
3. A quantity limit of four tablets per day will apply with a maximum approval duration of 10 days; and
4. The member must not exceed 3,250mg of acetaminophen per day from all sources.
5. Tier structure rules still apply.

Approval Criteria for Greater than 12 Claims of Hydrocodone Products:

1. Members may be approved for greater than 12 claims per year of hydrocodone products if the member has a pain contract with a single prescriber. A copy of the pain

contract should be submitted with the prior authorization request. Requests outside of the plan outlined in the contract will not be approved.

2. Members with a current oncology-related diagnosis or hemophilia diagnosis do not require a contract for additional approvals.

Suboxone® (Buprenorphine/Naloxone Tablets and Film), Subutex® (Buprenorphine Sublingual Tablets), Zubsolv® (Buprenorphine/Naloxone Sublingual Tablets) and Bunavail™ (Buprenorphine/Naloxone Buccal Films) Approval Criteria:

1. Suboxone® and Zubsolv® are the preferred products. Bunavail™ authorization requires a patient-specific, clinically significant reason why Suboxone® or Zubsolv® are not appropriate.
2. Subutex® (buprenorphine) 2mg and 8mg tablets will only be approved if the member is pregnant, or has a documented serious allergy or adverse reaction to naloxone.
3. Buprenorphine products FDA approved for a diagnosis of opiate abuse/dependence must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a Drug Enforcement Agency (DEA) X number; and
4. Member must have an FDA approved diagnosis of opiate abuse/dependence; and
5. Concomitant treatment with opioids (including tramadol) will be denied; and
6. Approvals will be for the duration of 90 days to allow for concurrent medication monitoring; and
7. The following limitations will apply:
    a. **Suboxone®** 2mg/0.5mg, 4mg/1mg, and 8mg/2mg tablets and film: A quantity limit of 90 units per 30 days will apply.
    b. **Suboxone®** 12mg/3mg film: A quantity limit of 60 films per 30 days will apply.
    c. **Subutex®** 2mg and 8mg tablets: A quantity limit of 90 tablets per 30 days will apply.
    d. **Zubsolv®** 1.4mg/0.36mg, 2.9mg/0.71mg, and 5.7mg/1.4mg sublingual tablets: A quantity limit of 90 tablets per 30 days will apply.
    e. **Zubsolv®** 8.6mg/2.1mg sublingual tablets: A quantity limit of 60 tablets per 30 days will apply.
    f. **Zubsolv®** 11.4mg/2.9mg sublingual tablets: A quantity limit of 30 tablets per 30 days will apply.
    g. **Bunavail™** 2.1mg/0.3mg and 4.2mg/0.7mg buccal films: A quantity limit of 90 films per 30 days will apply.
    h. **Bunavail™** 6.3mg/1mg buccal films: A quantity limit of 60 films per 30 days will apply.

High-Dose Buprenorphine Products Approval Criteria:

1. Each request for greater than 24mg bioequivalent buprenorphine per day should be evaluated on a case-by-case basis.
2. A taper schedule should be documented on the petition or dates of an attempted taper with reason for failure should be documented or a patient-specific, clinically significant reason a taper schedule or attempt is not appropriate for the member; and

3. Opioid urine drug screens should be submitted with high-dose requests that plan to continue high-dose treatment longer than the duration of one month.
    a. Urine drug screens must show the absence of opioid medications other than buprenorphine products for continued approval; or
    b. Prescriber must document a patient-specific reason the member should continue therapy, reason for opioid use, and document a plan for member to discontinue opioid use; and
4. Symptoms associated with withdrawal at lower doses or symptoms requiring high doses should be listed on petition; and
5. Each approval will be for the duration of one month. If urine drug screen and other documentation are submitted indicating high-dose therapy is necessary an approval can be granted for the duration of three months.
6. Continued high-dose authorization after the three month approval will require a new (recent) urine drug screen.

Utilization of Opioid Analgesics and Buprenorphine Products: Calendar Year 2015

Comparison of Calendar Years: Opioid Analgesics

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	138,263	505,982	$18,149,018.79	$35.87	$2.02	35,960,190	8,993,850
2015	127,579	458,739	$18,262,221.74	$39.81	$2.11	32,037,192	8,653,317
% Change	**-7.70%**	**-9.30%**	**0.60%**	**11.00%**	**4.50%**	**-10.90%**	**-3.80%**
Change	**-10,684**	**-47,243**	**$113,202.95**	**$3.94**	**$0.09**	**-3,922,998**	**-340,533**

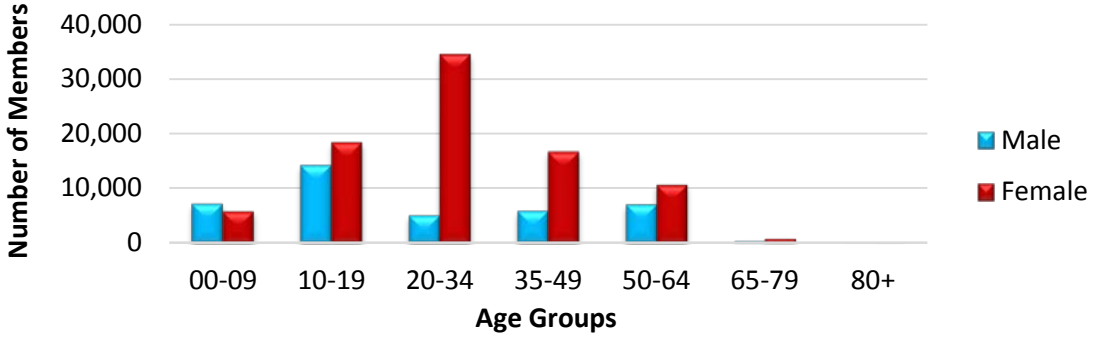
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Butrans® is included in the opioid analgesics data as it is only indicated for chronic pain and not treatment of opioid dependence.

Comparison of Calendar Years: Buprenorphine Products

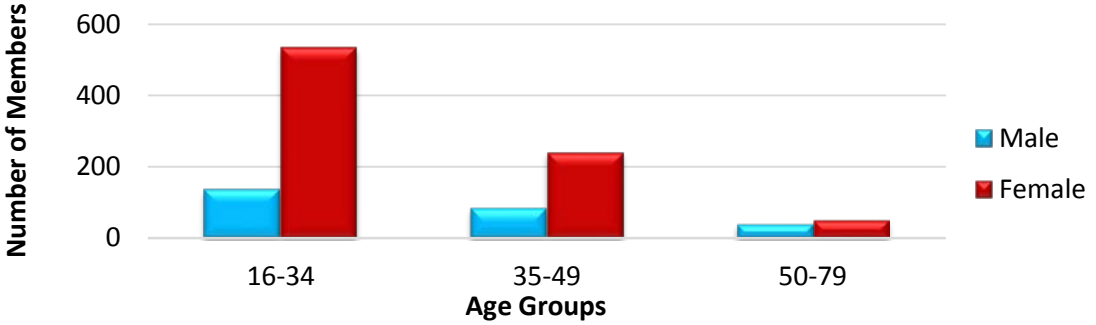
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	986	7,346	$2,709,892.89	$368.89	$14.41	412,118	188,114
2015	1,085	8,355	$3,303,407.06	$395.38	$15.09	500,924	218,933
% Change	**10.00%**	**13.70%**	**21.90%**	**7.20%**	**4.70%**	**21.50%**	**16.40%**
Change	**99**	**1,009**	**$593,514.17**	**$26.49**	**$0.68**	**88,806**	**30,819**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Does not include Butrans® claims.

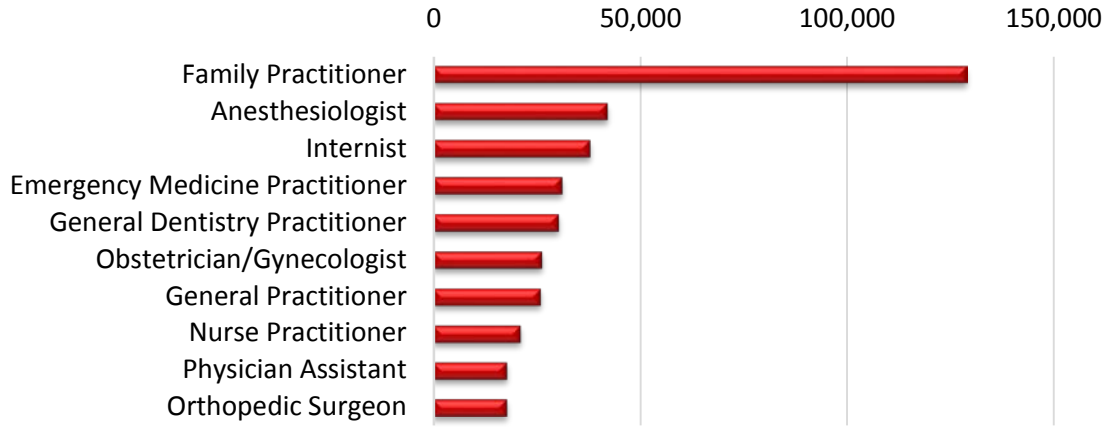
Demographics of Members Utilizing Opioid Analgesics



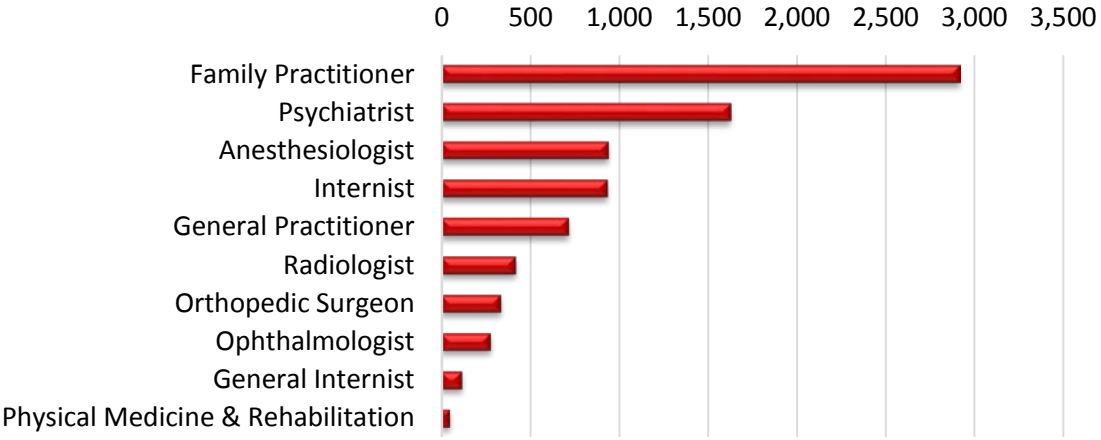
Demographics of Members Utilizing Buprenorphine Products



Top Prescriber Specialties of Opioid Analgesics by Number of Claims



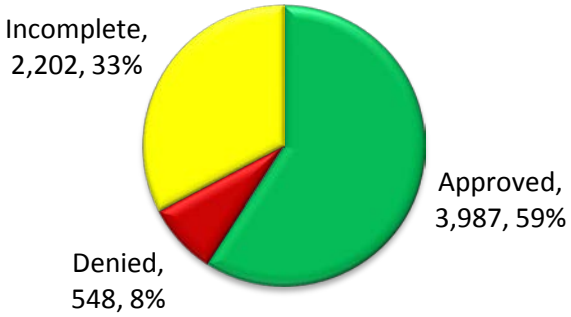
Top Prescriber Specialties of Buprenorphine Products by Number of Claims



Prior Authorization of Opioid Analgesics & Buprenorphine Products

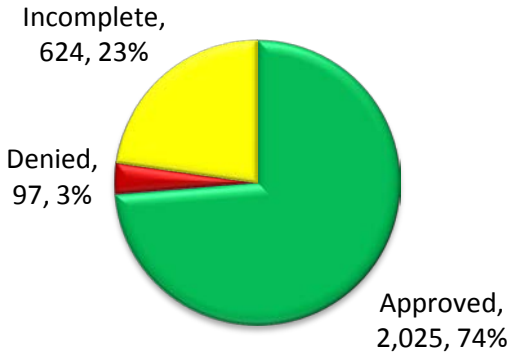
There were 6,737 prior authorization requests submitted for the opioid analgesics category during calendar year 2015. Computer edits are in place to detect Tier-1 medications in member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions: Opioid Analgesics



There were 2,746 prior authorization requests submitted for the buprenorphine products category during calendar year 2015. Computer edits are in place to detect diagnosis, concomitant opioid claims, and quantities/day supply and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

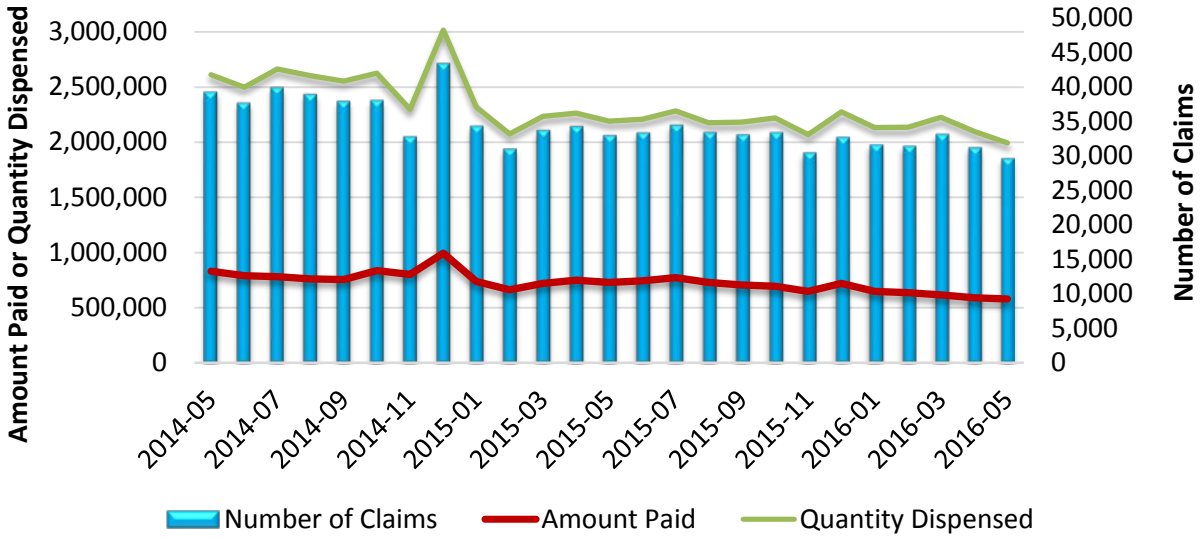
Status of Petitions: Buprenorphine Products



Opioid Analgesic Utilization Trends

In July of 2013 the Drug Utilization Review board voted to reduce the number of immediate-release narcotic units per claim resulting in a maximum quantity of 120 units per 30 day supply. In November of 2014, the College of Pharmacy and the Oklahoma Healthcare Authority began implementation of a quantity reduction on all immediate-release, solid dosage form opioid analgesics. The quantity limit was phased in over a three month period and was fully implemented by the end of January 2015 (*Of note, hydrocodone became a Schedule II medication 10/06/2014; mandatory prescription monitoring program (PMP) check implemented 11/01/2015 for prescribers of opioids to new patients or after 180 days elapsed since PMP check)*.

Short-Acting Opioid Analgesic Trends: May 2014-May 2016
Number of Claims, Amount Paid, Quantity Dispensed



Six Year Trend in Utilization of Opioid Analgesics

Calendar Year	Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2010	149,744	518,200	$15,301,884.16	$29.53	$1.97	34,389,996	7,771,934
2011	155,907	561,800	$16,043,606.57	$28.56	$1.83	38,278,004	8,760,325
2012	161,981	585,868	$16,414,461.71	$28.02	$1.75	40,194,163	9,391,441
2013	153,841	554,875	$16,221,644.55	$29.23	$1.76	38,315,636	9,219,592
2014	138,263	505,982	$18,149,018.79	$35.87	$2.02	35,960,190	8,993,850
2015	127,579	458,739	$18,262,221.74	$39.81	$2.11	32,037,192	8,653,317

Top 10 Products by Claims: Calendar Year 2015*

Medication	Claims	Members	Cost	Cost/ Day	Units/ Day
HYDROCO/APAP TAB 10-325MG	93,064	18,767	$2,157,933.97	$0.89	3.51
HYDROCO/APAP TAB 7.5-325MG	72,522	34,157	$1,081,314.20	$0.98	3.37
TRAMADOL HCL TAB 50MG	53,640	21,723	$286,098.15	$0.28	3.88
HYDROCO/APAP TAB 5-325MG	45,910	30,850	$362,557.50	$0.88	3.6
APAP/CODEINE TAB 300-30MG	25,852	18,405	$184,604.34	$0.77	3.66
OXYCOD/APAP TAB 10-325MG	24,294	6,414	$1,650,447.14	$2.79	3.66
OXYCOD/APAP TAB 5-325MG	22,213	17,529	$220,973.44	$1.35	4.71
OXYCOD/APAP TAB 7.5-325MG	10,910	5,311	$472,203.41	$2.56	3.62
APAP/CODEINE SOL 120-12/5ML	10,089	9,141	$60,021.85	$1.05	20.33
OXYCODONE TAB 30MG	9,565	1,495	$768,536.26	$2.78	3.71
SUBTOTAL	**368,059**		**$7,244,690.26**		
CATEGORY TOTAL	**467,523**		**$21,594,939.70**		
PERCENT OF TOTAL	**78.73%**		**33.55%**		

*Includes both opioid analgesics and buprenorphine products.

