Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
June 8, 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 – June 8, 2016

DATE: May 20, 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 June meeting.
Material is arranged in order of the agenda.

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir) – Appendix C

Action Item – 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 – Appendix D

Action Item – Vote to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®) and Update Makena® (Hydroxyprogesterone Caproate) Approval Criteria – Appendix E

Action Item – 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) – Appendix F

Action Item – Vote to Prior Authorize Entresto™ (Sacubitril/Valsartan) – Appendix G

30-Day Notice to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium Ra 223 Dichloride), and Provenge® (Sipuleucel-T) – Appendix H

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) – Appendix I

Annual Review of Cholbam® (Cholic Acid) – Appendix J

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

Annual Review of Anthelmintic Medications and 30-Day Notice to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole) – Appendix L

30-Day Notice to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection) – Appendix M

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) – Appendix N

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) – Appendix O

Annual Review of Topical Antifungal Products and 30-Day Notice to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution – Appendix P

Annual Review of Natpara® (Parathyroid Hormone Injection) – Appendix Q

FDA and DEA Updates – Appendix R

Future Business (Upcoming Product and Class Reviews)

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – June 8, 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. April 13, 2016 DUR Minutes – Vote
B. April 13, 2016 DUR Recommendations Memorandum
C. Correspondence

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

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

A. Medication Coverage Activity for April 2016
B. Pharmacy Help Desk Activity for April 2016
C. Medication Coverage Activity for May 2016
D. Pharmacy Help Desk Activity for May 2016
E. SoonerPsych Program Update

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

5. Action Item – Vote to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir) – See Appendix C

A. Introduction
B. Market News and Updates
C. Regimen Comparison
D. College of Pharmacy Recommendations

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

6. Action Item – 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 – See Appendix D

A. Introduction
B. Recommendations
C. Hemophilia Factor Dispensing Form
D. Hemophilia and Other Rare Bleeding Disorders Patient In-Home Assessment

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

7. Action Item – Vote to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®) and Update Makena® (Hydroxyprogesterone Caproate) Approval Criteria – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations
C. SoonerCare Coverage of Makena®, Crinone®, and Endometrin® - Algorithm
D. SoonerCare Coverage of Progesterone Products - Chart

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

8. Action Item – 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) – See Appendix F

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

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

9. Action Item – Vote to Prior Authorize Entresto™ (Sacubitril/Valsartan) – See Appendix G

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

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

10. 30-Day Notice to Prior Authorize Zytiga® (Abiraterone), Jevtana® (Cabazitaxel), Xtandi® (Enzalutamide), Xofigo® (Radium Ra 223 Dichloride), and Provenge® (Sipuleucel-T) – See Appendix H

A. Introduction
B. Utilization of Prostate Cancer Medications
C. Market News and Updates
D. Product Summaries
E. College of Pharmacy Recommendations
F. Utilization Details of Prostate Cancer Medications

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

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) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of ADHD & Narcolepsy Medications
C. Prior Authorization of ADHD & Narcolepsy Medications
D. Market News and Updates
E. Dyanavel™ XR (Amphetamine Extended-Release) Product Summary
F. QuilliChew ER™ (Methylphenidate Extended-Release) Product Summary
G. Adzenys XR-ODT™ (Amphetamine Extended-Release) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of ADHD & Narcolepsy Medications

Non-presentation; Questions only:

12. Annual Review of Cholbam® (Cholic Acid) – See Appendix J

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Cholbam® (Cholic Acid)
D. Prior Authorization of Cholbam® (Cholic Acid)
E. Market News and Updates
F. College of Pharmacy Recommendations

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

13. Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil) – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of Atypical Antipsychotic Medications
C. Prior Authorization of Atypical Antipsychotic Medications
D. Market News and Updates
E. Rexulti® (Brexpiprazole) Product Summary
F. Vraylar™ (Cariprazine) Product Summary
G. Aristada™ (Aripiprazole Lauroxil) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of Atypical Antipsychotic Medications

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

14. Annual Review of Anthelmintic Medications and 30-Day Notice to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole) – See Appendix L

A. Background Information
B. Utilization of Anthelmintic Medications
C. Market News and Updates
D. Regimen Comparison
E. Albenza® (Albendazole) Product Summary
F. Emverm™ (Mebendazole) Product Summary
G. College of Pharmacy Recommendations
H. Utilization Details of Anthelmintic Medications

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

15. 30-Day Notice to Prior Authorize H.P. Acthar® Gel (Corticotropin Injection) – See Appendix M

A. Introduction
B. Utilization of H.P. Acthar® Gel (Corticotropin Injection)
C. H.P. Acthar® Gel (Corticotropin Injection) Product Summary
D. College of Pharmacy Recommendations

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

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) – See Appendix N

A. Introduction
B. Utilization of Bowel Preparation Medications
C. Market News and Updates
D. Bowel Preparation Medications Summary
E. OsmoPrep® (Sodium Phosphate Monobasic/Sodium Phosphate Dibasic) Product Summary
F. Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid) Product Summary
G. Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/Sodium Chloride/Sodium Bicarbonate/Potassium Chloride) Product Summary
H. SUPREP® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) Product Summary
I. College of Pharmacy Recommendations
J. Utilization Details of Bowel Preparation Medications