Top 10 Products by Cost: Calendar Year 2015*

Medication	Claims	Members	Cost	Cost/ Day	Units/ Day
SUBOXONE SL FILM 8-2MG	5,477	764	$2,446,846.24	$16.61	2.24
HYDROCO/APAP TAB 10-325MG	93,064	18,767	$2,157,933.97	$0.89	3.51
OXYCONTIN TAB 80MG CR	1,479	190	$1,765,486.57	$40.93	2.57
OXYCOD/APAP TAB 10-325MG	24,294	6,414	$1,650,447.14	$2.79	3.66
HYDROCO/APAP TAB 7.5-325MG	72,522	34,157	$1,081,314.20	$0.98	3.37
OXYCONTIN TAB 60MG CR	1,132	193	$884,675.86	$26.59	2.09
OXYCODONE TAB 30MG	9,565	1,495	$768,536.26	$2.78	3.71
OXYCONTIN TAB 40MG CR	1,155	260	$634,147.73	$18.67	2.05
OXYCONTIN TAB 30MG CR	1,466	353	$630,405.39	$14.81	2.01
BUPREN/NALOX SL TAB 8-2MG	1,677	293	$619,162.11	$14.80	2.35
SUBTOTAL	**211,831**		**$12,638,955.47**		
CATEGORY TOTAL	**467,523**		**$21,594,939.70**		
PERCENT OF TOTAL	**45.31%**		**58.53%**		

*Includes both opioid analgesics and buprenorphine products.

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

Anticipated Patent Expiration(s):

- Butrans® (buprenorphine transdermal system): September 2017
- Abstral® (fentanyl sublingual tablet): September 2019
- Lazanda® (fentanyl nasal spray): October 2024
- Nucynta® (tapentadol immediate-release): June 2025
- Hysingla™ ER (hydrocodone bitartrate extended-release): August 2027
- Fentora® (fentanyl buccal tablet): June 2028
- Nucynta® ER (tapentadol extended-release): September 2028
- Embeda® (morphine/naltrexone): November 2029
- Subsys™ (fentanyl sublingual spray): April 2030
- Xartemis™ XR (oxycodone/acetaminophen extended-release): May 2032
- Zohydro™ ER (hydrocodone bitartrate extended-release): September 2034

Guideline Recommendation(s):

- **March 2016:** The Centers for Disease Control and Prevention (CDC) released guidelines for prescribing opioids for primary care clinicians who are prescribing opioids for chronic pain (i.e., pain lasting >3 months) outside of active cancer treatment, palliative care, and end-of-life care in outpatient settings. The guidelines outlined 12 recommendations based on the following assessments:
    - No evidence shows long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least one year later.
    - Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
    - Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

Summary of CDC Opioid Guideline Recommendations

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

Center for Medicaid and Chip Services (CMCS) Bulletin:

- **January 2016:** The Centers for Medicare and Medicaid Services (CMS) issued a CMCS informational bulletin regarding Medicaid strategies for preventing opioid-related harms. The bulletin specifically highlighted methods states could use to target prescribing of methadone for pain relief due to the disproportionate share of opioid-related overdose deaths associated with methadone when used for pain.
    - The bulletin highlighted several studies assessing methadone overdose deaths:
        - While methadone represented less than 5% of opioid prescriptions dispensed between 2002 and 2008, it was implicated in one-third of opioid-related deaths during that time period.
        - Between 2006 and 2010, the rate of methadone overdose was 10 times greater than that for other prescription opioids among the Washington Medicaid population.
        - Tennessee found that the risk of out-of-hospital death in non-cancer Medicaid patients receiving methadone was 46% greater than for those receiving morphine.
    - States are encouraged to consider additional steps to reduce the use of methadone prescribed for pain relief in order to reduce prescription opioid-related harms including reassessing preferred drug list placement, introducing clinical criteria, prior authorization, step therapy, and quantity limits.

Safety Update(s):

- **March 2016:** The U.S. Food and Drug Administration (FDA) announced required class-wide safety labeling changes for immediate-release opioids. The FDA is requiring a new boxed warning be added regarding the serious risks of misuse, abuse, addiction, overdose, and death.
- **May 2016:** An FDA advisory panel voted to modify the ER/LA opioid analgesic Risk Evaluation and Mitigation Strategies (REMS). The panel concluded that physician training on the risks of prescription opioids should be mandatory and include information on both immediate-release and extended-release formulations.

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

- **October 2015:** The FDA approved MorphaBond™ (morphine sulfate extended-release) tablets to treat pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate. MorphaBond™ has properties that are expected to reduce abuse of the drug when crushed and snorted or injected.
- **October 2015:** The FDA approved Belbuca™ (buprenorphine buccal film) for the treatment of chronic pain severe enough to require daily, around-the-clock, long-term opioid treatment, for whom alternative treatment options are inadequate. Belbuca™ is the first buccal film formulation of buprenorphine approved for pain management.
- **April 2016:** The FDA approved Xtampza™ ER (oxycodone extended-release) for the management of chronic pain requiring daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate. Xtampza™ ER uses

DETERx technology which is intended to preserve the drug's release profile despite manipulation such as chewing or crushing.

- **May 2016:** The FDA approved Probuphine®, the first buprenorphine implant for the maintenance treatment of opioid dependence. Probuphine® is designed to provide a constant, low-level dose of buprenorphine for six months in patients who are already stable on low-to-moderate doses of other forms of buprenorphine.

Product Discontinuation(s):

- **July 2015:** The FDA announced that Pfizer has discontinued Avinza® (morphine extended-release capsules). The company decided to remove Avinza® from the market since it does not have abuse-deterrent properties; Pfizer also makes Embeda® (morphine extended-release/naltrexone), an abuse-deterrent formulation of morphine extended-release.

Pipeline:

- **February 2016:** The FDA granted breakthrough status to oliceridine for the management of moderate-to-severe pain. If approved, oliceridine would be the first receptor G protein pathway-selective modulator (mGPS). Oliceridine binds mu-opioid receptors that stimulate analgesia but does not engage the beta-arrestin pathway and therefore does not promote respiratory depression or constipation.
- **February 2016:** Egalet Corporation announced that the FDA had accepted a new drug application (NDA) for Arymo™ ER (morphine extended-release) tablets. Arymo™ ER is being developed with abuse-deterrent properties via Guardian™ Technology making the tablets very hard, challenging to chew, and resistant to crushing.
- **April 2016:** Durect Corporation announced that the FDA had accepted an NDA for Remoxy® (oxycodone extended-release) capsules. Remoxy® is being developed with abuse-deterrent properties via Oradur® Technology.
- **May 2016:** The FDA awarded fast track-designation to KemPharm's hydromorphone candidate, KP511. KP511 is being developed with ligand-activated technology to produce abuse-deterrent properties at the molecular level.
- **June 2016:** An FDA advisory committee voted to approve Vantrela™ ER (hydrocodone extended-release) tablets for management of pain severe enough to require around-the-clock, long-term opioid treatment. The committee also approved labeling for Vantrela™ ER to reflect the drug's abuse-deterrent properties when manipulated.
- **June 2016:** The FDA issued a complete response letter (CRL) regarding KemPharm's NDA for Apadaz™ (benzhydrocodone/acetaminophen), an abuse-deterrent candidate for acute pain. The FDA considered the review of the application to be complete and that it was not ready for approval in its present state.
- **June 2016:** The FDA accepted Charleston Laboratories/Daiichi Sankyo's NDA for CL-108, an immediate-release tablet containing promethazine, hydrocodone, and acetaminophen.
- **June 2016:** Two FDA advisory committees voted to approve Pfizer's Troxyca™ ER (oxycodone/naltrexone extended-release) capsules for pain severe enough to require around-the-clock, long-term opioid treatment. The panel also recommended that Troxyca™ ER be labeled as abuse-deterrent for nasal and IV ingestion.

News:

- **May 2016:** The president of the American Medical Association, Stephen Stack, MD, called on prescribers to re-examine prescribing practices to reverse the opioid overdose epidemic including: not initiating opioids for new patients with chronic noncancer pain unless the benefits are anticipated to outweigh the risks; limiting the amount of opioids prescribed for postoperative care and acutely injured patients; and registering for and using the PDMP.
- **June 2016:** Yuhua Bao, PhD and colleagues used National Ambulatory Medical Care Survey (NAMCS) data to evaluate the effects of implementation of prescription drug monitoring programs. The study analyzed data from 24 states from 2001 through 2010. Researchers found that the rate of Schedule II prescribing decreased by more than 30% after implementation of PDMP programs.
- **June 2016:** Wayne Raye, PhD and colleagues conducted a retrospective cohort study using Tennessee Medicaid data from patients with chronic noncancer pain between 1999 and 2012. Researchers found that a "prescription of long-acting opioids, compared with anticonvulsants or cyclic antidepressants, was associated with a significantly increased risk of all-cause mortality, including deaths from causes other than overdose".[21]

Belbuca™ (Buprenorphine Buccal Film) Product Summary[22]

Indications: Belbuca™ (buprenorphine buccal film) is 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.

Limitations of Use:

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, Belbuca™ should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Belbuca™ is not indicated as an as-needed (prn) analgesic.

Boxed Warning:

- Addiction, Abuse, and Misuse: Belbuca™ exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death.
- Life-Threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression may occur with use of Belbuca™. Misuse or abuse of Belbuca™ by chewing, swallowing, snorting, or injecting buprenorphine extracted from the buccal film will result in the uncontrolled delivery of buprenorphine and pose a significant risk of overdose and death.
- Accidental Exposure: Accidental exposure to even one dose of Belbuca™, especially in children, can result in a fatal overdose of buprenorphine.
- Neonatal Opioid Withdrawal Syndrome: Prolonged use of Belbuca™ during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts.

Dosing:

- Belbuca™ is available as a buccal film supplied in cartons of 60 individual child-resistant foil packages in the following strengths: 75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 750mcg, and 900mcg.
- Belbuca™ should be applied to the buccal mucosa every 12 hours. The patient should use the tongue to wet the inside of the cheek for placement. Belbuca™ is placed against the inside of the cheek, held in place with clean, dry fingers for five seconds, and then left in place until fully dissolved. Belbuca™ will completely dissolve usually within 30 minutes. Eating food and drinking liquids should be avoided until the film has dissolved.
- Patients should avoid applying Belbuca™ to areas of the mouth with any open sores or lesions. Belbuca™ should not be used if the buccal film is cut.
- The dosing regimen for each patient should be individualized, taking into account the patient's severity of pain, response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.
- Opioid-naïve patients should initiate treatment with a 75mcg film once daily or, if tolerated, every 12 hours for at least four days, then increased in increments of 150mcg every 12 hours, no more frequently than every four days.
- There is a potential for buprenorphine to precipitate withdrawal in patients who are already on opioids. To reduce the risk of opioid withdrawal, patients should be tapered to no more than 30mg morphine sulfate equivalents (MSE) daily before beginning Belbuca™. Following analgesic taper, the starting dose should be based on the patient's daily opioid dose prior to taper (*see following table*).

Initial Belbuca™ Dose Based on Prior Opioid Expressed as Oral MSE	
Prior Daily Dose of Opioid Analgesic Before Taper to 30mg Oral MSE	**Initial Belbuca™ Dose**
< 30 mg MSE	75mcg once daily or every 12 hours
30mg to 89mg MSE	150mcg every 12 hours
90mg to 160mg MSE	300mcg every 12 hours
> 160mg MSE	Consider alternate analgesic

- Belbuca™ may not provide adequate analgesia for patients requiring greater than 160mg oral MSE per day. The maximum Belbuca™ dose is 900mcg every 12 hours. A dose of 900mcg every 12 hours should not be exceeded due to the potential for QTc interval prolongation. If pain is not adequately managed on 900mcg, an alternate analgesic should be considered.
- In severe hepatic impairment or mucositis the starting dose and titration should be reduced by half from 150mcg to 75mcg.

Efficacy: The efficacy of Belbuca™ was evaluated in three 12-week double-blind, placebo-controlled clinical trials in patients with moderate-to-severe chronic low back pain using pain scores as the primary efficacy variable. Two of the studies demonstrated efficacy; one study did not show a statistically significant pain reduction for Belbuca™ compared to placebo.

- Study 1: A total of 749 patients with chronic low back pain entered an open-label, dose-titration period for up to eight weeks. Patients who achieved adequate analgesia on Belbuca™ for at least 2 weeks were then randomized to continue their titrated dose of

Belbuca™ or matching placebo into a 12-week, double-blind treatment period. The mean pain (SD) scores on a 0 to 10 numeric rating scale (NRS) were 7.1 (1.06) and 7.2 (1.05) prior to open-label titration and 2.8 (1.01) and 2.8 (1.12) at the beginning of the double-blind period for Belbuca™ and placebo. The change from baseline to week 12 in mean pain (SD) NRS score was statistically significant favoring Belbuca™ compared with placebo. A higher proportion of Belbuca™ patients (62%) had at least a 30% reduction in pain score compared to patients who received placebo buccal film (47%). A higher proportion of Belbuca™ patients (41%) also had at least a 50% reduction in pain score compared to placebo (33%).

- Study 2: A total of 810 patients on chronic opioid therapy (total daily dose 30mg to 160mg MSE for at least 4 weeks) entered an open-label, dose-titration period with Belbuca™ for up to 8 weeks, following taper of their prior opioids to 30mg oral MSE daily. After a dose was reached with adequate analgesia for a period of 2 weeks, patients were randomized to continue their titrated dose of Belbuca™ or matching placebo into a 12-week double-blind treatment phase. The mean pain (SD) NRS scores were 6.8 (1.28) and 6.6 (1.32) prior to open-label titration and 2.9 (0.985) and 2.8 (1.05) at the beginning of the double-blind period for Belbuca™ and placebo. The change from baseline to week 12 in mean pain (SD) NRS score was statistically significant in favor of Belbuca™ compared with placebo. A higher proportion of Belbuca™ patients (64%) had at least a 30% reduction in pain score compared placebo (31%). A higher proportion of Belbuca™ patients (39%) also had at least a 50% reduction in pain score compared to placebo (17%).

Cost:

Product	Strength	Cost Per Unit	Cost Per 30 Days
Belbuca™ (buprenorphine) buccal film	**75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 750mcg, 900mcg**	**$4.50-$11.09[+]**	**$270.00-$665.40**
morphine sulfate ER tablet[Δ]	15mg, 30mg, 60mg, 100mg	$0.47-$2.44*	$28.20-$146.40
Butrans® (buprenorphine) transdermal patch[¥]	5mcg, 7.5mcg, 10mcg, 15mcg, 20mcg	$59.11-$156.96[+]	$236.44-$627.84

Costs do not reflect rebated prices or net costs.
[+] Costs based on estimated acquisition cost (EAC).
*Costs based on state maximum allowable cost (SMAC).
[Δ] Morphine sulfate ER 200mg tablet not included as it exceeds recommended MSE (160mg) for Belbuca™.
[¥] Butrans® 20 mcg/hour may not provide adequate analgesia for patients requiring greater than 80mg/day MSE.
ER = extended-release; Unit = film, tablet, or patch

MorphaBond™ (Morphine Extended-Release) Product Summary[23]

Indications: MorphaBond™ (morphine extended-release) is 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.

Limitations of Use:

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release

opioid formulations, MorphaBond™ should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- MorphaBond™ is not indicated as an as-needed (prn) analgesic.

Boxed Warning:

- Addiction, Abuse, and Misuse: MorphaBond™ exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death.
- Life-Threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression may occur with use of MorphaBond™. Crushing, chewing, or dissolving MorphaBond™ tablets can cause rapid release and absorption of a potentially fatal dose of morphine.
- Accidental Ingestion: Accidental ingestion of even one dose of MorphaBond™, especially by children, can result in a fatal overdose of morphine.
- Neonatal Opioid Withdrawal Syndrome: Prolonged use of MorphaBond™ during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts.

Dosing:

- MorphaBond™ is available as oral extended-release tablets in the following strengths: 15mg, 30mg, 60mg, and 100mg.
- MorphaBond™ is administered orally every 12 hours. MorphaBond™ tablets must be swallowed whole.
- The dosing regimen for each patient should be individualized, taking into account the patient's prior analgesic treatment experience and risk factors for addiction, abuse, and misuse.
- MorphaBond™ 100mg tablets, a single dose greater than 60mg, or a total daily dose greater than 120mg, are only for use in patients in whom tolerance to an opioid of comparable potency has been established. The starting dosage for patients who are opioid-naïve is 15mg orally every 12 hours.
- Patients receiving other oral morphine formulations may be converted to MorphaBond™ by administering one-half of the patient's 24-hour requirement as MorphaBond™ on an every-12-hour schedule.
- There are no established conversion ratios for conversion from other opioids to MorphaBond™ defined by clinical trials. MorphaBond™ titration should be individualized to a dose that provides adequate analgesia and minimizes adverse reactions.

Clinical Abuse Potential Studies: MorphaBond™ is formulated with inactive ingredients that make the tablet more difficult to adulterate for misuse and abuse while maintaining extended-release characteristics even if the tablet is subjected to physical manipulation, or chemical extraction.

- A randomized, double-blind, placebo-controlled, crossover study in 25 non-dependent opioid users with a history of intranasal drug abuse was performed to determine the abuse potential of crushed intranasal MorphaBond™ 60mg tablets compared with

crushed intranasal morphine sulfate extended-release 60mg tablets. Drug liking and response to whether the subject would take the study drug again were measured on a 100mm bipolar visual analog scale (VAS). Intranasal administration of crushed MorphaBond™ was associated with statistically significantly lower drug liking (Emax) scores ($P < 0.0001$), and significantly lower willingness to take the drug again (Emax) scores ($P = 0.034$), compared to crushed extended-release morphine.

Cost:

Product	Strength	Cost Per Unit	Cost Per 30 Days
MorphaBond™ (morphine ER) tablet	**15mg, 30mg, 60mg, 100mg**	**Not Available**	**Not Available**
morphine sulfate ER tablet[Δ]	15mg, 30mg, 60mg, 100mg	$0.47-$2.44*	$28.20-$146.40
Embeda® (morphine ER/naltrexone) capsule	20mg/0.8mg, 30mg/1.2mg, 50mg/2mg, 60mg/2.4mg, 80mg/3.2mg, 100mg/4mg	$6.28-$24.79[+]	$188.40-$1,487.40

Costs do not reflect rebated prices or net costs.
[+] Costs based on estimated acquisition cost (EAC).
*Costs based on state maximum allowable cost (SMAC).
[Δ] Morphine sulfate ER 200mg tablet not included as it exceeds MSE for MorphaBond™.
ER = extended-release; Unit = tablet or capsule

Xtampza™ ER (Oxycodone Extended-Release) Product Summary[24]

Indications: Xtampza™ ER (oxycodone extended-release) is 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.

Limitations of Use:

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, Xtampza™ ER should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Xtampza™ ER is not indicated as an as-needed (prn) analgesic.

Boxed Warning:

- Addiction, Abuse, and Misuse: Xtampza™ ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death.
- Life-Threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression may occur with use of Xtampza™ ER.
- Accidental Ingestion: Accidental ingestion of even one dose of Xtampza™ ER, especially by children, can result in a fatal overdose of oxycodone.
- Neonatal Opioid Withdrawal Syndrome: Prolonged use of Xtampza™ ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts.
- Cytochrome P450 3A4 Interaction: The concomitant use of Xtampza™ ER with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma

concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentration.

Dosing:

- Xtampza™ ER is available as oral extended-release capsules in the following strengths (strengths are in oxycodone base): 9mg, 13.5mg, 18mg, 27mg, and 36mg.
- Xtampza™ ER is administered by mouth twice daily, every 12 hours, with food.
- Patients who are unable to swallow Xtampza™ ER should be instructed to sprinkle the capsule contents on soft foods or into a cup and then administer directly into the mouth and immediately swallowed. Xtampza™ ER may also be administered through a gastrostomy or nasogastric feeding tube.
- Xtampza™ ER is formulated with oxycodone base. The following table describes the equivalent amount of oxycodone HCl present in other oxycodone products.

Equivalence Table for Dosage Strengths of Oxycodone HCL and Oxycodone Base Extended-Release	
Oxycodone HCL	**Oxycodone Base (Xtampza™ ER)**
10mg	9mg
15mg	13.5mg
20mg	18mg
30mg	27mg
40mg	36mg

- The dosing regimen for each patient should be individualized, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.
- The starting dose for patients who are opioid-naïve is 9mg every 12 hours. The dosage may be adjusted every 1 to 2 days. Single doses greater than 36mg or a total daily dose greater than 72mg are only for patients who are opioid-tolerant.
- Patients receiving other oral oxycodone formulations, may be converted to Xtampza™ ER, using the same total daily dose of oxycodone, by administering one-half of the patient's total daily oral oxycodone dose as Xtampza™ ER every 12 hours. There are no established conversion ratios for conversion from other opioids to Xtampza™ ER defined by clinical trials. While tables of opioid equivalents are available, there is substantial inter-patient variability in the relative potency of different opioid drugs and products.
- The maximum daily dose of Xtampza™ ER is 288mg per day (eight 36mg capsules, equivalent to 320mg oxycodone HCl per day) as the safety of the excipients in Xtampza™ ER for doses over 288mg/day has not been established.
- For patients with hepatic impairment, the starting dose should be 1/3 to 1/2 the usual starting dose followed by careful dose titration.

Efficacy: The efficacy of Xtampza™ ER was established in a randomized, double-blind, placebo-controlled study conducted in 740 patients with moderate-to-severe chronic lower back pain. Patients were titrated to a stable Xtampza™ ER dose between 18mg twice daily and 72mg twice daily during the first six weeks of the trial. Following the titration phase, 389 subjects (53%)

entered the 12-week randomized, double-blind maintenance phase. Patients were randomized with their fixed dose of Xtampza™ ER or matching placebo. There was a significant difference in pain reduction, favoring Xtampza™ ER, between doses of 36mg to 144mg per day and placebo, based on the primary endpoint of change in average pain intensity from randomization baseline to Week 12 ($p<0.0001$).

Clinical Abuse Potential Studies: Xtampza™ ER capsules contain microspheres formulated with inactive ingredients intended to make the formulation more difficult to manipulate for misuse.

- Oral Abuse Potential Study: A randomized, double-blind, active-controlled, crossover study evaluated the oral abuse potential of Xtampza™ ER. A total of 61 recreational opioid users with a history of oral drug abuse were randomized to the following treatment arms: intact Xtampza™ ER, chewed Xtampza™ ER, and crushed immediate-release oxycodone HCl in water. Drug liking and response to whether the subject would take the study drug again were measured on a bipolar 100-point Visual Analog Scale (VAS) where 50 represents a neutral response, 0 represents maximum disliking, and 100 represents maximum liking. The oral administration of chewed and intact Xtampza™ ER was associated with statistically lower mean drug liking scores compared with crushed oxycodone HCl (Intact: 68.8, Chewed: 73.4, Crushed: 81.8). The differences for Xtampza™ ER chewed and intact compared with crushed oxycodone HCl for the take drug again scores were small and not statistically significant (Intact: 70.2, Chewed: 73.7, Crushed: 75.4).
- Nasal Abuse Potential Study: In a randomized, double-blind, active-controlled, crossover study, 39 recreational opioid users with a history of intranasal drug abuse were randomized to the following treatment arms: crushed Xtampza™ ER 36mg dosed intranasally, intact Xtampza™ ER 36mg dosed orally, and crushed immediate-release oxycodone HCl 40mg dosed intranasally. Intranasal administration of crushed Xtampza™ ER was associated with statistically lower mean drug liking and take drug again scores compared with crushed immediate-release oxycodone ([drug liking: Xtampza™ ER: 61.8, oxycodone: 82.7], [take drug again: Xtampza™ ER: 47.7, oxycodone: 71.4]). Approximately 92% of subjects had some reduction in drug liking with Xtampza™ ER compared to oxycodone HCl. Approximately 78% of subjects had a reduction of at least 30% in drug liking with Xtampza™ ER compared to oxycodone HCl, and approximately 58% of subjects had a reduction of at least 50% in drug liking with Xtampza™ ER compared to oxycodone HCl.

Cost:

Product	Strength	Cost Per Unit[+]	Cost Per 30 Days
Xtampza™ ER (oxycodone ER) capsules	**9mg, 13.5mg, 18mg, 27mg, 36mg**	**$3.56-$11.37**	**$213.60-$682.20**
Oxycontin® (oxycodone ER) tablets[Δ]	10mg, 15mg, 20mg, 30mg, 40mg	$3.24-$10.60	$194.40-$636.00

Costs do not reflect rebated prices or net costs.
[+] Costs based on estimated acquisition cost (EAC).
[Δ] Oxycontin® 60mg and 80mg tablets not included they exceed equivalent dose for 36mg Xtampza™ ER.
ER = extended-release; Unit = tablet or capsule

Probuphine® (Buprenorphine Implant) Product Summary[25]

Indications: Probuphine® (buprenorphine implant) is a partial opioid agonist indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine containing products (i.e., doses of no more than 8mg per day of Subutex® or Suboxone® sublingual tablet or generic equivalent).

- Probuphine® should be used as part of a complete treatment program to include counseling and psychosocial support.
- Probuphine® is not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8mg per day or less of a Subutex® or Suboxone® sublingual tablet or generic equivalent.

Patient Selection:

- Probuphine® implants are only for use in patients who meet all of the following criteria:
    - Achieved and sustained prolonged clinical stability on transmucosal buprenorphine.
    - Are currently on a maintenance dose of 8mg per day or less of a Subutex® or Suboxone® sublingual tablet or its transmucosal buprenorphine product equivalent (patients should not be tapered to a lower dose for the sole purpose of transitioning to Probuphine®).
    - Stable transmucosal buprenorphine dose (of 8mg per day or less) for three months or longer without any need for supplemental dosing or adjustments.
- Consideration should be given to the following factors in determining clinical stability and suitability for Probuphine®:
    - Period free from illicit opioid drug use
    - Stability of living environment
    - Participation in a structured activity/job
    - Consistency in participation in recommended behavioral therapy/peer support program
    - Consistency in compliance with clinic visit requirements
    - Minimal to no desire or need to use illicit opioids
    - Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis interventions
    - Social support system

Boxed Warning:

- <u>Risk Associated with Insertion and Removal:</u> Insertion and removal of Probuphine® are associated with the risk of implant migration, protrusion, and expulsion resulting from the procedure. Rare but serious complications including nerve damage and migration resulting in embolism and death may result from improper insertion of drug implants inserted in the upper arm. Incomplete insertions or infections may lead to protrusion or expulsion.
- Because of the risks associated with insertion and removal, Probuphine® is available only through a restricted program called the Probuphine® REMS Program. All healthcare

providers must successfully complete a live training program on the insertion and removal procedures and become certified, prior to performing insertions or prescribing Probuphine® implants. Patients must be monitored to ensure that Probuphine® is removed by a healthcare provider certified to perform insertions.

Drug Addiction Treatment Act: Under the Drug Addiction Treatment Act (DATA) codified at 21 United States Code (U.S.C.) 823(g), use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe or dispense this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.

Dosing:

- Probuphine® is available as a kit containing four individually packaged sterile implants and one individually packaged sterile disposable applicator. Each implant is 26mm in length and 2.5mm in diameter and contains 74.2mg of buprenorphine (equivalent to 80mg of buprenorphine hydrochloride).
- Each dose consists of four Probuphine® implants inserted subdermally under aseptic conditions in the inner side of the upper arm. Probuphine® subdermal implants are intended to be in place for six months of treatment and removed by the end of the sixth month.
- New implants may be inserted subdermally in an area of the inner side of either upper arm that has not been previously used at the time of removal. If new implants are not inserted on the same day as the removal of implants, patients should be maintained on their previous dosage of transmucosal buprenorphine. After one insertion in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment. There is no experience with inserting additional implants into other sites in the arm to recommend an approach to a second insertion into a previously-used arm.
- The insertion site should be examined one week following insertion for signs of infection or any problems with wound healing, including evidence of implant extrusion from the skin. The recommended visit schedule for most patients is a frequency of no less than once-monthly for continued counseling and psychosocial support.
- Some patients may require occasional supplemental dosing with buprenorphine, however patients should not be provided with prescriptions for transmucosal buprenorphine-containing products for as-needed use. Ongoing use of supplemental dosing with transmucosal buprenorphine indicates that the amount of buprenorphine delivered by Probuphine® is not adequate for stable maintenance. Consideration should be given to use of alternate buprenorphine products for maintenance of treatment.

Efficacy: The efficacy of Probuphine® was demonstrated in one randomized, double-blind study in adults with opioid dependence who were considered clinically stable on a sublingual buprenorphine dose of no more than 8mg per day. Healthcare Providers attested to their patient's clinical stability and endorsed criteria on a clinical stability checklist that included the following factors: no reports of any illicit opioid use; no reports of significant withdrawal symptoms; reports of low to no desire/need to use illicit opioids; no episodes of hospitalizations

(addiction or mental health issues), emergency room visits, or crisis interventions in the past 90 days; stable living environment, participation in a structured activity/job that contributes to the community, consistent participation in recommended cognitive behavioral therapy/peer support program; and consistent compliance with clinic visit requirements. Patients had no positive urine toxicology results for illicit opioids for the last 90 days, and were intended to have been on sublingual buprenorphine treatment for at least the last six months prior to randomization. Subjects were randomized 1:1 to either Probuphine® (4 implants) or treatment with their pre-randomization dose of sublingual buprenorphine. Patients were required to provide four randomly-scheduled urine samples for toxicology. Efficacy was evaluated through urine toxicology screening and patient self-report to detect opioid use over the 6-month treatment period. Protocol permitted supplemental buprenorphine use for patients in both arms however, the use of supplemental buprenorphine in patients on Probuphine®, may be interpreted to indicate that the dose of buprenorphine provided by Probuphine® was inadequate for that patient (to maintain stability) and so patients who required supplemental dosing were not included as successfully maintained, even if they did not have evidence of opioid use. There were 11 patients in the Probuphine® arm who required supplemental sublingual buprenorphine, but had no evidence of opioid use.

Proportion of patients with no evidence of illicit opioid use throughout the 6 months		
Probuphine® Only (N=87)	**Sublingual Buprenorphine (N=89)**	**Treatment Difference (95% CI)**
55 (63%)	57 (64%)	-1% (-15%, 13%)

CI = Confidence Interval

Two additional studies in patients who were new entrants to buprenorphine treatment suggested that Probuphine® should not be used for patients who are new entrants to buprenorphine treatment or who have not achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product, because the dose appears to be too low to be effective in these populations.

Cost:

Product	Dosing	Cost Per Unit	Cost Per 6 Months
Probuphine® (buprenorphine implant)	**4 implants every six months**	**$1,306.80[+]**	**$5,227.20[◊]**
Suboxone® 8mg/2mg (buprenorphine/naloxone sublingual tablets)	One tablet sublingually daily	$5.53*	$995.40

Costs do not reflect rebated prices or net costs.
[+]Costs based on estimated acquisition cost (EAC).
[◊]Probuphine® will require an additional cost for implantation. Procedural costs are expected to average $156.37.
*Costs based on state maximum allowable cost (SMAC).
Unit = implant or tablet

Recommendations

The College of Pharmacy recommends the following:

1. The placement of Belbuca™ (buprenorphine buccal film), MorphaBond™ (morphine extended-release), and Xtampza™ ER (oxycodone extended-release) into Tier-3 of the

Opioid Analgesics Product Based Prior Authorization (PBPA) category. Current Tier-3 criteria for this category will apply.

2. Moving methadone from Tier-1 to Tier-3 of the Opioid Analgesics PBPA category based on CMS recommendations and the disproportionate share of opioid-related overdose deaths associated with methadone when used for pain. Current Tier-3 criteria for this category will apply. A quantity limit of 120 tablets per 30 days will apply.
3. The prior authorization of Probuphine® (buprenorphine implant) with the criteria listed in red.

Probuphine® (Buprenorphine Implant) Approval Criteria:

1. An FDA approved diagnosis of maintenance treatment of opioid dependence; and
2. Members must be currently on a maintenance dose of 8mg per day or less of a Subutex® or Suboxone® sublingual tablet or its transmucosal buprenorphine product equivalent; and
3. Member must have been stable on current transmucosal buprenorphine dose (of 8mg per day or less) for three months or longer without any need for supplemental dosing or adjustments; and
4. Members must have had no positive urine toxicology results or paid claims for opioids for the last three months. Concomitant treatment with opioids (including tramadol) will be denied; and
5. Probuphine® must be prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a DEA (X) number; and
6. Prescribers must verify they have considered the following factors in determining clinical stability and suitability for Probuphine®:
    a. Period free from illicit opioid drug use
    b. Stability of living environment
    c. Participation in a structured activity/job
    d. Consistency in participation in recommended behavioral therapy/peer support program
    e. Consistency in compliance with clinic visit requirements
    f. Minimal to no desire or need to use illicit opioids
    g. Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis interventions
    h. Social support system
7. The prescriber must verify enrollment in the Probuphine® Risk Evaluation and Mitigation Strategy (REMS) program; and
8. Approvals will be for one kit (four implants) per six months. Reauthorizations for an additional six months may be granted if the member does not have ongoing use of supplemental dosing with transmucosal buprenorphine or opioid analgesics while utilizing Probuphine®.