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

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) – See Appendix O

A. Introduction
B. Current Prior Authorization Criteria

C. Utilization of Special Formulations
D. Prior Authorization of Special Formulations
E. Nuvessa™ (Metronidazole Vaginal Gel 1.3%) Product Summary
F. Zyclara® (Imiquimod Cream) Product Summary
G. Kristalose® (Lactulose Packets) Product Summary
H. College of Pharmacy Recommendations

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

18. Annual Review of Topical Antifungal Products and 30-Day Notice to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution – See Appendix P

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

Non-presentation; Questions only:

19. Annual Review of Natpara® (Parathyroid Hormone Injection) – See Appendix Q

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Natpara® (Parathyroid Hormone)
D. Prior Authorization of Natpara® (Parathyroid Hormone)
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Natpara® (Parathyroid Hormone)

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

20. FDA and DEA Updates – See Appendix R

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

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

A. Opioid Analgesics and Buprenorphine Products
B. Antidepressant Medications
C. Alzheimer's Medications
D. Anti-Ulcer Medications
E. Nasal Allergy Medications

**Future business subject to change.*

22. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF APRIL 13, 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): Not applicable		

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:		
Debbie Parent, EBSI	Brent Tabor, Merck	Aaron Shaw, BI
Shane Melton, EBSI	Sean Seago, Merck	Brian Maves, Pfizer
Greg Pappas, CSL Behring	Quynh Doan, AbbVie	Ron Schnare, Shire
Danielle Walters, Sanofi	Matthew Flores, BioRx	Sarah Hawk, OUHSC
Matt Walchle, NNI	Bobby White, UCB	Jignsen Patel, Novo Nordisk
John Cheppo, Grifols USA LLC	Angie Dale, CSL	Tyrone McBayne, Baxalta
Erk Hecht, NNI	Jeff Knappen, Allergan	Mark Kaiser, Otsuka America
Edie Dodson, Genzyme	John Dunham, Accredo	Clint Degner, Novartis
Mai Duong, Novartis	Justin Springfield, CSL	Holly Turner, Merck
Sasha Cheatham, BioRx	Courtney Walker, Novo Nordisk	Jim Chapman, AbbVie
Lynne Szott, CSL	Dana Koehn, Baxalta	Nima Nabavi, Novo Nordisk
Melivin Nwamadi, Abbott	Jim Fowler, AstraZeneca	Richard Ponder, J&J

PRESENT FOR PUBLIC COMMENT:	
Jignesh Patel	Novo Nordisk
Tyrone McBayne	Baxalta
Mai Duong	Novartis
Justin Springfield	CSL Behring
Courtney Walker	Novo Nordisk
Brian Holling	Merck
Angie Dale	CSL Behring
Sarah Hawk	OUHSC

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA NO. 10 BRIAN HOLLING
2B: AGENDA NO. 11 JIGNESH PATEL
2C: AGENDA NO. 11 TYRONE MCBAYNE
2D: AGENDA NO. 11 JUSTIN SPRINGFIELD
2E: AGENDA NO. 11 ANGIE DALE
2F: AGENDA NO. 11 SARAH HAWK
2G: AGENDA NO. 13 COURTNEY WALKER
2H: AGENDA NO. 14 MAI DUONG

ACTION: NONE REQUIRED

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

3A: MARCH 9, 2016 DUR MINUTES – VOTE
3B: MARCH 9, 2016 DUR RECOMMENDATIONS MEMORANDUM

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

ACTION: MOTION CARRIED

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

4A: MEDICATION COVERAGE ACTIVITY FOR MARCH 2016
4B: PHARMACY HELP DESK ACTIVITY FOR MARCH 2016
4C: CHRONIC MEDICATION ADHERENCE PROGRAM UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE UPTRAVI® (SELEXIPAG)

5A: INDICATION AND TREATMENT

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE CEREZYME® (IMIGLUCERASE), ELELYSO® (TALIGLUCERASE ALFA), VPRIV® (VELAGLUCERASE ALFA), CERDELGA® (ELIGLUSTAT), AND ZAVESCA® (MIGLUSTAT)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented Dr. Abbott

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE ELESTRIN® (ESTRADIOL GEL 0.06%)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE EVZIO® (NALOXONE AUTO-INJECTOR)

8A: INTRODUCTION

8B: MARKET NEWS AND UPDATES

8C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF SOONERCARE PHARMACY BENEFIT

9A: PHARMACY BENEFIT MANAGEMENT

9B: SUMMARY

9C: TRADITIONAL VERSUS SPECIALTY PHARMACY PRODUCTS

9D: TOP 10 THERAPEUTIC CLASSES BY REIMBURSEMENT

9E: TOP 10 MEDICATIONS BY REIMBURSEMENT

9F: MEDICAID DRUG REBATE PROGRAM

9G: MEDICATION PRICE INCREASES

9H: PHARMACY TREND: SPENDING PER MEMBER PER YEAR (PMPY)

9I: CONCLUSION

9J: TOP 100 REIMBURSED DRUGS BY FISCAL YEAR

9K: TOP 50 MEDICATIONS BY TOTAL NUMBER OF CLAIMS

9L: TOP TRADITIONAL THERAPEUTIC CLASSES BY FISCAL YEAR

9M: TOP SPECIALTY THERAPEUTIC CLASSES BY FISCAL YEAR

Materials included in agenda packet; presented by Dr. Holderread, Dr. Nesser

ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: 30-DAY NOTICE TO PRIOR AUTHORIZE ZEPATIER™ (ELBASVIR/GRAZOPREVIR)

10A: INTRODUCTION

10B: CURRENT PRIOR AUTHORIZATION CRITERIA

10C: MARKET NEWS AND UPDATES

10D: ZEPATIER™ (ELBASVIR/GRAZOPREVIR) PRODUCT SUMMARY

10E: REGIMEN COMPARISON
10F: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF FACTOR REPLACEMENT PRODUCTS AND 30-DAY NOTICE 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
11A: HEMOPHILIA AND OTHER RARE BLEEDING DISORDERS OVERVIEW
11B: COMPLICATIONS OF HEMOPHILIA
11C: ACQUIRED HEMOPHILIA
11D: FACTOR X DEFICIENCY
11E: FACTOR XII DEFICIENCY
11F: UTILIZATION OF FACTOR REPLACEMENT PRODUCTS
11G: PRODUCT SUMMARIES
11H: STANDARDS OF CARE FOR PHARMACY PROVIDERS FOR THE HOME USE OF FACTOR REPLACEMENT PRODUCTS FOR PATIENTS WITH BLEEDING DISORDERS
11I: RECOMMENDATIONS
11J: UTILIZATION DETAILS OF FACTOR REPLACEMENT PRODUCTS
Materials included in agenda packet; presented by Dr. Ratterman
ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF MAKENA® (HYDROXYPROGESTERONE CAPROATE) AND 30-DAY NOTICE TO PRIOR AUTHORIZE VAGINAL PROGESTERONE PRODUCTS (CRINONE® AND ENDOMETRIN®)
12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF MAKENA® (HYDROXYPROGESTERONE CAPROATE)
12C: PRIOR AUTHORIZATION OF MAKENA® (HYDROXYPROGESTERONE CAPROATE)
12D: MARKET NEWS AND UPDATES
12E: PRETERM BIRTH
12F: EXPANSION OF MAKENA® (HYDROXYPROGESTERONE CAPROATE) START WINDOW
12G: MANAGEMENT GUIDELINES FOR SHORT CERVIX
12H: ESTIMATED COST SAVINGS
12I: COLLEGE OF PHARMACY RECOMMENDATIONS
12J: UTILIZATION DETAILS OF HYDROXYPROGESTERONE AND VAGINAL PROGESTERONE
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF DIABETES MEDICATIONS AND 30-DAY NOTICE 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)
13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF DIABETES MEDICATIONS
13C: PRIOR AUTHORIZATION OF DIABETES MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: PRODUCT SUMMARIES
13F: COLLEGE OF PHARMACY RECOMMENDATIONS
13G: UTILIZATION DETAILS OF DIABETIC MEDICATIONS

13H: UTILIZATION DETAILS OF INSULIN MEDICATIONS

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ANTIHYPERTENSIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ENTRESTO™ (SACUBITRIL/VALSARTAN)

14A: UTILIZATION OF ANTIHYPERTENSIVE MEDICATIONS

14B: PRIOR AUTHORIZATION OF ANTIHYPERTENSIVE MEDICATIONS

14C: MARKET NEWS AND UPDATES

14D: ENTRESTO™ (SACUBITRIL/VALSARTAN) PRODUCT SUMMARY

14E: COLLEGE OF PHARMACY RECOMMENDATIONS

14F: UTILIZATION DETAILS OF ANTIHYPERTENSIVE MEDICATIONS

14G: CURRENT PRIOR AUTHORIZATION CRITERIA

Materials included in agenda packet; presented by Dr. Abbott

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF DIABETIC SUPPLIES

15A: CURRENT PRIOR AUTHORIZATION CRITERIA

15B: UTILIZATION OF DIABETIC SUPPLIES

15C: PRIOR AUTHORIZATION OF DIABETIC SUPPLIES

15D: MARKET NEWS AND UPDATES

15E: COLLEGE OF PHARMACY RECOMMENDATIONS

15F: UTILIZATION DETAILS OF DIABETIC SUPPLIES

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: FDA AND DEA UPDATES

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

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

NO MEETING SCHEDULED FOR MAY 2016

17A: ADHD AND NARCOLEPSY MEDICATIONS

17B: ATYPICAL ANTIPSYCHOTIC MEDICATIONS

17C: ANTHELMINTIC MEDICATIONS

17D: PROSTATE CANCER MEDICATIONS

17E: CHOLBAM® (CHOLIC ACID)

17F: NATPARA® (PARATHYROID HORMONE)

17G: VARIOUS SPECIAL FORMULATIONS

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

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: ADJOURNMENT

The meeting was adjourned at 5:46 pm

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

Memorandum

Date: April 14, 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 April 13, 2016

Recommendation 1: Chronic Medication Adherence Program Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Uptravi® (Selexipag)

MOTION CARRIED by unanimous approval.

Uptravi® (Selexipag) Tablets Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension (PAH); and
2. Member must be 18 years of age or older; and
3. Previous failed trials of at least one of each of the following categories (alone or in combination):
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    c. Adempas® (riociguat); and
    d. Orenitram™ (treprostinil); and
4. Medical supervision by a pulmonary specialist and/or cardiologist; and
5. A quantity limit of two tablets daily will apply for all strengths with an upper dose limit of 1,600mcg twice daily.

Recommendation 3: Vote to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat)

MOTION CARRIED by unanimous approval.

Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), and Vpriv® (Velaglucerase Alfa) Approval Criteria:

1. A diagnosis of symptomatic (e.g., anemia, thrombocytopenia, bone disease, splenomegaly, or hepatomegaly) Type 1 or Type 3 Gaucher disease (GD); and
2. Member's weight (kg) must be provided and have been taken within the last four weeks to ensure accurate weight based dosing; and
3. Prescriber must verify that the member will not take requested therapy concurrently with another therapy for GD.
4. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

Cerdelga® (Eliglustat) Approval Criteria:

1. An FDA approved indication of Type 1 Gaucher disease (GD1); and
2. Member is classified as one of the following as detected by an FDA-cleared test:
    a. CYP2D6 extensive metabolizers (EMs); or
    b. CYP2D6 intermediate metabolizers (IMs); or
    c. CYP2D6 poor metabolizers (PMs); and
3. Prescriber must verify that the member will not take Cerdelga® concurrently with another therapy for GD1.
4. For CYP2D6 EMs and IMs, a quantity limit of 56 capsules per 28 days will apply. For CYP2D6 PMs, a quantity limit of 28 capsules per 28 days will apply.
5. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

Zavesca® (Miglustat) Approval Criteria:

1. An FDA approved indication of mild/moderate Type 1 Gaucher disease (GD1); and
2. A patient-specific, clinically significant reason why the member cannot use one of the following enzyme replacement therapies:
    a. Cerezyme® (imiglucerase); or
    b. Elelyso® (taliglucerase alfa); or
    c. Vpriv® (velaglucerase alfa); and
3. Prescriber must verify that the member will not take Zavesca® concurrently with another therapy for GD1.
4. A quantity limit of 90 capsules per 30 days will apply.
5. Approvals will be for the duration of six months, at which time the prescriber must verify the patient is responding to the medication.

Recommendation 4: Vote to Prior Authorize Elestrin® (Estradiol Gel 0.06%)

MOTION CARRIED by unanimous approval.

Elestrin® (Estradiol Gel 0.06%) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe vasomotor symptoms due to menopause; and
2. Member must not have any contraindications for use of Elestrin®; and
3. A patient-specific, clinically significant reason why other topical estradiol formulations (e.g., Divigel®) are not appropriate for the member; and
4. Members greater than 65 years of age will generally not be approved without supporting information; and
5. Approvals will be for the duration of six months to ensure the need for continued therapy is reassessed periodically and the medication is being used for the shortest duration possible; and
6. A quantity limit of 52 grams per 30 days will apply.

Recommendation 5: Vote to Prior Authorize Evzio® (Naloxone Auto-Injector)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Evzio® (naloxone auto-injector) with the following criteria:

Evzio® (Naloxone Auto-Injector) Approval Criteria:

1. An FDA approved diagnosis of potential or risk for opioid overdose; and
2. A patient-specific, clinically significant reason why the member cannot use other formulations of naloxone.

Additionally, the College of Pharmacy recommends further education via letter or newsletter for prescribers and pharmacies who have patients utilizing high-dose opioid analgesics. Education should include the available naloxone medications reimbursable by SoonerCare and the importance of training and access to these medications.

Recommendation 6: Annual Review of SoonerCare Pharmacy Benefit

NO ACTION REQUIRED.

Recommendation 7: 30-Day Notice to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Factor Replacement Products and 30-Day Notice 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

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Makena® (Hydroxyprogesterone Caproate) and 30-Day Notice to Prior Authorize Vaginal Progesterone Products (Crinone® and Endometrin®)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Diabetes Medications and 30-Day Notice 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)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Entresto™ (Sacubitril/Valsartan)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Diabetic Supplies

NO ACTION REQUIRED.

NATIONAL HEMOPHILIA FOUNDATION

for all bleeding disorders

April 12, 2016

Nancy Nesser, Pharm D., J.D.
Pharmacy Director
Oklahoma Health Care Authority
4345 N. Lincoln Blvd.
Oklahoma City, Oklahoma 73105

RE: Drug Utilization Review Board (DUR Board) Review of Factor Replacement Products and Pharmacy Provider Standards of Care

Dear Dr. Nesser,

The National Hemophilia Foundation (NHF) is the nation's leading advocacy organization for individuals with hemophilia and related bleeding disorders. Our mission is to ensure that individuals affected by hemophilia and related bleeding disorders have timely access to quality medical care, therapies and services, regardless of financial circumstances or place of residence. We are writing in advance of your April 13th DUR Board review of factor replacement products and establishing pharmacy provider standards of care. Specifically, we ask that the state maintain the current policy of including all FDA approved clotting factor therapies on the drug formulary, thereby allowing Oklahoma beneficiaries timely access to care delivered by uniquely qualified medical and pharmacy providers.

NHF applauds the state's continued efforts to help ensure that individuals with hemophilia and related bleeding disorders covered under Oklahoma Medicaid have timely access to a range of clotting factor therapies to treat their disorder, and for providing a comprehensive explanation of the intent and recommendations for stakeholder review. We commend the state for recognizing the value of multidisciplinary care provided by the hemophilia treatment center (HTC) and acknowledging NHF's Medical and Scientific Advisory Council (MASAC) as the leading authority for advancing the standard of clinical care and issuing treatment recommendations for individuals with bleeding disorders. These efforts clearly demonstrate Oklahoma Medicaid's commitment to improving the health and well-being of the bleeding disorder community.