Opioid Analgesics*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Long-Acting: oxycodone ER 10mg, 15mg, 20mg only (Oxycontin®)◊ **Short-Acting:** ASA/butalbital/caffeine/codeine (Fiorinal with Codeine®) codeine codeine/APAP hydrocodone/APAP (Norco®) hydrocodone/IBU (Vicoprofen®, Ibudone®, Reprexain™) hydromorphone (Dilaudid®) morphine IR (MSIR®) oxycodone IR (Oxy IR®) oxycodone/APAP (Percocet®) oxycodone/ASA (Percodan®) oxycodone/ibuprofen (Combunox™) tramadol/APAP (Ultracet®) tramadol (Ultram®)	**Long-Acting:** buprenorphine (Butrans®) fentanyl patches (Duragesic®) hydrocodone bitartrate ER (Hysingla™ ER) morphine ER tablets (MS Contin®) oxycodone ER (Oxycontin®)◊ **Short-Acting:** tapentadol IR (Nucynta®) oxymorphone IR (Opana®)	**Long-Acting:** **buprenorphine ER buccal film (Belbuca™)** hydrocodone bitartrate ER (Zohydro™ ER) hydromorphone ER (Exalgo®) **methadone (Dolophine®)** ~~**morphine sulfate ER (Avinza®)**~~ morphine sulfate ER (Kadian®) **morphine sulfate ER (MorphaBond™)** morphine/naltrexone (Embeda®) **oxycodone ER (Xtampza™ ER)** oxymorphone (Opana® ER)+ tapentadol ER (Nucynta® ER) tramadol ER (Ultram ER®, Ryzolt®) **Short-Acting:** hydrocodone/APAP (Xodol®, Zamicet®, Liquicet®) hydrocodone/APAP/caffeine (Trezix™) oxycodone/APAP (Primlev™, Xolox®) oxycodone (Oxecta®)	**Long-Acting:** oxycodone/APAP ER (Xartemis™ XR) **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
*Tier Structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications subject to move to Tier-3.
◊Brand name preferred.
+Brand name Opana® ER preferred. Generic oxymorphone extended-release tablets require special authorization as they are not abuse-deterrent.

Opioid Analgesics Tier-2 Approval Criteria:

1. A documented 30-day trial/titration period with at least one Tier-1 medication within the last 90 days is required for a Tier-2 long-acting medication; or
2. A documented 30-day trial with at least two Tier-1 short-acting medications within the last 90 days is required for a Tier-2 short-acting medication; or
3. A chronic pain diagnosis requiring time-released medication (for long-acting medications).

Opioid Analgesics Tier-3 Approval Criteria:

1. A documented 30-day trial with at least two Tier-2 long-acting medications within the last 90 days is required for approval of a long-acting Tier-3 medication; or
2. A documented 30-day trial with at least two Tier-2 short-acting medications within the last 90 days is required for approval of a Tier-3 short-acting medication; or
3. A documented allergy or contraindication to all available Tier-2 medications.

Utilization Details of Opioid Analgesics: Calendar Year 2015

Short-Acting Opioid Analgesics

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
Immediate-Release Hydrocodone Products					
HYDROCO/APAP TAB 10-325MG	93,064	18,767	$2,157,933.97	4.96	$23.19
HYDROCO/APAP TAB 7.5-325MG	72,522	34,157	$1,081,314.20	2.12	$14.91
HYDROCO/APAP TAB 5-325MG	45,910	30,850	$362,557.50	1.49	$7.90
HYDROCO/APAP SOL 7.5-325MG	9,335	8,397	$374,172.14	1.11	$40.08
HYDROCOD/IBU TAB 7.5-200MG	1,511	728	$33,754.72	2.08	$22.34
HYDROCOD/IBU TAB 10-200MG	153	46	$56,245.31	3.33	$367.62
XYLON TAB 10-200MG	127	52	$41,584.76	2.44	$327.44
IBUDONE TAB 10-200MG	61	14	$6,517.21	4.36	$106.84
HYDROCOD/IBU TAB 5-200MG	46	20	$7,379.94	2.3	$160.43
HYDROCO/APAP TAB 7.5-300MG	9	3	$772.58	3	$85.84
LORTAB ELX 10-300MG	9	9	$649.13	1	$72.13
HYDROCO/APAP TAB 2.5-325MG	5	4	$131.73	1.25	$26.35
IBUDONE TAB 5-200MG	4	3	$196.34	1.33	$49.09
VICODIN HP TAB 10-300MG	2	1	$444.82	2	$222.41
ZAMICET SOL 10-325MG	1	1	$44.88	1	$44.88
HYDROCO/APAP TAB 7.5-500MG	1	1	$5.43	1	$5.43
HYDROCO/APAP TAB 5-500MG	1	1	$4.73	1	$4.73
HYDROCO/APAP TAB 7.5-650MG	1	1	$0.38	1	$0.38
Subtotal	**222,762**	**78,279**	**$4,123,709.77**	**2.85**	**$18.51**
Immediate-Release Oxycodone Products					
OXYCOD/APAP TAB 10-325MG	24,294	6,414	$1,650,447.14	3.79	$67.94
OXYCOD/APAP TAB 5-325MG	22,213	17,529	$220,973.44	1.27	$9.95
OXYCOD/APAP TAB 7.5-325MG	10,910	5,311	$472,203.41	2.05	$43.28
OXYCODONE TAB 30MG	9,565	1,495	$768,536.26	6.4	$80.35
OXYCODONE TAB 15MG	7,983	1,683	$242,423.64	4.74	$30.37
OXYCODONE TAB 10MG	4,831	1,519	$114,812.47	3.18	$23.77
OXYCODONE TAB 20MG	2,958	623	$143,777.51	4.75	$48.61
OXYCODONE TAB 5MG	2,233	1,149	$33,424.40	1.94	$14.97
ENDOCET TAB 10-325MG	1,387	561	$107,776.47	2.47	$77.70
ENDOCET TAB 7.5-325MG	245	135	$13,611.02	1.81	$55.56
ENDOCET TAB 5-325MG	170	153	$1,351.39	1.11	$7.95
OXYCODONE SOL 5MG/5ML	150	103	$11,392.19	1.46	$75.95
OXYCODONE CAP 5MG	94	69	$6,800.36	1.36	$72.34
OXYCOD/ASA TAB 4.8355-325MG	75	46	$3,104.72	1.63	$41.40
OXYCODONE CON 100MG/5ML	21	8	$10,008.99	2.63	$476.62
PERCOCET TAB 5-325MG	12	10	$161.34	1.2	$13.45
OXYCOD/APAP TAB 2.5-325MG	11	7	$551.17	1.57	$50.11
ROXICET SOL 5-325MG/5ML	5	5	$39.41	1	$7.88
OXYCODONE CON 20MG/ML	3	3	$1,045.71	1	$348.57
Subtotal	**87,160**	**6,414**	**$3,802,441.04**	**2.83**	**$43.63**
Codeine Products					
APAP/CODEINE TAB 300-30MG	25,852	18,405	$184,604.34	1.4	$7.14
APAP/CODEINE SOL 120-12MG/5ML	10,089	9,141	$60,021.85	1.1	$5.95
APAP/CODEINE TAB 300-60MG	6,444	2,398	$129,434.80	2.69	$20.09
BUT/APAP/CAF/COD CAP 30MG	837	326	$52,959.04	2.57	$63.27

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
ASCOMP/COD CAP 30MG	237	73	$30,881.66	3.25	$130.30
APAP/CODEINE TAB 300-15MG	224	187	$1,972.50	1.2	$8.81
BUT/ASA/CAF/COD CAP 30MG	185	77	$21,298.28	2.4	$115.13
CODEINE SULF TAB 30MG	56	23	$1,918.94	2.43	$34.27
CAPITAL/COD SUS 120-12MG/5ML	3	1	$1,353.89	3	$451.30
CODEINE SULF TAB 15MG	3	2	$57.85	1.5	$19.28
CODEINE SULF SOL 30MG/5ML	2	2	$47.16	1	$23.58
CODEINE POW PHOSPHAT	1	1	$18.16	1	$18.16
DIHYDROCOD/ASA/CAFF CAP 16MG	1	1	$194.80	1	$194.80
SYNALGOS-DC CAP 16MG	1	1	$76.06	1	$76.06
Subtotal	**43,935**	**29,575**	**$484,839.33**	**1.49**	**$11.04**
Immediate-Release Hydromorphone Products					
HYDROMORPHON TAB 4MG	1,436	405	$17,874.30	3.55	$12.45
HYDROMORPHON TAB 2MG	669	413	$5,170.26	1.62	$7.73
HYDROMORPHON TAB 8MG	493	103	$24,117.98	4.79	$48.92
HYDROMORPHON LIQ 1MG/ML	22	3	$2,960.04	7.33	$134.55
DILAUDID TAB 8MG	10	1	$5,375.76	10	$537.58
HYDROMORPHON POW HCL	8	1	$943.87	8	$117.98
Subtotal	**2,638**	**845**	**$56,442.21**	**3.12**	**$21.40**
Immediate-Release Morphine Products					
MORPHINE SUL TAB 15MG	2,976	767	$36,331.61	3.88	$12.21
MORPHINE SUL TAB 30MG	1,305	270	$28,898.25	4.83	$22.14
MORPHINE SUL SOL 100/5ML	147	81	$5,449.78	1.81	$37.07
MORPHINE SUL SOL 10MG/5ML	69	37	$1,057.42	1.86	$15.32
MORPHINE SUL SOL 20MG/5ML	29	13	$777.47	2.23	$26.81
MORPHINE SUL INJ 5MG/ML	4	4	$19.04	1	$4.76
MORPHINE POW SULFATE	3	1	$11.19	3	$3.73
MORPHINE SUL INJ 10MG/ML	2	2	$20.81	1	$10.41
MORPHINE SUL INJ 15MG/ML	2	1	$70.50	2	$35.25
MORPHINE SUL INJ 25MG/ML	2	1	$47.38	2	$23.69
MORPHINE SUL INJ 50MG/ML	2	2	$36.65	1	$18.33
MORPHINE SUL INJ 10MG/ML	1	1	$27.97	1	$27.97
MORPHINE SUL SOL 20MG/ML	1	1	$193.19	1	$193.19
Subtotal	**4,543**	**1,071**	**$72,941.26**	**4.24**	**$16.06**
Immediate-Release Tramadol Products					
TRAMADOL HCL TAB 50MG	53,640	21,723	$286,098.15	2.47	$5.33
TRAMADL/APAP TAB 37.5-325MG	1,100	787	$14,344.14	1.4	$13.04
ULTRAM TAB 50MG	6	1	$245.85	6	$40.98
Subtotal	**54,746**	**22,321**	**$300,688.14**	**2.45**	**$5.49**
Immediate-Release Tapentadol Products					
NUCYNTA TAB 100MG	85	13	$36,556.65	6.54	$430.08
NUCYNTA TAB 50MG	33	22	$10,461.61	1.5	$317.02
NUCYNTA TAB 75MG	30	12	$10,548.92	2.5	$351.63
Subtotal	**148**	**42**	**$57,567.18**	**3.52**	**$388.97**
Immediate-Release Oxymorphone Products					
OXYMORPHONE TAB HCL 10MG	502	72	$157,614.27	6.97	$313.97
OXYMORPHONE TAB HCL 5MG	111	32	$20,542.06	3.47	$185.06
Subtotal	**613**	**96**	**$178,156.33**	**6.39**	**$290.63**
Immediate-Release Fentanyl Products					
FENTANYL CIT INJ 100MCG	35	10	$178.71	3.5	$5.11

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
FENTANYL OT LOZ 800MCG	11	1	$19,162.94	11	$1,742.09
FENTORA TAB 200MCG	9	5	$20,988.93	1.8	$2,332.10
FENTANYL OT LOZ 200MCG	3	1	$1,150.30	3	$383.43
FENTORA TAB 100MCG	2	2	$5,511.51	1	$2,755.76
FENTANYL OT LOZ 600MCG	1	1	$1,614.17	1	$1,614.17
Subtotal	**61**	**19**	**$48,606.56**	**3.21**	**$796.83**
Pentazocine/Naloxone Products					
PENTAZ/NALOX TAB 50-0.5MG	1,121	546	$158,308.01	2.05	$141.22
Subtotal	**1,121**	**546**	**$158,308.01**	**2.05**	**$141.22**
Meperidine Products					
MEPERIDINE TAB 50MG	817	552	$18,367.02	1.48	$22.48
MEPERIDINE SOL 50MG/5ML	693	500	$3,693.48	1.39	$5.33
MEPERIDINE TAB 100MG	67	27	$3,504.18	2.48	$52.30
DEMEROL INJ 100MG/ML	12	4	$303.06	3	$25.26
MEPERIDINE POW	9	9	$222.66	1	$24.74
DEMEROL INJ 50MG/ML	9	9	$51.16	1	$5.68
Subtotal	**1,607**	**1,094**	**$26,141.56**	**1.47**	**$16.27**
Total	**419,334**	**127,247***	**$9,309,841.39**	**3.3**	**$22.20**

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

Long-Acting Opioid Analgesics

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
Extended-Release Hydrocodone Products					
HYSINGLA ER TAB 20 MG	314	150	$63,858.30	2.09	$203.37
HYSINGLA ER TAB 40 MG	262	138	$104,508.41	1.9	$398.89
HYSINGLA ER TAB 30 MG	247	128	$73,822.89	1.93	$298.88
HYSINGLA ER TAB 60 MG	123	58	$69,114.83	2.12	$561.91
HYSINGLA ER TAB 80 MG	35	14	$25,811.17	2.5	$737.46
HYSINGLA ER TAB 100 MG	15	5	$14,611.55	3	$974.10
HYSINGLA ER TAB 120 MG	7	3	$6,753.92	2.33	$964.85
Subtotal	**1,003**	**408**	**$358,481.07**	**2.46**	**$357.41**
Extended-Release Oxycodone Products					
OXYCONTIN TAB 20MG CR	2,019	598	$601,058.41	3.38	$297.70
OXYCONTIN TAB 80MG CR	1,479	190	$1,765,486.57	7.78	$1,193.70
OXYCONTIN TAB 30MG CR	1,466	353	$630,405.39	4.15	$430.02
OXYCONTIN TAB 10MG CR	1,172	495	$179,229.93	2.37	$152.93
OXYCONTIN TAB 40MG CR	1,155	260	$634,147.73	4.44	$549.05
OXYCONTIN TAB 60MG CR	1,132	193	$884,675.86	5.87	$781.52
OXYCONTIN TAB 15MG CR	1,003	314	$235,135.03	3.19	$234.43
OXYCODONE TAB 40MG ER	169	61	$70,458.73	2.77	$416.92
OXYCODONE TAB 80MG ER	167	44	$168,091.68	3.8	$1,006.54
OXYCODONE TAB 20MG ER	161	83	$39,637.92	1.94	$246.20
OXYCODONE TAB 10MG ER	71	54	$7,052.91	1.31	$99.34
Subtotal	**9,994**	**1,868**	**$5,215,380.16**	**5.35**	**$521.85**
Extended-Release Hydromorphone Products					
HYDROMORPHON TAB 16MG ER	43	10	$34,453.55	4.3	$801.25

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
EXALGO TAB 12MG	24	5	$17,476.04	4.8	$728.17
EXALGO TAB 32MG	22	2	$53,008.78	11	$2,409.49
HYDROMORPHON TAB 12MG ER	19	9	$13,088.40	2.11	$688.86
HYDROMORPHON TAB 8MG ER	19	7	$5,804.30	2.71	$305.49
HYDROMORPHON TAB 32MG ER	6	3	$21,450.76	2	$3,575.13
Subtotal	**133**	**27**	**$145,281.83**	**4.93**	**$1,092.34**
Extended-Release Morphine Products					
MORPHINE SUL TAB 30MG ER	5,493	1,077	$350,890.53	5.1	$63.88
MORPHINE SUL TAB 15MG ER	5,161	1,218	$183,661.46	4.24	$35.59
MORPHINE SUL TAB 60MG ER	2,496	429	$288,682.14	5.82	$115.66
MORPHINE SUL TAB 100MG ER	921	146	$200,538.84	6.31	$217.74
MORPHINE SUL TAB 200MG ER	136	20	$45,364.74	6.8	$333.56
MORPHINE SUL CAP 80MG ER	60	10	$30,608.32	6	$510.14
MORPHINE SUL CAP 30MG ER	58	12	$11,711.67	4.83	$201.93
MORPHINE SUL CAP 100MG ER	34	7	$25,887.73	4.86	$761.40
MORPHINE SUL CAP 90MG ER	31	4	$13,111.16	7.75	$422.94
MORPHINE SUL CAP 20MG ER	31	14	$5,362.85	2.21	$173.00
MORPHINE SUL CAP 50MG ER	29	6	$7,839.14	4.83	$270.32
MORPHINE SUL CAP 60MG ER	26	6	$12,166.92	4.33	$467.96
KADIAN CAP 200MG ER	21	3	$76,032.13	7	$3,620.58
KADIAN CAP 50MG ER	14	1	$10,992.64	14	$785.19
MORPHINE SUL CAP 120MG ER	12	1	$12,008.76	12	$1,000.73
MS CONTIN TAB 60MG CR	11	1	$41,005.82	11	$3,727.80
EMBEDA CAP 20-0.8MG	10	3	$3,023.48	3.33	$302.35
MORPHINE SUL CAP 10MG ER	8	5	$1,317.59	1.6	$164.70
AVINZA CAP 90MG	4	1	$1,963.72	4	$490.93
EMBEDA CAP 50-2MG	1	1	$694.77	1	$694.77
KADIAN CAP 40MG ER	1	1	$340.71	1	$340.71
MORPHINE SUL CAP 30MG ER	1	1	$144.92	1	$144.92
Subtotal	**14,559**	**2,423**	**$1,323,350.04**	**6.01**	**$90.90**
Extended-Release Tramadol Products					
TRAMADOL HCL TAB 100MG ER	10	3	$691.37	3.33	$69.14
TRAMADOL HCL TAB 200MG ER	6	2	$655.42	3	$109.24
Subtotal	**16**	**5**	**$1,346.79**	**3.2**	**$84.17**
Extended-Release Tapentadol Products					
NUCYNTA ER TAB 250MG	40	6	$35,633.86	6.67	$890.85
NUCYNTA ER TAB 200MG	39	6	$30,822.52	6.5	$790.32
NUCYNTA ER TAB 100MG	24	11	$9,628.06	2.18	$401.17
NUCYNTA ER TAB 50MG	20	13	$4,385.07	1.54	$219.25
NUCYNTA ER TAB 150MG	17	8	$10,767.50	2.13	$633.38
Subtotal	**140**	**34**	**$91,237.01**	**4.12**	**$651.69**
Extended-Release Oxymorphone Products					
OPANA ER TAB 20MG	253	38	$123,002.17	6.66	$486.17
OPANA ER TAB 40MG	172	23	$172,182.30	7.48	$1,001.06
OPANA ER TAB 30MG	144	27	$103,738.41	5.33	$720.41
OPANA ER TAB 10MG	127	31	$35,473.68	4.1	$279.32
OPANA ER TAB 15MG	81	18	$31,141.42	4.5	$384.46
OPANA ER TAB 5MG	22	8	$3,152.04	2.75	$143.27