NHF supports the state's effort to establish standards of service for specialty pharmacy providers that are aligned with MASAC 188 in providing a multitude of consumer protections to meet the needs of this patient population.[3] The proposed standards recognize the importance of having specialty pharmacy providers uniquely qualified to supply factor replacement products, helping to ensure patients receive the level of care necessary to improve patient outcomes and reduce costs.

This therapeutic class has previously been excluded from strategies typically employed to control costs, such as establishing a preferred drug list (PDL) and step therapy edits. We recognize that

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the complexities involved in treating hemophilia and related bleeding disorders can result in high medical expenses for patients and payers. In addition, we are acutely aware that states need to balance budgets and are being forced to make difficult decisions on best to control costs. While the need to identify cost containment strategies is necessary, it is critical that such strategies not compromise continuity of care for those with complex medical conditions. Moreover, establishing a PDL contradicts MASAC recommended treatment of bleeding disorders.[1]

Hemophilia and related bleeding disorders are rare, complex genetic conditions for which there are no known cures. Individuals often experience spontaneous and prolonged internal bleeding into the joints and soft tissues. To effectively manage these disorders, patients often require life-long infusions of clotting factor therapies that replace the missing or deficient blood proteins, thus preventing debilitating and life-threatening internal bleeding. While today's therapies are safer and more effective than ever, they are also costlier than other types of medication. For example, cost of treatment for a person with severe hemophilia can reach $250,000 per year or more. Developing an inhibitor (i.e., an immune response to treatment) or other complications such as HIV/AIDS, hepatitis, chronic joint disease, or bleeding as a result of trauma or surgery can increase those costs to over $1 million.

Clotting factor therapies are biological products either derived from human blood plasma or else produced by using recombinant technology; there are no generic equivalents. Moreover, how clotting factor therapies are manufactured (i.e., recombinant or plasma-derived), purity, and half-life, among other factors, means that these therapies are neither pharmacologically nor therapeutically equivalent. Collectively, these characteristics make an individual's response and tolerability for a specific product unique. For these reasons, MASAC recommends that individuals retain access to the full range of FDA-approved clotting factor products.[1] Limiting access through the use of restrictive drug formularies such as those requiring prior authorization, PDLs, and fail first/step therapy, negatively impacts patient care and ultimately results in higher drug spends. Therefore, drug benefit designs employing these methods should be avoided, and the choice of product used by an individual should remain a decision between patient and physician.[2]

However, should the state move to using one of these strategies, we request that there be a clearly defined path to access this drug class. For example, the state could have prescribing physicians complete a short, standardized form that can be submitted electronically for approval. Due to urgency in which bleeding episodes must be treated, we ask that any prior authorization process be completed in a timely manner (with a wait no longer than 12 hours to access the drug).[3]

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[1] MASAC Document #235 (2015) Recommendation Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available at www.hemophilia.org
[2] MASAC Document #166 (2005) MASAC Resolution Regarding Preferred Drug Lists. Available at www.hemophilia.org
[3] MASAC Document #188 (2008) Recommendations Regarding Standards of Service for Pharmacy Providers of Clotting Factor Concentrates for Home Use to Patients with Bleeding Disorders. Available at www.hemophilia.org

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NATIONAL HEMOPHILIA FOUNDATION

for all bleeding disorders

On behalf of individuals in the State of Oklahoma affected by bleeding disorders, we urge you to continue the practice of allowing patient access to all FDA-approved therapies available to treat hemophilia and related bleeding disorders. Thank you for your consideration of our request. If you would like additional information or have questions, please feel free to contact Michelle Rice, Vice President, NHF Public Policy and Stakeholder Relations, at 317-517-3032 or via email at mrice@hemophilia.org.

Sincerely,

Val D. Bias
Chief Executive Officer
National Hemophilia Foundation

Marion A. Koerper MD
Medical Advisor, NHF
Vice Chair, MASAC, NHF

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Nancy Nesser
Pharmacy Director
OK Healthcare Authority
4345 N. Lincoln Blvd.
Oklahoma City, OK 73105
nancy.nesser@okhca.org

April 10th, 2016

To whom it may concern:

It is my understanding that the new drug for congestive heart failure, Entresto, is going to be reviewed later this week at the Medicaid DUR Board meeting. I am a cardiologist with a significant amount Medicaid patients and have been practicing in South Oklahoma City for almost 14 years now. I would kindly request you to give my plea ample consideration in an attempt to reduce medical care costs during these difficult times and above all improve the lives of the Medicaid patients.

My Plea: Remove the requirement for prior authorization paperwork for the use of Entresto.

Rationale:

1. Ernesto is a novel agent for patients with CHF, indicated as first line therapy and has been shown to reduce the risk of CV death and hospitalization.
2. The data from the Paradigm HF Trial was so significant that they had to stop the trial prematurely due to the magnitude of mortality benefit. This benefit was on top of the standard of care therapy. If discontinuation of the trial was done on ethical grounds, then depriving CHF patients of the drug or making it difficult for them to get the drug, should also be considered unethical.
3. The benefit was not just in mortality, but more importantly, decrease in recurrent hospitalizations for CHF. This will lead to significant reductions in medical costs for the patients on this drug.
4. In my practice, almost all of the my patients who are on Entresto have a significantly increased quality of life and have not had any further hospitalizations for CHF.