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
OXYMORPHONE TAB 20MG ER	5	2	$1,569.10	2.5	$313.82
OPANA ER TAB 7.5MG	5	2	$1,094.25	2.5	$218.85
OPANA ER TAB 20MG	1	1	$407.15	1	$407.15
OXYMORPHONE TAB 10MG ER	1	1	$176.14	1	$176.14
Subtotal	**811**	**114**	**$471,936.66**	**7.11**	**$581.92**
Extended-Release Fentanyl Products					
FENTANYL DIS 50MCG/HR	2,184	524	$173,377.17	4.17	$79.39
FENTANYL DIS 25MCG/HR	2,150	648	$99,304.00	3.32	$46.19
FENTANYL DIS 75MCG/HR	1,540	298	$188,530.38	5.17	$122.42
FENTANYL DIS 100MCG/H	1,505	245	$260,743.62	6.14	$173.25
FENTANYL DIS 12MCG/HR	719	270	$107,520.83	2.66	$149.54
FENTANYL DIS 37.5MCG	37	14	$16,730.40	2.64	$452.17
DURAGESIC DIS 100MCG/H	24	2	$30,828.00	12	$1,284.50
DURAGESIC DIS 50MCG/HR	6	1	$3,837.48	6	$639.58
FENTANYL DIS 62.5MCG	1	1	$834.88	1	$834.88
Subtotal	**8,166**	**1,440**	**$881,706.76**	**5.67**	**$107.97**
Methadone Products					
METHADONE TAB 10MG	2,961	399	$78,553.02	7.42	$26.53
METHADONE TAB 5MG	380	96	$5,993.25	3.96	$15.77
METHADONE SOL 5MG/5ML	121	78	$1,825.10	1.55	$15.08
METHADOSE CON 10MG/ML	17	2	$609.06	8.5	$35.83
METHADONE CON 10MG/ML	5	3	$98.37	1.67	$19.67
Subtotal	**3,484**	541	**$87,078.80**	**6.44**	**$24.99**
Buprenorphine Transdermal Products					
BUTRANS DIS 10MCG/HR	494	289	$148,440.12	1.71	$300.49
BUTRANS DIS 15MCG/HR	204	91	$90,947.46	2.24	$445.82
BUTRANS DIS 5MCG/HR	198	117	$40,466.74	1.69	$204.38
BUTRANS DIS 20MCG/HR	167	54	$86,129.91	3.09	$515.75
BUTRANS DIS 7.5/HR	36	23	$10,597.00	1.57	$294.36
Subtotal	**1,099**	**437**	**$376,581.23**	**2.51**	**$342.66**
Total	**39,405**	**6,105***	**$8,952,380.35**	**6.45**	**$227.19**

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

Utilization Details of Buprenorphine Products: Calendar Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
SUBOXONE MIS 8-2MG	5,477	764	$2,446,846.24	7.17	$446.75
BUPREN/NALOX SUB 8-2MG	1,677	293	$619,162.11	5.72	$369.21
BUPRENORPHIN SUB 8MG	832	143	$123,715.56	5.82	$148.70
SUBOXONE MIS 2-0.5MG	110	36	$20,912.66	3.06	$190.12
ZUBSOLV SUB 5.7-1.4	70	22	$31,389.59	3.18	$448.42
BUPRENORPHIN SUB 2MG	44	11	$3,845.14	4	$87.39
SUBOXONE MIS 12-3MG	43	8	$26,748.52	5.38	$622.06
SUBOXONE MIS 4-1MG	39	15	$12,533.45	2.6	$321.37
BUPREN/NALOX SUB 2-0.5MG	39	20	$7,035.31	1.95	$180.39
BUNAVAIL MIS 4.2-0.7	18	9	$7,757.22	2	$430.96
BUNAVAIL MIS 6.3-1MG	5	5	$3,253.59	1	$650.72

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
ZUBSOLV SUB 1.4-0.36	1	1	$207.67	1	$207.67
Total	**8,355**	**1,085***	**$3,303,407.06**	**7.7**	**$395.38**

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

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Appendix M

Fiscal Year 2015 Annual Review of Anti-Ulcer Medications and 30-Day Notice to Prior Authorize Dexilant™ SoluTab (Dexlansoprazole Delayed-Release Orally Disintegrating Tablets)

Oklahoma Health Care Authority
July 2016

Current Prior Authorization Criteria

Anti-Ulcer Medications*		
Tier-1	**Tier-2**	**Tier-3**
omeprazole (Prilosec®)	dexlansoprazole (Dexilant®)	esomeprazole magnesium (Nexium®)
pantoprazole (Protonix®)	lansoprazole (Prevacid® and ODT)	esomeprazole strontium
	rabeprazole (Aciphex®)	omeprazole suspension (Prilosec®)
		pantoprazole (Protonix® suspension)
		rabeprazole (Aciphex® sprinkles)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
ODT = orally disintegrating tablet

Anti-Ulcer Medications Tier-2 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 medications titrated up to the recommended dose that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 medications; or
3. An indication not covered by lower tiered medications.

Anti-Ulcer Medications Tier-3 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 and Tier-2 medications that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 and Tier-2 medications; or
3. An indication not covered by lower tiered medications.
4. Special formulations including orally disintegrating tablets (ODTs), sprinkle capsules, granules, suspensions, and solutions for intravenous (IV) use require patient-specific, clinically significant reasoning why the member cannot use standard dosage formulations.

Proton-Pump Inhibitors for Pediatric Members Approval Criteria:

1. A recent 14-day trial of a histamine (H_2) receptor antagonist that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. Recurrent or severe disease such as:
    a. Gastrointestinal (GI) bleed; or
    b. Zollinger-Ellison Syndrome or similar disease

Anti-Ulcer Medications Special Prior Authorization Approval Criteria:

1. Authorization of ranitidine (Zantac® Effervescent Tablets) requires a patient-specific, clinically significant reason why the member cannot use other dosage formulations.
2. Pepcid® Suspension (famotidine) is reserved for members less than 1 month of age when no other anti-ulcer medications are indicated.
3. Authorization of omeprazole/sodium bicarbonate combination products requires a patient-specific, clinically significant reason for use in place of the individual components.

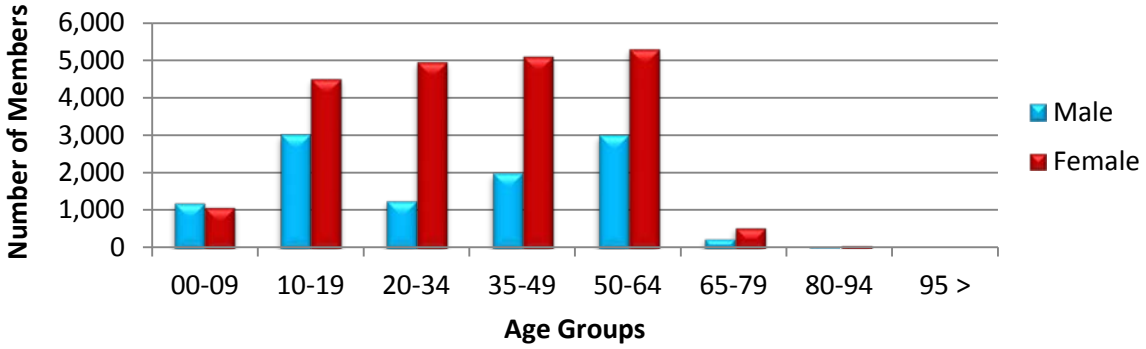
Utilization of Anti-Ulcer Medications: Fiscal Year 2015

Comparison of Fiscal Years

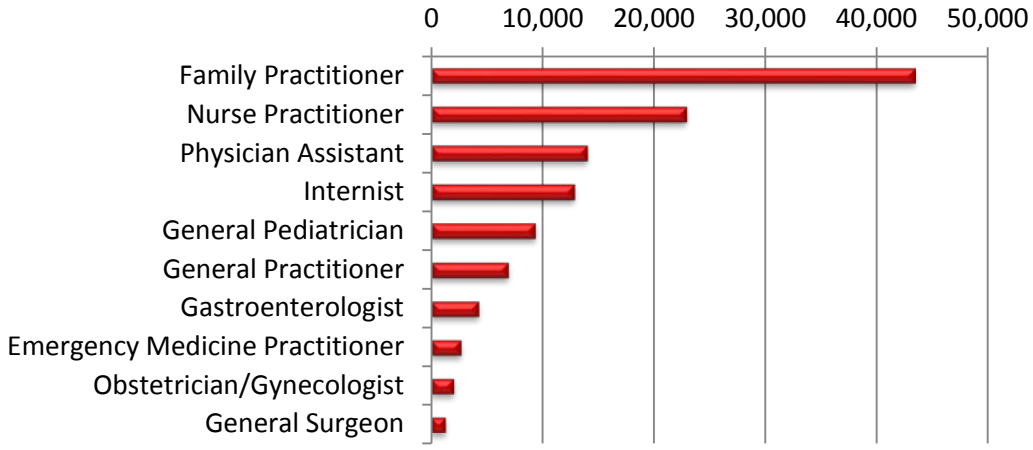
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	34,916	134,808	$2,622,379.12	$19.45	$0.60	5,354,294	4,385,775
2015	32,355	128,306	$2,152,743.46	$16.78	$0.52	5,118,745	4,174,176
% Change	**-7.30%**	**-4.80%**	**-17.90%**	**-13.70%**	**-13.30%**	**-4.40%**	**-4.80%**
Change	**-2,561**	**-6,502**	**-$469,635.66**	**-$2.67**	**-$0.08**	**-235,549**	**-211,599**

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

Demographics of Members Utilizing Anti-Ulcer Medications



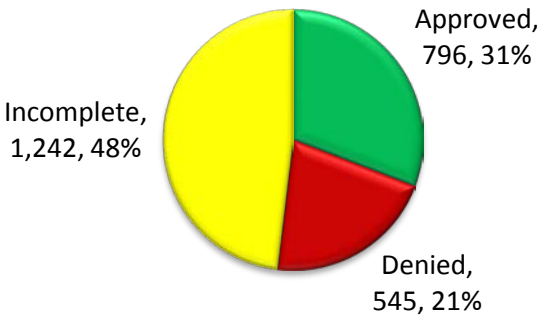
Top Prescriber Specialties of Anti-Ulcer Medications by Number of Claims



Prior Authorization of Anti-Ulcer Medications

There were 2,583 prior authorization requests submitted for the anti-ulcer medications category during fiscal year 2015. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expirations:

- Aciphex® Sprinkle (rabeprazole): September 2016
- Dexilant® capsules (dexlansoprazole): September 2030

New FDA Approvals and Indications:

- **January 2016:** The U.S. Food and Drug Administration (FDA) approved a 30mg delayed-release orally disintegrating formulation of Dexilant® (dexlansoprazole). This is in addition to the currently available Dexilant® oral capsules.

New Safety Information and Updates:

- **June 2015:** According to a data-mining study published online in the *Public Library of Science (PLOS) ONE Journal*, proton pump inhibitors (PPIs), but not H_2-antagonists appear to be associated with an elevated risk for myocardial infarction. This association has not yet been demonstrated in randomized clinical trials.
- **January 2016:** According to a recent study published in *The Journal of the American Medical Association (JAMA) Internal Medicine*, PPIs are associated with an increased risk of chronic kidney disease (CKD). Further research is required to determine whether PPI use itself causes kidney damage and, if so, to investigate the underlying mechanism of the association between PPIs and CKD.
- **April 2016:** According to a recent prospective cohort study published in *JAMA Neurology*, PPIs are associated with an increased risk of incident dementia. Randomized, prospective clinical trials are needed to examine this connection in more detail.

Dexilant™ SoluTab (Dexlansoprazole) Product Summary[6]

Indications: Dexilant™ SoluTab (dexlansoprazole) delayed-release orally disintegrating tablet is a proton pump inhibitor (PPI) indicated in adults for the following:

- Maintaining healing of erosive esophagitis (EE); and
- Treating heartburn associated with gastroesophageal reflux disease (GERD).

Dosing:

- Dexilant™ SoluTab is available as a delayed-release orally disintegrating 30mg tablet.
- Two 30mg Dexilant™ SoluTab are not interchangeable with one 60mg Dexilant™ capsule.
- The FDA approved dosing for maintenance healing of EE is 30mg once daily for up to six months.
- The FDA approved dosing for treatment of symptomatic non-erosive GERD is 30mg once daily for four weeks.
- Dexilant™ SoluTab should be taken at least 30 minutes before a meal and should not be cut or broken.
- Dexilant™ SoluTab should be placed on the tongue, allowed to disintegrate, and swallowed without water. Patients should not chew the microgranules. Dexilant™ SoluTab may also be swallowed whole with water.
- Alcohol use should be avoided when taking Dexilant™ SoluTab.

Mechanism of Action:

- Dexlansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H^+, K^+)-ATPase at the secretory surface of the gastric parietal cell. Since this enzyme is regarded as the acid (proton) pump within the parietal cell, dexlansoprazole has been characterized as a gastric proton pump inhibitor, in that it blocks the final step of acid production.

Contraindications:

- Patients with known hypersensitivity to any component of the formulation.
- Patients receiving a rilpivirine-containing product.

Safety:

- Gastric Malignancy: Relief of symptoms with dexlansoprazole does not rule out other serious stomach conditions including the presence of gastric malignancy.
- Acute Interstitial Nephritis: Acute interstitial nephritis has been observed in patients taking PPIs. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Dexlansoprazole should be discontinued if acute interstitial nephritis develops.
- Cyanocobalamin (Vitamin B-12) Deficiency: Daily long-term use of dexlansoprazole (e.g., longer than three years) may lead to malabsorption or a deficiency of cyanocobalamin.
- *Clostridium difficile*-Associated Diarrhea: PPI therapy may be associated with increased risk of *Clostridium difficile*-associated diarrhea.

- Bone Fracture: Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine.
- Hypomagnesemia: Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
- Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Increases in intragastric pH may result in hypergastrinemia and enterochromaffin-like cell hyperplasia and increased chromogranin A levels which may interfere with diagnostic investigations for neuroendocrine tumors.
- Interaction with Methotrexate: Concomitant use with PPIs may elevate and/or prolong serum concentrations of methotrexate and/or its metabolite, possibly leading to toxicity. With high-dose methotrexate administration, consideration should be given to a temporary withdrawal of dexlansoprazole.

Adverse Reactions: The most commonly reported adverse reactions (≥ 2%) during clinical trials include the following:

- Diarrhea
- Abdominal pain
- Nausea
- Upper respiratory tract infection
- Vomiting
- Flatulence

Efficacy: The efficacy of Dexilant™ SoluTab was based on demonstration of the bioequivalence of dexlansoprazole capsules in a pharmacokinetic/pharmacodynamics study. The bioavailability (C_{max} and AUC) of dexlansoprazole was similar when Dexilant™ SoluTab 30mg tablets were mixed with water and administered via oral syringe, nasogastric tube, or swallowed intact with water compared to Dexilant™ SoluTab 30mg tablets administered on the tongue, allowed to disintegrate, and swallowed without water. Two 30mg Dexilant™ SoluTab are not interchangeable with one 60mg Dexilant™ capsule because systemic exposure is lower and two 30mg Dexilant™ SoluTab are not recommended for the healing of EE.

Cost Comparison:
Information regarding the anticipated cost and launch date of Dexilant™ SoluTab is unknown at this time.

Recommendations

The College of Pharmacy recommends the placement of Dexilant™ SoluTab into Tier-3 of the Anti-Ulcer Product Based Prior Authorization (PBPA) category. Current Tier-3 criteria for this category would apply.

Anti-Ulcer Medications*		
Tier-1	**Tier-2**	**Tier-3**
omeprazole (Prilosec®)	dexlansoprazole (Dexilant®)	**dexlansoprazole (Dexilant™ SoluTab)**
pantoprazole (Protonix®)	lansoprazole (Prevacid® and ODT)	esomeprazole magnesium (Nexium®)
	rabeprazole (Aciphex®)	esomeprazole strontium
		omeprazole suspension (Prilosec®)
		pantoprazole (Protonix® suspension)
		rabeprazole (Aciphex® sprinkles)

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
ODT = orally disintegrating tablet

Anti-Ulcer Medications Tier-2 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 medications titrated up to the recommended dose that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 medications; or
3. An indication not covered by lower tiered medications.

Anti-Ulcer Medications Tier-3 Approval Criteria:

1. A recent 14-day trial of all available Tier-1 and Tier-2 medications that has resulted in inadequate relief of symptoms or intolerable adverse effects; or
2. A contraindication to all available Tier-1 and Tier-2 medications; or
3. An indication not covered by lower tiered medications.
4. Special formulations including orally disintegrating tablets (ODTs), sprinkle capsules, granules, suspensions, and solutions for intravenous (IV) use require patient-specific, clinically significant reasoning why the member cannot use standard dosage formulations.

Utilization Details of Anti-Ulcer Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM
TIER-1 PRODUCTS					
OMEPRAZOLE PRODUCTS					
OMEPRAZOLE CAP 20MG	61,522	18,401	$353,665.23	$0.16	$5.75
OMEPRAZOLE CAP 40MG	30,238	8,243	$260,531.42	$0.28	$8.62
OMEPRAZOLE CAP 10MG	2,317	917	$32,219.31	$0.46	$13.91
PRILOSEC CAP 20MG	89	41	$576.27	$0.22	$6.47
SUBTOTAL	**94,166**	**27,602**	**$646,992.23**	**$0.21**	**$6.87**
PANTOPRAZOLE PRODUCTS					
PANTOPRAZOLE TAB 40MG	21,532	5,843	$150,022.61	$0.23	$6.97
PANTOPRAZOLE TAB 20MG	2,748	908	$20,717.29	$0.25	$7.54
PROTONIX TAB 40MG	27	17	$257.25	$0.32	$9.53
SUBTOTAL	**24,307**	**6,768**	**$170,997.15**	**$0.23**	**$7.03**
TIER-1 SUBTOTAL	**118,473**	**34,370**	**$817,989.38**	**$0.21**	**$6.90**
TIER-2 PRODUCTS					
LANSOPRAZOLE PRODUCTS					
LANSOPRAZOLE CAP 30MG	3,798	538	$76,743.25	$0.68	$20.21
PREVACID TAB 15MG STB	672	176	$197,648.24	$9.56	$294.12
PREVACID TAB 30MG STB	467	77	$135,809.41	$9.80	$290.81
LANSOPRAZOLE CAP 15MG	416	77	$12,668.99	$1.02	$30.45
SUBTOTAL	**5,353**	**868**	**$422,869.89**	**$2.65**	**$79.00**
RABEPRAZOLE PRODUCTS					
RABEPRAZOLE TAB 20MG	411	81	$11,282.00	$0.92	$27.45
SUBTOTAL	**411**	**81**	**$11,282.00**	**$0.92**	**$27.45**
DEXLANSOPRAZOLE PRODUCTS					
DEXILANT CAP 60MG DR	2,333	352	$469,178.51	$6.78	$201.11
DEXILANT CAP 30MG DR	334	67	$71,047.53	$7.11	$212.72
SUBTOTAL	**2,667**	**419**	**$540,226.04**	**$6.82**	**$202.56**
TIER-2 SUBTOTAL	**8,431**	**1,368**	**$974,377.93**	**$3.89**	**$115.57**
TIER-3 PRODUCTS					
ESOMEPRAZOLE PRODUCTS					
NEXIUM CAP 40MG	808	113	$212,816.07	$8.76	$263.39
ESOMEPRA MAG CAP 40MG	147	57	$32,920.27	$7.36	$223.95
NEXIUM GRA 10MG DR	105	22	$29,818.17	$9.65	$283.98
NEXIUM CAP 20MG	33	8	$8,550.86	$8.64	$259.12
NEXIUM GRA 40MG DR	26	4	$6,034.51	$7.83	$232.10
NEXIUM GRA 20MG DR	25	5	$6,373.04	$8.50	$232.10
NEXIUM GRA 5MG DR	23	9	$6,115.30	$8.86	$232.10
NEXIUM GRA 2.5MG DR	20	7	$5,089.19	$8.48	$232.10
ESOMEPRA MAG CAP 20MG	6	3	$1,302.20	$7.23	$232.10
ESOMEPRAZOLE CAP	1	1	$215.75	$7.19	$215.75
SUBTOTAL	**1,194**	**229**	**$309,235.36**	**$8.62**	**$258.99**
OMEPRAZOLE PRODUCTS					

PRILOSEC POW 10MG	100	21	$21,468.46	$8.14	$214.68
PRILOSEC POW 2.5MG	48	18	$13,419.76	$9.32	$279.58
SUBTOTAL	**148**	**39**	**$34,888.22**	**$8.56**	**$235.73**
PANTOPRAZOLE PRODUCTS					
PROTONIX PAK	44	9	$11,989.28	$9.08	$272.48
PROTONIX INJ 40MG	**3**	3	$91.61	$5.73	$30.54
SUBTOTAL	**47**	**12**	**$12,080.89**	**$9.04**	**$257.04**
RABEPRAZOLE PRODUCTS					
ACIPHEX SPR CAP 5MG	8	3	$2,591.48	$12.46	$323.94
ACIPHEX SPR CAP 10MG	5	3	$1,580.20	$10.53	$316.04
SUBTOTAL	**13**	**6**	**$4,171.68**	**$11.65**	**$320.90**
TIER-3 SUBTOTAL	**1,402**	**286**	**$360,376.15**	**$8.66**	**$257.04**
TOTAL	**128,306**	**32,355***	**$2,152,743.46**	**$0.52**	**$16.78**

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

[1] U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/2015. Last accessed 06/2016.
[2] PR Newswire. "FDA Approves Takeda's Dexilant SoluTab (dexlansoprazole)." Available online at: http://www.prnewswire.com/news-releases/fda-approves-takedas-dexilant-solutab-dexlansoprazole-300210700.html. Issued 01/27/2016. Last accessed 06/2016.
[3] Lazarus B, Chen Y, Wilson FP, et al. Proton pump inhibitor use and the risk of chronic kidney disease. *JAMA Internal Medicine*. 2016; 176(2): 238-246.
[4] Gomm W, Von Holt K, Thome F, et al. Proton Pump Inhibitors and Risk of Dementia. *JAMA Neurology*. 2016; 73(4): 410-416.
[5] Pullen, LC. "Chronic Use of Proton Pump Inhibitors Increases Heart Risk." *Medscape*. Available online at: http://www.medscape.com/viewarticle/846202. Issued 06/2015. Last accessed 06/2016.
[6] Dexilant™ SoluTab Prescribing Information. Takeda Pharmaceuticals America, Inc. Available online at: http://general.takedapharm.com/content/file.aspx?filetypecode=DEXILANTPI&cacheRandomizer=0daa0e2f-c2aa-489f-aa10-5e346cb2d43d. Last revised 01/2016. Last accessed 06/2016.

Appendix N

Calendar Year 2015 Annual Review of Antidepressants

Oklahoma Health Care Authority
July 2016

Current Prior Authorization Criteria

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®)	levomilnacipran (Fetzima®)	desvenlafaxine (Khedezla®)	bupropion ER (Aplenzin®)
duloxetine (Cymbalta®)	vilazodone (Viibryd®)	desvenlafaxine (Pristiq®)	bupropion ER (Forfivo XL®)
mirtazapine (Remeron®, Remeron® SolTab™)		nefazodone (Serzone®)	duloxetine 40mg (Irenka™)
trazodone (Desyrel®)			trazodone ER (Oleptro®)
venlafaxine (Effexor®, Effexor XR® capsules)			venlafaxine ER tablets (Effexor XR® tablets)
Monoamine Oxidase Inhibitors (MAOIs)			
		phenelzine (Nardil®)	
		selegiline (Emsam®)	
		tranylcypromine (Parnate®)	
Unique Mechanisms of Action			
		vortioxetine (Trintellix®)	

*Tier structure based on State Maximum Allowable Cost (SMAC) and/or supplemental rebate participation.
CR = Controlled-Release; DR = Delayed-Release; ER = Extended-Release

Antidepressant 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 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 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.

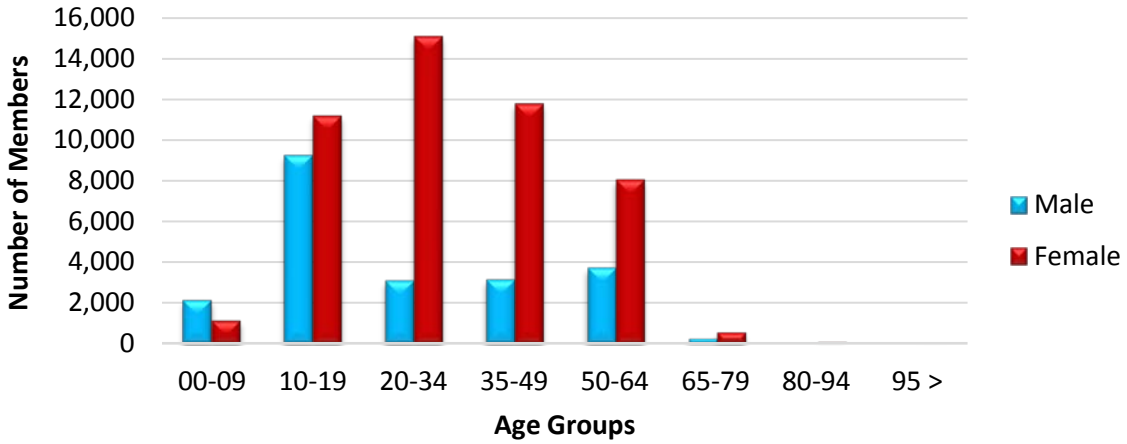
Utilization of Antidepressants: Calendar Year 2015

Comparison of Calendar Years

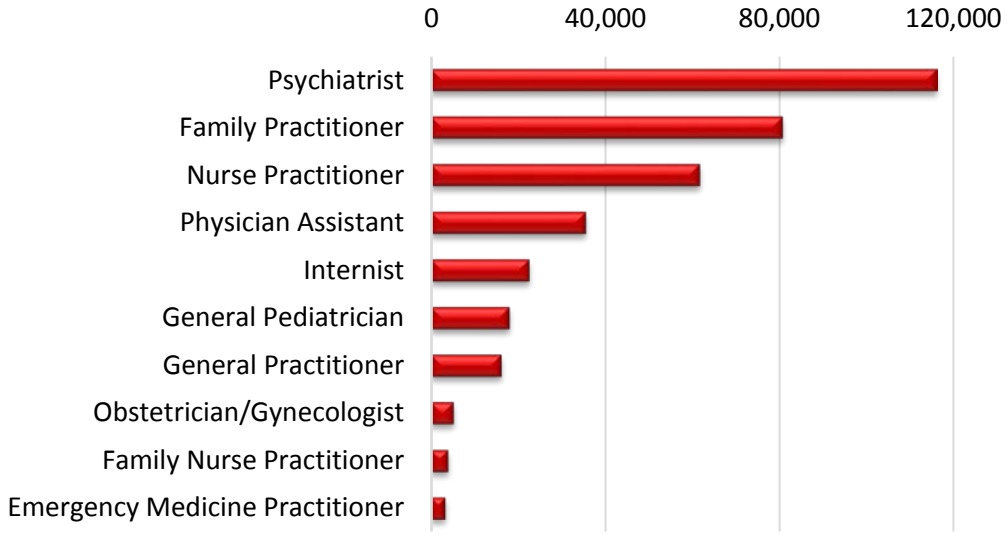
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	68,940	371,532	$6,914,861.32	$18.61	$0.57	14,289,100	12,222,572
2015	69,494	377,909	$5,140,905.91	$13.60	$0.41	14,598,078	12,489,561
% Change	**0.80%**	**1.70%**	**-25.70%**	**-26.90%**	**-28.10%**	**2.20%**	**2.20%**
Change	**554**	**6,377**	**-$1,773,955.41**	**-$5.01**	**-$0.16**	**308,978**	**266,989**

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

Demographics of Members Utilizing Antidepressants



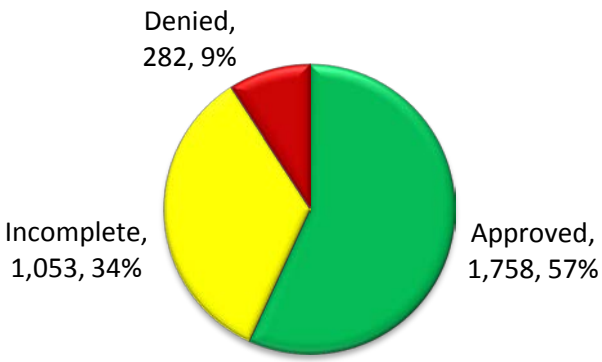
Top Prescriber Specialties of Antidepressants by Number of Claims



Prior Authorization of Antidepressants

There were 3,093 prior authorization requests submitted for antidepressants during calendar year 2015. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated Patent Expirations:

- Emsam® (selegiline ER transdermal patches): June 2018
- Viibryd® (vilazodone tablets): June 2022
- Pexeva® (paroxetine tablets): May 2025
- Aplenzin® (bupropion ER tablets): June 2026
- Pristiq® (desvenlafaxine ER tablets): July 2027
- Oleptro® (trazodone ER tablets): March 2029
- Trintellix® (vortioxetine tablets): June 2031
- Fetzima® (levomilnacipran ER capsules): May 2032

News:

- **June 2015:** A randomized, double-blind, placebo-controlled, fluoxetine-referenced Phase 3 study of Pristiq® (desvenlafaxine ER) in pediatric patients ages seven to seventeen with major depressive disorder (MDD) failed to meet its primary objective of demonstrating superior efficacy versus placebo. Efficacy results indicate that both Pristiq® and the positive control, fluoxetine, were not statistically significantly different than placebo. This trial was the first completed study of four late-stage pediatric trials being conducted as part of a U.S. Food and Drug Administration (FDA) post-marketing commitment under the Pediatric Research Equity Act (PREA). Pristiq® was approved by the FDA in 2008 for the treatment of MDD in adults.
- **October 2015:** The FDA determined that Oleptro® (trazodone ER) is no longer being marketed, but was not withdrawn from sale for reasons of safety or effectiveness. When Oleptro® (trazodone ER) is determined to be permanently discontinued, it will be removed from the antidepressants tier chart at that time. Oleptro® was approved by the FDA in 2010 for the treatment of MDD in adults.

- **March 2016:** In a complete response letter (CRL), the FDA denied an expanded indication for Brintellix® (vortioxetine). Despite a recommendation from an FDA advisory committee in February 2016, the FDA declined to add new data to the label for Brintellix® supporting use of the drug for the treatment of cognitive dysfunction in adults with MDD. This rejection is unusual as the FDA typically follows the recommendation of the relevant advisory committee. The pharmaceutical companies of Brintellix® were pleased, however, that the FDA did acknowledge that cognitive dysfunction in MDD is a legitimate target for drug development, and are looking forward to reviewing the CRL with the FDA to determine the appropriate path forward. Brintellix® was FDA approved in 2013 for the treatment of MDD in adults.
- **May 2016:** The FDA approved a brand name change for Brintellix® (vortioxetine) to decrease the risk of prescribing and dispensing errors resulting from name confusion with the antiplatelet medication Brilinta® (ticagrelor). The FDA issued a Drug Safety Communication in July 2015 regarding the potential brand name confusion. The new brand name of Brintellix® (vortioxetine) is Trintellix®. Trintellix® became available on the market in June 2016, and no other changes will be made to the label or packaging. The antidepressants tier chart has been updated to reflect this brand name change from Brintellix® to Trintellix®.
- **June 2016:** A meta-analysis was completed comparing the efficacy and tolerability of antidepressants for the treatment of MDD in children and adolescents. The meta-analysis included both published and unpublished, double-blind, randomized, controlled trials for the acute treatment of MDD in children and adolescents, and included trials of amitriptyline, citalopram, clomipramine, desipramine, duloxetine, escitalopram, fluoxetine, imipramine, mirtazapine, nefazodone, nortriptyline, paroxetine, sertraline, and venlafaxine. The primary outcomes were efficacy and tolerability. Thirty-four trials were deemed eligible for the meta-analysis, which included 5,260 patients and compared 14 antidepressants or placebo. Significant findings and conclusions from the meta-analysis include:
    - For efficacy, only fluoxetine was statistically significantly more effective than placebo.
    - In terms of tolerability, fluoxetine was better tolerated than duloxetine and imipramine. Patients given imipramine, venlafaxine, and duloxetine had more discontinuations due to adverse events than did those given placebo.
    - Venlafaxine was associated with a significantly increased risk of suicidal behavior or ideation compared with placebo and five other antidepressants (escitalopram, imipramine, duloxetine, fluoxetine, and paroxetine).
    - The study concludes that when considering the risk-benefit profile of antidepressants in the acute treatment of MDD, these drugs do not seem to offer a clear advantage for children and adolescents, and that fluoxetine is probably the best option to consider when a pharmacological treatment is indicated.

Recommendations

The College of Pharmacy does not recommend any changes to the Antidepressants Product Based Prior Authorization (PBPA) category at this time, other than updating the antidepressants tier chart to reflect the brand name change from Brintellix® to Trintellix® (included above in market news and reflected in the tier chart found in Current Prior Authorization Criteria).