Recommendations for modifications to the approval criteria:

1. #3 is a basic requirement for all CHF patients except those who cannot tolerate or not on beta blockers for valid reasons. To actually mandate that is like you requiring us to document using aspirin before you would approve any cardiac drugs for the treatment of CAD. I feel it is just like red tape which insurance companies sometimes use if they don't want to pay for anything.
2. #4 requiring ACE inhibitors for 4 weeks prior to starting Entresto confuses me. I speculate misinterpretation of the study which had 2-4 week run-in period to check for tolerability. That 4 week pre-trial period had no effect on the primary endpoints of the study other than eliminate those who could not tolerate either the ACE or Entresto .
3. #5, #6 are basically contraindications of the drug. You could add several more to that list. It does not do anything but make it difficult to prescribe Entresto. As physicians we are mandated to follow contraindications as stated in package inserts.

Final Comments:

1. Entresto is the first of a new class of drugs in the treatment of CHF patients.
2. Entresto undoubtedly saves lives and keeps patients from hospitalizations for CHF, which in turn saves significant medical costs when used instead of ACE inhibitors.
3. CHF is one of the most common diagnosis on hospital admissions and adds to the rising costs of medical care in the US.
4. More than 20% of my practice is comprised of Medicaid patients and feel they deserve the same care as you feel your family deserves. Improving access to Entresto will change many Medicaid lives in Oklahoma.
5. I don't think my plea is unreasonable as it is my understanding that other states have lifted the requirement for prior authorization paperwork for Entresto.
6. If for some reason, you are still not convinced, I would at least make a second plea to remove the requirement for prior authorization paperwork on Entresto for cardiologists only.

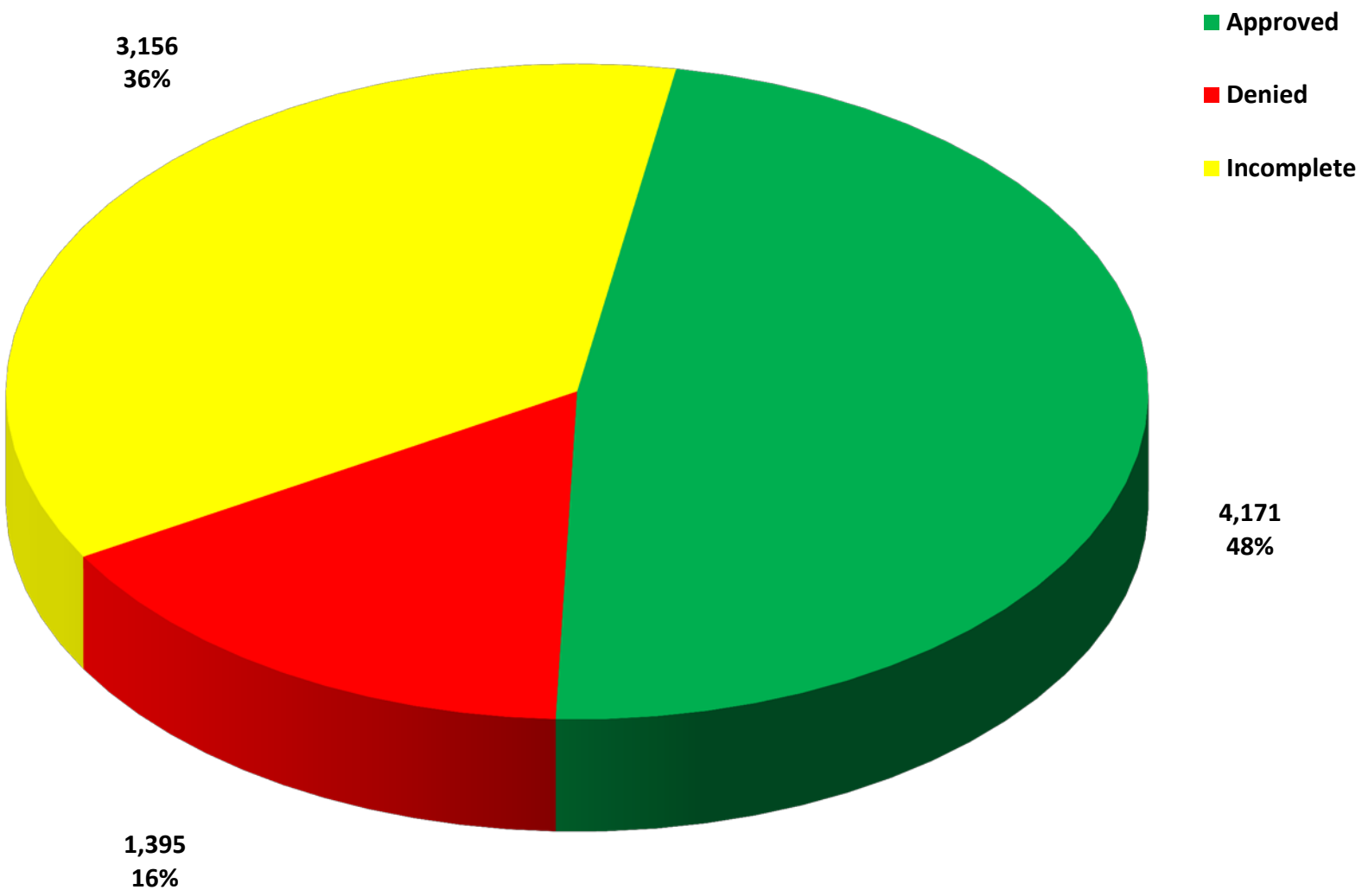
Thank you for your consideration.

Sincerely,

Riaz A Sirajuddin, MD, FSCAI
Interventional Cardiologist
Medical Director of Heart Solutions of Oklahoma
Member of the Oklahoma State Medical Board

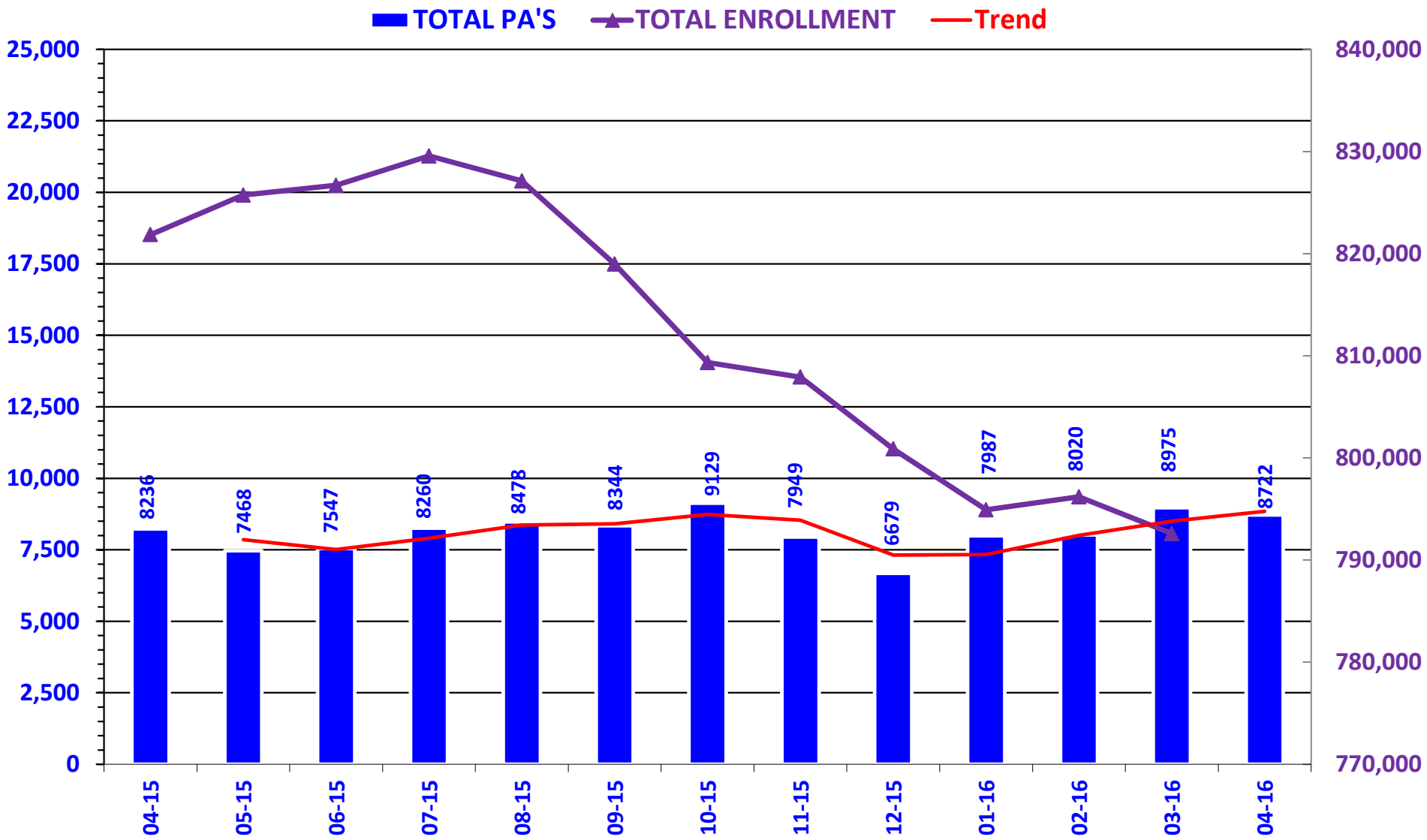
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: APRIL 2016