Utilization Details of Antidepressants: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 MEDICATIONS						
SERTRALINE PRODUCTS						
SERTRALINE TAB 100MG	30,144	7,122	$203,213.62	$0.20	$6.74	3.95%
SERTRALINE TAB 50MG	27,135	9,602	$169,479.53	$0.19	$6.25	3.30%
SERTRALINE TAB 25MG	11,668	4,160	$73,610.55	$0.20	$6.31	1.43%
SERTRALINE CON 20MG/ML	429	121	$30,720.95	$2.20	$71.61	0.60%
SERTRALINE TAB 50MG	223	88	$1,400.67	$0.19	$6.28	0.03%
SERTRALINE TAB 100MG	60	16	$450.48	$0.21	$7.51	0.01%
ZOLOFT TAB 100MG	9	2	$4,047.80	$10.62	$449.76	0.08%
SUBTOTAL	**69,668**	**21,111**	**$482,923.60**	**$0.21**	**$6.93**	**9.39%**
TRAZODONE PRODUCTS						
TRAZODONE TAB 50MG	28,173	8,460	$140,580.75	$0.16	$4.99	2.73%
TRAZODONE TAB 100MG	20,876	5,814	$115,785.41	$0.17	$5.55	2.25%
TRAZODONE TAB 150MG	12,371	3,193	$89,714.89	$0.22	$7.25	1.75%
TRAZODONE TAB 300MG	347	139	$37,767.38	$3.18	$108.84	0.73%
SUBTOTAL	**61,767**	**17,606**	**$383,848.43**	**$0.19**	**$6.21**	**7.47%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 20MG	29,307	9,080	$145,125.69	$0.15	$4.95	2.82%
FLUOXETINE CAP 40MG	13,766	3,704	$134,489.29	$0.29	$9.77	2.62%
FLUOXETINE CAP 10MG	11,597	4,133	$62,271.97	$0.17	$5.37	1.21%
FLUOXETINE TAB 10MG	3,149	1,160	$78,348.38	$0.81	$24.88	1.52%
FLUOXETINE TAB 20MG	1,595	636	$78,134.22	$1.54	$48.99	1.52%
FLUOXETINE SOL 20MG/5ML	1,076	262	$9,767.23	$0.31	$9.08	0.19%
PROZAC CAP 20MG	28	5	$20,958.29	$25.62	$748.51	0.41%
PROZAC CAP 40MG	1	1	$1,699.03	$18.88	$1,699.03	0.03%
SUBTOTAL	**60,519**	**18,981**	**$530,794.10**	**$0.27**	**$8.77**	**10.32%**
CITALOPRAM PRODUCTS						
CITALOPRAM TAB 20MG	21,898	7,526	$92,513.31	$0.12	$4.22	1.80%
CITALOPRAM TAB 40MG	13,572	3,800	$56,300.24	$0.11	$4.15	1.10%
CITALOPRAM TAB 10MG	7,848	2,695	$40,112.38	$0.16	$5.11	0.78%
CITALOPRAM SOL	134	36	$4,829.17	$1.22	$36.04	0.09%
CELEXA TAB 20MG	2	2	$13.00	$0.22	$6.50	0.00%
CELEXA TAB 10MG	2	2	$12.54	$0.21	$6.27	0.00%
CELEXA TAB 40MG	1	1	$69.87	$6.99	$69.87	0.00%
SUBTOTAL	**43,457**	**14,062**	**$193,850.51**	**$0.13**	**$4.46**	**3.77%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
ESCITALOPRAM PRODUCTS						
ESCITALOPRAM TAB 20MG	14,250	3,476	$114,436.94	$0.24	$8.03	2.23%
ESCITALOPRAM TAB 10MG	14,108	5,030	$102,487.29	$0.22	$7.26	1.99%
ESCITALOPRAM TAB 5MG	1,142	469	$8,526.89	$0.24	$7.47	0.17%
ESCITALOPRAM SOL	177	44	$23,557.09	$4.69	$133.09	0.46%
LEXAPRO TAB 10MG	25	4	$5,886.12	$6.82	$235.44	0.11%
LEXAPRO TAB 20MG	17	4	$6,826.83	$7.85	$401.58	0.13%
SUBTOTAL	**29,719**	**9,027**	**$261,721.16**	**$0.26**	**$8.81**	**5.09%**
BUPROPION PRODUCTS						
BUPROPION TAB 150MG SR	7,167	2,483	$114,314.15	$0.51	$15.95	2.22%
BUPROPN HCL TAB 150MG	6,247	2,318	$179,558.38	$0.85	$28.74	3.49%
BUPROPN HCL TAB 300MG	5,975	1,553	$164,278.30	$0.75	$27.49	3.20%
BUPROPION TAB 100MG SR	1,997	761	$28,212.87	$0.47	$14.13	0.55%
BUPROPION TAB 100MG	1,944	741	$66,683.25	$1.12	$34.30	1.30%
BUPROPION TAB 75MG	1,809	696	$46,527.35	$0.84	$25.72	0.91%
BUPROPION TAB 200MG SR	1,025	264	$24,695.45	$0.78	$24.09	0.48%
WELLBUTRIN TAB XL 150MG	91	35	$54,224.89	$18.36	$595.88	1.05%
BUPROPION TAB 150MG ER	17	11	$223.33	$0.44	$13.14	0.00%
WELLBUTRIN TAB XL 300MG	13	2	$12,592.15	$32.29	$968.63	0.24%
WELLBUTRIN TAB 150MG SR	7	1	$1,113.58	$5.30	$159.08	0.02%
WELLBUTRIN TAB 200MG SR	1	1	$32.99	$1.10	$32.99	0.00%
BUPROPION TAB 100MG ER	1	1	$18.09	$0.60	$18.09	0.00%
SUBTOTAL	**26,294**	**8,867**	**$692,474.78**	**$0.80**	**$26.34**	**13.47%**
VENLAFAXINE PRODUCTS						
VENLAFAXINE CAP 150MG	8,665	2,190	$107,803.02	$0.36	$12.44	2.10%
VENLAFAXINE CAP 75MG ER	6,788	2,558	$65,788.73	$0.28	$9.69	1.28%
VENLAFAXINE TAB 75MG	2,360	783	$43,029.88	$0.57	$18.23	0.84%
VENLAFAXINE CAP 37.5 ER	2,163	1,098	$17,807.91	$0.27	$8.23	0.35%
VENLAFAXINE TAB 37.5MG	903	398	$14,100.14	$0.52	$15.61	0.27%
VENLAFAXINE TAB 100MG	518	135	$13,485.65	$0.83	$26.03	0.26%
VENLAFAXINE TAB 50MG	228	77	$5,006.08	$0.70	$21.96	0.10%
VENLAFAXINE TAB 25MG	94	37	$1,821.11	$0.66	$19.37	0.04%
EFFEXOR XR CAP 75MG	41	5	$20,927.72	$15.81	$510.43	0.41%
EFFEXOR XR CAP 150MG	33	7	$13,340.27	$12.04	$404.25	0.26%
SUBTOTAL	**21,793**	**7,288**	**$303,110.51**	**$0.41**	**$13.91**	**5.90%**
DULOXETINE PRODUCTS						
DULOXETINE CAP 60MG	14,366	3,619	$550,474.40	$1.07	$38.32	10.71%
DULOXETINE CAP 30MG	6,469	2,554	$267,471.03	$1.29	$41.35	5.20%
DULOXETINE CAP 20MG	823	348	$39,232.03	$1.53	$47.67	0.76%
CYMBALTA CAP 60MG	47	20	$10,351.71	$6.27	$220.25	0.20%
CYMBALTA CAP 30MG	33	16	$5,616.92	$4.31	$170.21	0.11%
SUBTOTAL	**21,738**	**6,557**	**$873,146.09**	**$1.16**	**$40.17**	**16.98%**
MIRTAZAPINE PRODUCTS						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
MIRTAZAPINE TAB 15MG	10,635	3,426	$91,131.95	$0.27	$8.57	1.77%
MIRTAZAPINE TAB 30MG	6,921	2,014	$71,327.86	$0.32	$10.31	1.39%
MIRTAZAPINE TAB 45MG	2,804	632	$37,935.62	$0.40	$13.53	0.74%
MIRTAZAPINE TAB 7.5MG	461	154	$19,354.64	$1.41	$41.98	0.38%
MIRTAZAPINE TAB 15MG	222	76	$7,300.87	$1.03	$32.89	0.14%
MIRTAZAPINE TAB 30MG	120	43	$3,602.42	$0.96	$30.02	0.07%
MIRTAZAPINE TAB 45MG	56	14	$1,982.45	$1.19	$35.40	0.04%
SUBTOTAL	**21,219**	**6,359**	**$232,635.81**	**$0.35**	**$10.96**	**4.53%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 20MG	5,857	2,270	$33,293.47	$0.16	$5.68	0.65%
PAROXETINE TAB 40MG	4,299	1,120	$38,917.04	$0.25	$9.05	0.76%
PAROXETINE TAB 10MG	2,454	1,008	$15,679.90	$0.19	$6.39	0.31%
PAROXETINE TAB 30MG	1,820	476	$15,294.35	$0.24	$8.40	0.30%
PAXIL SUS 10MG/5ML	88	19	$15,999.09	$6.33	$181.81	0.31%
PAXIL TAB 40MG	4	1	$2,103.63	$5.84	$525.91	0.04%
SUBTOTAL	**14,522**	**4,894**	**$121,287.48**	**$0.24**	**$8.35**	**2.36%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE TAB 100MG	1,492	282	$27,286.81	$0.60	$18.29	0.53%
FLUVOXAMINE TAB 50MG	974	247	$12,881.08	$0.44	$13.22	0.25%
FLUVOXAMINE TAB 25MG	319	82	$4,244.43	$0.42	$13.31	0.08%
SUBTOTAL	**2,785**	**611**	**$44,412.32**	**$0.52**	**$15.95**	**0.86%**
TIER-1 SUBTOTAL	**373,481**	**115,363**	**$4,120,204.79**	**$0.33**	**$11.03**	**80.15%**
TIER-2 MEDICATIONS						
VILAZODONE PRODUCTS						
VIIBRYD TAB 40MG	604	134	$119,645.45	$6.62	$198.09	2.33%
VIIBRYD TAB 20MG	167	70	$35,217.93	$6.81	$210.89	0.69%
VIIBRYD TAB 10MG	53	32	$11,467.28	$8.08	$216.36	0.22%
VIIBRYD KIT	20	20	$4,019.70	$6.70	$200.99	0.08%
SUBTOTAL	**844**	**256**	**$170,350.36**	**$6.74**	**$201.84**	**3.31%**
LEVOMILNACIPRAN PRODUCTS						
FETZIMA CAP 80MG	82	20	$21,965.26	$8.93	$267.87	0.43%
FETZIMA CAP 40MG	62	20	$17,060.65	$9.34	$275.17	0.33%
FETZIMA CAP 120MG	25	10	$6,731.00	$8.97	$269.24	0.13%
FETZIMA CAP 20MG	10	6	$2,370.49	$8.72	$237.05	0.05%
SUBTOTAL	**179**	**56**	**$48,127.40**	**$9.07**	**$268.87**	**0.94%**
TIER-2 SUBTOTAL	**1,023**	**312**	**$218,477.76**	**$7.15**	**$213.57**	**4.25%**
TIER-3 MEDICATIONS						
DESVENLAFAXINE PRODUCTS						
PRISTIQ TAB 100MG	389	64	$119,159.27	$8.67	$306.32	2.32%
PRISTIQ TAB 50MG	306	63	$98,695.38	$8.44	$322.53	1.92%
DESVENLAFAX TAB 50MG ER	26	4	$3,221.22	$4.94	$123.89	0.06%
DESVENLAFAX TAB 100MG	17	3	$3,626.91	$4.91	$213.35	0.07%
PRISTIQ TAB 25MG	9	3	$2,193.70	$8.22	$243.74	0.04%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
DESVENLAFAX TAB 50MG ER	3	1	$452.46	$5.03	$150.82	0.01%
SUBTOTAL	**750**	**138**	**$227,348.94**	**$8.36**	**$303.13**	**4.42%**
VORTIOXETINE PRODUCTS+						
BRINTELLIX TAB 10MG	145	61	$40,757.26	$9.38	$281.08	0.79%
BRINTELLIX TAB 20MG	114	40	$31,826.55	$9.35	$279.18	0.62%
BRINTELLIX TAB 5MG	11	7	$3,103.27	$10.17	$282.12	0.06%
SUBTOTAL	**270**	**108**	**$75,687.08**	**$9.40**	**$280.32**	**1.47%**
NEFAZODONE PRODUCTS						
NEFAZODONE TAB 200MG	20	2	$1,042.75	$1.74	$52.14	0.02%
NEFAZODONE TAB 100MG	14	3	$673.84	$1.60	$48.13	0.01%
NEFAZODONE TAB 250MG	13	1	$654.09	$1.68	$50.31	0.01%
NEFAZODONE TAB 150MG	2	1	$126.96	$2.12	$63.48	0.00%
SUBTOTAL	**49**	**7**	**$2,497.64**	**$1.70**	**$50.97**	**0.05%**
SELEGILINE PRODUCTS						
EMSAM DIS 12MG/24H	6	1	$8,157.51	$45.32	$1,359.59	0.16%
SUBTOTAL	**6**	**1**	**$8,157.51**	**$45.32**	**$1,359.59**	**0.16%**
TIER-3 SUBTOTAL	**1,075**	**254**	**$313,691.17**	**$8.50**	**$291.81**	**6.10%**
SPECIAL PA MEDICATIONS						
VENLAFAXINE PRODUCTS						
VENLAFAXINE TAB 225MG	783	205	$214,697.78	$7.21	$274.20	4.18%
VENLAFAXINE TAB 150MG	255	88	$29,119.54	$3.12	$114.19	0.57%
VENLAFAXINE TAB 75MG ER	73	33	$6,500.72	$2.70	$89.05	0.13%
VENLAFAXINE TAB 37.5 ER	47	19	$3,988.98	$2.71	$84.87	0.08%
SUBTOTAL	**1,158**	**345**	**$254,307.02**	**$5.92**	**$219.61**	**4.95%**
PAROXETINE PRODUCTS						
PAROXETINE TAB 25MG ER	453	111	$61,893.78	$3.96	$136.63	1.20%
PAROXETIN ER TAB 37.5MG	222	45	$32,000.38	$4.06	$144.15	0.62%
PAROXETIN ER TAB 12.5MG	146	51	$20,082.89	$3.88	$137.55	0.39%
PEXEVA TAB 40MG	10	1	$2,826.43	$10.35	$282.64	0.05%
PEXEVA TAB 20MG	4	2	$2,824.99	$9.42	$706.25	0.05%
PAXIL CR TAB 37.5MG	3	1	$514.37	$5.72	$171.46	0.01%
SUBTOTAL	**838**	**211**	**$120,142.84**	**$4.09**	**$143.37**	**2.34%**
FLUVOXAMINE PRODUCTS						
FLUVOXAMINE CAP 100MG	140	28	$63,728.77	$15.30	$455.21	1.24%
FLUVOXAMINE CAP 150MG	103	23	$35,772.55	$11.40	$347.31	0.70%
LUVOX CR CAP 100MG	1	1	$714.87	$39.72	$714.87	0.01%
SUBTOTAL	**244**	**52**	**$100,216.19**	**$13.69**	**$410.72**	**1.95%**
FLUOXETINE PRODUCTS						
FLUOXETINE CAP 90MG DR	59	9	$8,171.05	$4.86	$138.49	0.16%
FLUOXETINE TAB 60MG	29	6	$5,492.91	$5.97	$189.41	0.11%
SUBTOTAL	**88**	**15**	**$13,663.96**	**$5.25**	**$155.27**	**0.27%**
TRAZODONE PRODUCTS						
OLEPTRO TAB 24HR150	2	1	$202.18	$3.37	$101.09	0.00%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SUBTOTAL	**2**	**1**	**$202.18**	**$3.37**	**$101.09**	**0.00%**
SPECIAL PA SUBTOTAL	**2,330**	**624**	**$488,532.19**	**$5.94**	**$209.67**	**9.50%**
TOTAL	**377,909**	**69,494***	**$5,140,905.91**	**$0.41**	**$13.60**	**100.00%**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
[+]The FDA approved a brand name change for Brintellix® (vortioxetine) to Trintellix® in May 2016; therefore, the product was still available as Brintellix® in calendar year 2015, as is reflected in the utilization details above.

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[4] Takeda and Lundbeck Press Release. "Takeda and Lundbeck Receive Complete Response Letter for Brintellix® (vortioxetine) sNDA." Available online at: https://www.lundbeck.com/upload/us/files/pdf/2016_Releases/Brintellix%20sNDA%20CRL%20Release_3%2028%2016_541pm%20FINAL.pdf. Issued 03/29/2016. Last accessed 06/16/2016.
[5] Anderson, Pauline. "FDA Panel Backs Vortioxetine for Cognitive Dysfunction in MDD." *Medscape*. Available online at: http://www.medscape.com/viewarticle/858539. Issued 02/08/2016. Last accessed 06/16/2016.
[6] U.S. Food and Drug Administration (FDA) Drug Safety Communication. "FDA Approves Brand Name Change for Antidepressant Brintellix (vortioxetine) to Avoid Confusion with Antiplatelet Drug Brilinta (ticagrelor)." Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm497942.htm. Issued 05/02/2016. Last accessed 06/16/2016.
[7] Cipriani A, Zhou X, et al. Comparative Efficacy and Tolerability of Antidepressants for Major Depressive Disorder in Children and Adolescents: A Network Meta-Analysis. *The Lancet*, published online at doi: 10.1016/S0140-6736(16)30385-3. Issued 06/08/2016. Last accessed 06/16/2016.

Appendix O

Calendar Year 2015 Annual Review of Myalept® (Metreleptin)

Oklahoma Health Care Authority
July 2016

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

Generalized lipodystrophy is a rare condition associated with complete or partial lack of adipose tissue. Patients with congenital generalized lipodystrophy are born with little or no adipose tissue, whereas, patients with acquired generalized lipodystrophy lose adipose tissue over time. This leads to abnormal deposition of triglycerides in other tissues such as muscle, liver, and pancreas. Additionally, due to the lack of adipose tissue, these patients may also have a leptin deficiency. Leptin is a hormone secreted by adipocytes, which is involved in regulation of food intake, energy homeostasis, and other hormones such as insulin.

Clinical manifestations include severe insulin resistance, hyperlipidemia, progressive liver disease, pancreatitis, heart disease, and increased metabolic rate. Insulin resistance is noted at an early age and diabetes mellitus usually develops in the early teen years. Diabetes in this population is typically refractory to insulin therapy. Hypertriglyceridemia associated with congenital and acquired lipodystrophy is difficult to treat and frequently leads to pancreatitis and hepatic steatosis.

The prevalence of generalized lipodystrophy has been estimated to be less than one case per one million people. In congenital generalized lipodystrophy, the absence of subcutaneous fat is often noted at or soon after birth. Acquired generalized lipodystrophy can occur in previously healthy children or adults and predominates in females.

Myalept® (metreleptin) was approved by the U.S. Food and Drug Administration (FDA) as an orphan drug in February 2014 and is the first FDA approved therapy indicated for treating the complications of congenital and acquired generalized lipodystrophy.

Current Prior Authorization Criteria

Myalept® (Metreleptin) Approval Criteria:

1. An FDA approved diagnosis of leptin deficiency in patients with congenital or acquired generalized lipodystrophy; and
2. Approvals will not be granted for the following diagnoses:
    a. Metabolic disease without current evidence of generalized lipodystrophy; or
    b. HIV-related lipodystrophy; or
    c. General obesity not associated with congenital leptin deficiency; and
3. Myalept® must be prescribed by an endocrinologist; and
4. Prescriber must agree to test for neutralizing antibodies in patients who experience severe infections or if they suspect Myalept® is no longer effective.
    a. Baseline HbA1c, fasting glucose, and fasting triglycerides must be provided on prior authorization request; and
    b. Re-approvals will require recent lab values (HbA1c, fasting glucose, and fasting triglycerides) to ensure neutralizing antibodies have not developed; and

5. Prescriber and pharmacy must be enrolled in the Myalept® REMS program; and
6. Approvals will be for the duration of three months to evaluate compliance and ensure the prescriber is assessing continued efficacy; and
7. A quantity limit of one vial per day will apply.

Utilization of Myalept® (Metreleptin): Calendar Year 2015

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	1	1	$46,636.67	$46,636.67	$1,554.56	30	30
2015	1	13	$1,199,077.09	$92,236.70	$3,312.37	362	362
% Change	**0.0%**	**1,200.0%**	**2,471.1%**	**97.8%**	**113.1%**	**1,106.7%**	**1,106.7%**
Change	**0**	**12**	**$1,152,440.42**	**$45,600.03**	**$1,757.81**	**332**	**332**

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

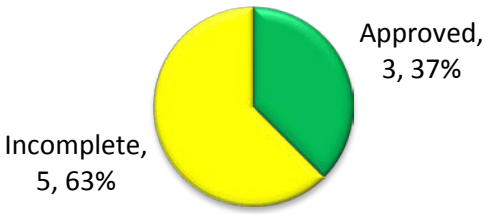
Top Prescriber Specialties of Myalept® (Metreleptin) by Number of Claims

- The only prescriber specialty listed on paid claims for Myalept® during calendar year 2015 was a pediatric endocrinologist.

Prior Authorization of Myalept® (Metreleptin)

There were 8 prior authorization requests submitted for Myalept® during calendar year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



Recommendations

The College of Pharmacy does not recommend any changes at this time.

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[1] Mantzoros, Christos. "Lipodystrophic Syndromes." *UpToDate*. Available online at: http://www.uptodate.com/contents/lipodystrophic-syndromes?source=search_result&search=lipodystrophic+syndromes&selectedTitle=1%7E150. Last revised 07/27/2015. Last accessed 06/16/2016.
[2] Oral, Elif A. "Generalized Lipodystrophy." *Medscape*. Available online at: http://emedicine.medscape.com/article/128355-overview. Last revised 12/11/2015. Last accessed 06/16/2016.
[3] National Organization for Rare Disorders (NORD). "Congenital Generalized Lipodystrophy." Available online at: http://rarediseases.org/rare-diseases/congenital-generalized-lipodystrophy/. Last revised 2015. Last accessed 06/16/2016.
[4] NORD. "Acquired Lipodystrophy." Available online at: http://rarediseases.org/rare-diseases/acquired-lipodystrophy/. Last revised 2015. Last accessed 06/16/2016.
[5] Myalept® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/myalept-1/. Last revised 06/30/2014. Last accessed 06/16/2016.
[6] Micromedex 2.0. "Metreleptin Drug Information." Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 01/26/2016. Last accessed 06/16/2016.

Appendix P

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

FDA NEWS RELEASE

For Immediate Release: June 28th, 2016

FDA approves Epclusa for treatment of chronic Hepatitis C virus infection

First regimen to treat all six major HCV genotypes

The U.S. Food and Drug Administration (FDA) approved Epclusa to treat adult patients with chronic hepatitis C virus (HCV) both with and without cirrhosis (advanced liver disease). For patients with moderate to severe cirrhosis (decompensated cirrhosis), Epclusa is approved for use in combination with the drug ribavirin. Epclusa is a fixed-dose combination tablet containing sofosbuvir, a drug approved in 2013, and velpatasvir, a new drug, and is the first to treat all six major forms of HCV.

Hepatitis C is a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. There are at least six distinct HCV genotypes, or strains, which are genetically distinct groups of the virus. Knowing the genotype helps inform treatment recommendations and the duration of treatment. Approximately 75 percent of Americans with HCV have genotype 1; 20-25 percent have genotypes 2 or 3; and a small numbers of patients are infected with genotypes 4, 5 or 6. According to the Centers for Disease Control and Prevention, HCV infection becomes chronic in approximately 75 to 85 percent of cases. Patients who suffer from chronic HCV infection over many years may have complications, such as bleeding, jaundice, fluid accumulation in the abdomen, infections, liver cancer and death.

The safety and efficacy of Epclusa for 12 weeks was evaluated in three Phase III clinical trials of 1,558 subjects without cirrhosis or with compensated cirrhosis (mild cirrhosis). Results demonstrated that 95–99 percent of patients who received Epclusa had no virus detected in the blood 12 weeks after finishing treatment, suggesting the patients' infections had been cured. The safety and efficacy of Epclusa was also evaluated in a clinical trial of 267 subjects with decompensated cirrhosis (moderate to severe cirrhosis), of whom 87 subjects received Epclusa in combination with ribavirin for 12 weeks, and 94 percent of these patients had no virus detected in the blood 12 weeks after finishing treatment.

The most common side effects of Epclusa include headache and fatigue. Epclusa and ribavirin combination regimens are contraindicated for patients for whom ribavirin is contraindicated.

Epclusa carries a warning for patients and health care providers that serious slowing of the heart rate (symptomatic bradycardia) and cases requiring pacemaker intervention have been reported when amiodarone is used with sofosbuvir in combination with another HCV direct-acting antiviral. Co-administration of amiodarone with Epclusa is not recommended. Epclusa also carries a warning not to use with certain drugs that may reduce the amount of Epclusa in the blood which could lead to reduced efficacy of Epclusa.

Epclusa was reviewed under the FDA's priority review program, which provides for an expedited review of drugs that treat serious conditions and, if approved, would provide significant improvement in safety or effectiveness.

Epclusa is manufactured and marketed by Gilead Sciences, Inc., of Foster City, California.

Safety Announcements

FDA Drug Safety Communication: FDA warns about serious bleeding risk with over-the-counter antacid products containing aspirin

[6-6-2016] The FDA is warning consumers about the risk of serious bleeding when using nonprescription (OTC) aspirin-containing antacid products to treat heartburn, sour stomach, acid indigestion, or upset stomach. Many other products for these conditions are available that do not contain aspirin.

These widely used products already contain warnings about this bleeding risk on their labels; however, the FDA is continuing to receive reports of this serious safety issue. As a result, the FDA will continue to evaluate this safety concern and plans to convene an advisory committee of external experts to provide input regarding whether additional FDA actions are needed.

OTC aspirin-antacid products are sold under various trade names, including Alka-Seltzer Original, Bromo Seltzer, Medique Medi Seltzer, Picot Plus Effervescent, Vida Mia Pain Relief, Winco Foods Effervescent Antacid and Pain Relief, and Zee-Seltzer Antacid and Pain Reliever. They are also available as generic products.

Consumers should always read the Drug Facts label carefully when purchasing or taking an OTC product to treat heartburn, acid indigestion, or sour or upset stomach. If the product contains aspirin, consumers should consider whether they should choose a product without aspirin to relieve their symptoms.
Aspirin is a commonly used pain reducer and fever reducer. It is a nonsteroidal anti-inflammatory drug (NSAID) that can increase the risk of bleeding, including in the stomach and gastrointestinal (GI) tract.
Consumers should ask their pharmacist if they need help reading the Drug Facts label.
If consumers have one or more of the following risk factors, they may have a higher chance of serious bleeding when taking aspirin-containing antacid products:

- Are 60 years or older
- Have a history of stomach ulcers or bleeding problems
- Take a blood-thinning or steroid medicine
- Take other medicines containing NSAIDs such as ibuprofen or naproxen
- Drink three or more alcoholic drinks every day

Taking more of these medicines than the amount recommended or for a longer period than recommended will increase the risk of serious bleeding.
In 2009, a warning about the risk of serious bleeding was added to the labels of all OTC products that contain NSAIDs, including aspirin-containing antacid products. However, a search of the FDA Adverse Event Reporting System (FAERS) database identified eight cases of serious bleeding events associated with these products after the warning was added. All of these patients were hospitalized. Patients had underlying conditions such as the risk factors above that put them at greater risk for developing serious bleeding events. The FAERS database includes only reports submitted to FDA so there are likely additional cases which have not been reported.

Safety Announcements

FDA Drug Safety Communication: FDA warns about serious heart problems with high doses of the antidiarrheal medicine loperamide (Imodium), including from abuse and misuse

[6-7-2016] The FDA is warning that taking higher than recommended doses of the common over-the-counter (OTC) and prescription diarrhea medicine loperamide (Imodium), including through abuse or misuse of the product, can cause serious heart problems that can lead to death. The risk of these serious heart problems, including abnormal heart rhythms, may also be increased when high doses of loperamide are taken with several kinds of medicines that interact with loperamide.
**This is not a complete list, and the extent of the effects of each drug are unknown.*

Generic Name	Examples of Brand Name(s)
cimetidine	Tagamet HB
clarithromycin	Biaxin, Prevpac
erythromycin	E.E.S., Ery-Tab, Eryc, Eryped, PCE
gemfibrozil	Lopid
itraconazole	Onmel,Sporanox
ketoconazole	Available by generic only
quinidine†	Nuedexta
quinine†	Qualaquin
ranitidine	Zantac
ritonavir	Kaletra, Norvir, Technivie, Viekira Pak

†Quinine and its isomer quinidine are also present in Tonic Water.

The majority of reported serious heart problems occurred in individuals who were intentionally misusing and abusing high doses of loperamide in attempts to self-treat opioid withdrawal symptoms or to achieve a feeling of euphoria. This safety issue will continue to be evaluated and will determine if additional FDA actions are needed.
Health care professionals should be aware that use of higher than recommended doses of loperamide can result in serious cardiac adverse events. Consider loperamide as a possible cause of unexplained cardiac events including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest. In cases of abuse, individuals often use other drugs together with loperamide in attempts to increase its absorption and penetration across the blood-brain barrier, inhibit loperamide metabolism, and enhance its euphoric effects. If loperamide toxicity is suspected, the drug should be promptly discontinued and necessary therapy started. If loperamide ingestion is suspected, blood levels should be measured, which

may require specific testing. For some cases of Torsades de Pointes in which drug treatment is ineffective, electrical pacing or cardioversion may be required.
Patients taking loperamide should be advised to follow the dosing recommendations on the label because taking higher than recommended doses, either intentionally or unintentionally, may lead to abnormal heart rhythms and serious cardiac events leading to death. Also patients should be advised that drug interactions with commonly used medicines also increase the risk of serious cardiac adverse events. Patients with opioid use disorders should be refered for treatment.
Patients and consumers should only take loperamide in the dose directed by their health care professionals or according to the OTC Drug Facts label. They should not use more than the dose prescribed or listed on the label, as doing so can cause severe heart rhythm problems or death. If diarrhea lasts more than 2 days, patients should stop taking loperamide and contact their health care professional. They should seek medical attention immediately if they experience any of the following:

- Fainting
- Rapid heartbeat or irregular heart rhythm
- Unresponsiveness

Patients should ask a pharmacist or health care professional if they are not sure how much loperamide to take, how often to take it, or whether a medicine they are taking may interact with loperamide. Patients should always tell their health care professionals about all the medicines they are taking, including OTC medicines.
Loperamide is approved to help control symptoms of diarrhea, including Travelers' Diarrhea. The maximum approved daily dose for adults is 8mg per day for OTC use and 16mg per day for prescription use. It is sold under the OTC brand name Imodium A-D, as store brands, and as generics.
In the 39 years from when loperamide was first approved in 1976 through 2015, FDA received reports of 48 cases of serious heart problems associated with use of loperamide. This number includes only reports submitted to FDA, so there are likely additional cases which have not been reported. Thirty-one of these cases resulted in hospitalizations, and 10 patients died. More than half of the 48 cases were reported after 2010. The serious heart problems occurred mostly in patients who were taking doses that were much higher than recommended. In other cases, patients were taking the recommended dose of loperamide, but they were also taking interacting medicines, causing an increase in loperamide levels. Additional cases of serious heart problems associated with the use of loperamide were reported in the medical literature. Cases reported to FDA and in the medical literature indicate that individuals are taking significantly high doses of loperamide in situations of both misuse and abuse, often attempting to achieve euphoria or self-treat opioid withdrawal. They are also combining loperamide with interacting drugs in attempts to increase these effects.
The FDA urges patients, consumers, and health care professionals to report side effects involving loperamide or other medicines to the FDA MedWatch program,

Safety Announcements

FDA Drug Safety Communication: FDA strengthens kidney warnings for diabetes medicines canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR)

[6-14-2016] The FDA has strengthened the existing warning about the risk of acute kidney injury for the type 2 diabetes medicines canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR). Based on recent reports, the FDA has revised the warnings in the drug labels to include information about acute kidney injury and added recommendations to minimize this risk.
Patients should seek medical attention immediately if they experience signs and symptoms of acute kidney injury. This is a serious condition in which the kidneys suddenly stop working, causing dangerous levels of wastes to build up in the body. Signs and symptoms of acute kidney injury may include decreased urine or swelling in the legs or feet. Patients should not stop taking their medicine without first talking to their health care professionals. Doing so can lead to uncontrolled blood sugar levels that can be harmful.
Health care professionals should consider factors that may predispose patients to acute kidney injury prior to starting them on canagliflozin or dapagliflozin. These include decreased blood volume; chronic kidney insufficiency; congestive heart failure; and taking other medications such as diuretics, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs (NSAIDs). Kidney function should be assessed prior to starting canagliflozin or dapagliflozin and monitored periodically thereafter. If acute kidney injury occurs, the drug should be promptly discontinued and the kidney impairment treated.

Canagliflozin and dapagliflozin are prescription medicines used with diet and exercise to help lower blood sugar in adults with type 2 diabetes. They belong to a class of drugs called sodium-glucose cotransporter-2 (SGLT2) inhibitors. Canagliflozin and dapagliflozin lower blood sugar by causing the kidneys to remove sugar from the body through the urine. Untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease.
From March 2013, when canagliflozin was approved, to October 2015, FDA received reports of 101 confirmable cases of acute kidney injury, some requiring hospitalization and dialysis, with canagliflozin or dapagliflozin use. This number includes only reports submitted to FDA, so there are likely additional cases which have not been reported. In approximately half of the cases, the events of acute kidney injury occurred within 1 month of starting the drug, and most patients improved after stopping it. Some cases occurred in patients who were younger than 65 years. Some patients were dehydrated, had low blood pressure, or were taking other medicines that can affect the kidneys.
The FDA urges health care professionals and patients to report side effects involving canagliflozin, dapagliflozin, or other medicines to the FDA MedWatch program.

Current Drug Shortages Index (as of June 30th, 2016):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Bleomycin Sulfate for Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Desmopressin Acetate Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin Lyophilized Powder for Injection	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fomepizole 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***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
LifeCare PCA™ Sterile Empty Vial and Injector	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***

Methylprednisolone Sodium Succinate for Injection, USP	***Currently in Shortage***
Morphine Sulfate Injection, USP, CII, (Preservative-Free)(For PCA Use Only)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***
Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Penicillin G Benzathine (Bicillin L-A) Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***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***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sumatriptan (Imitrex) Nasal Spray	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Theophylline Extended Release Tablets and Capsules	***Currently in Shortage***
Tigecycline (Tygacil) Injection	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Tretinoin Capsules	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***