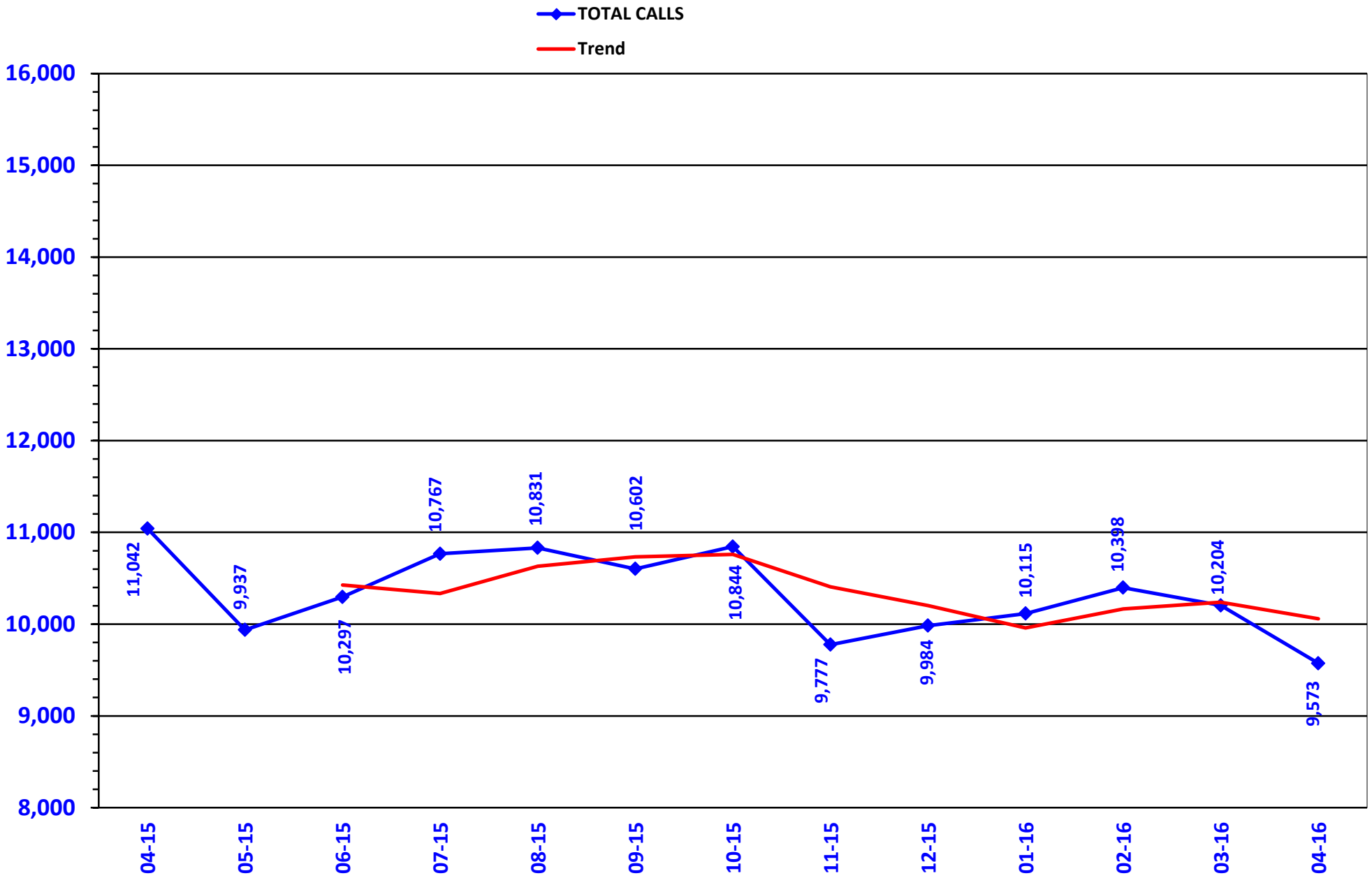
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: APRIL 2015 – APRIL 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
APRIL 2015 – APRIL 2016



Prior Authorization Activity

4/1/2016 Through 4/30/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	395	170	51	174	357
Analgesic - NonNarcotic	33	0	10	23	0
Analgesic, Narcotic	439	249	44	146	156
Angiotensin Receptor Antagonist	18	3	5	10	358
Anorectal	11	0	9	2	0
Antiasthma	90	31	16	43	315
Antibiotic	21	11	1	9	235
Anticonvulsant	57	23	12	22	303
Antidepressant	131	24	29	78	331
Antidiabetic	225	108	30	87	349
Antifungal	20	4	4	12	60
Antigout	14	6	5	3	299
Antihistamine	185	144	13	28	358
Antimigraine	42	12	9	21	217
Antineoplastic	28	14	5	9	170
Antiulcers	175	50	50	75	123
Anxiolytic	72	56	4	12	250
Atypical Antipsychotics	525	290	41	194	342
Benign Prostatic Hypertrophy	11	0	6	5	0
Biologics	126	71	17	38	300
Bladder Control	64	29	9	26	348
Blood Thinners	157	95	10	52	300
Botox	28	17	8	3	356
Calcium Channel Blockers	14	3	4	7	246
Cardiovascular	97	42	15	40	321
Cephalosporins	13	6	0	7	4
Chronic Obstructive Pulmonary Disease	92	12	25	55	359
Contraceptive	31	28	0	3	309
Corticosteroid	11	3	2	6	65
Dermatological	115	11	64	40	131
Diabetic Supplies	546	299	18	229	181
Endocrine & Metabolic Drugs	62	50	2	10	120
Erythropoietin Stimulating Agents	13	7	2	4	105
Fibromyalgia	201	34	88	79	335
Fish Oils	10	2	2	6	360
Gastrointestinal Agents	122	34	32	56	94
Growth Hormones	82	61	5	16	149
Hematopoietic Agents	74	20	16	38	25
Hepatitis C	215	116	53	46	7
HFA Rescue Inhalers	62	18	6	38	329
Insomnia	35	8	11	16	178
Insulin	58	9	22	27	359
Linzess/Amitiza/Relistor/Movantik	150	18	62	70	146
Miscellaneous Antibiotics	34	6	4	24	69
Multiple Sclerosis	63	33	11	19	184
Muscle Relaxant	66	15	22	29	73
Nasal Allergy	147	27	42	78	206
Neurological Agents	58	31	10	17	330
NSAIDs	230	28	79	123	265
Ocular Allergy	64	11	19	34	212
Ophthalmic Anti-infectives	20	3	7	10	125
Osteoporosis	20	8	6	6	346
Other*	259	55	69	135	212
Pediculicide	39	9	8	22	14
Statins	51	11	10	30	356
Stimulant	920	441	102	377	331

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

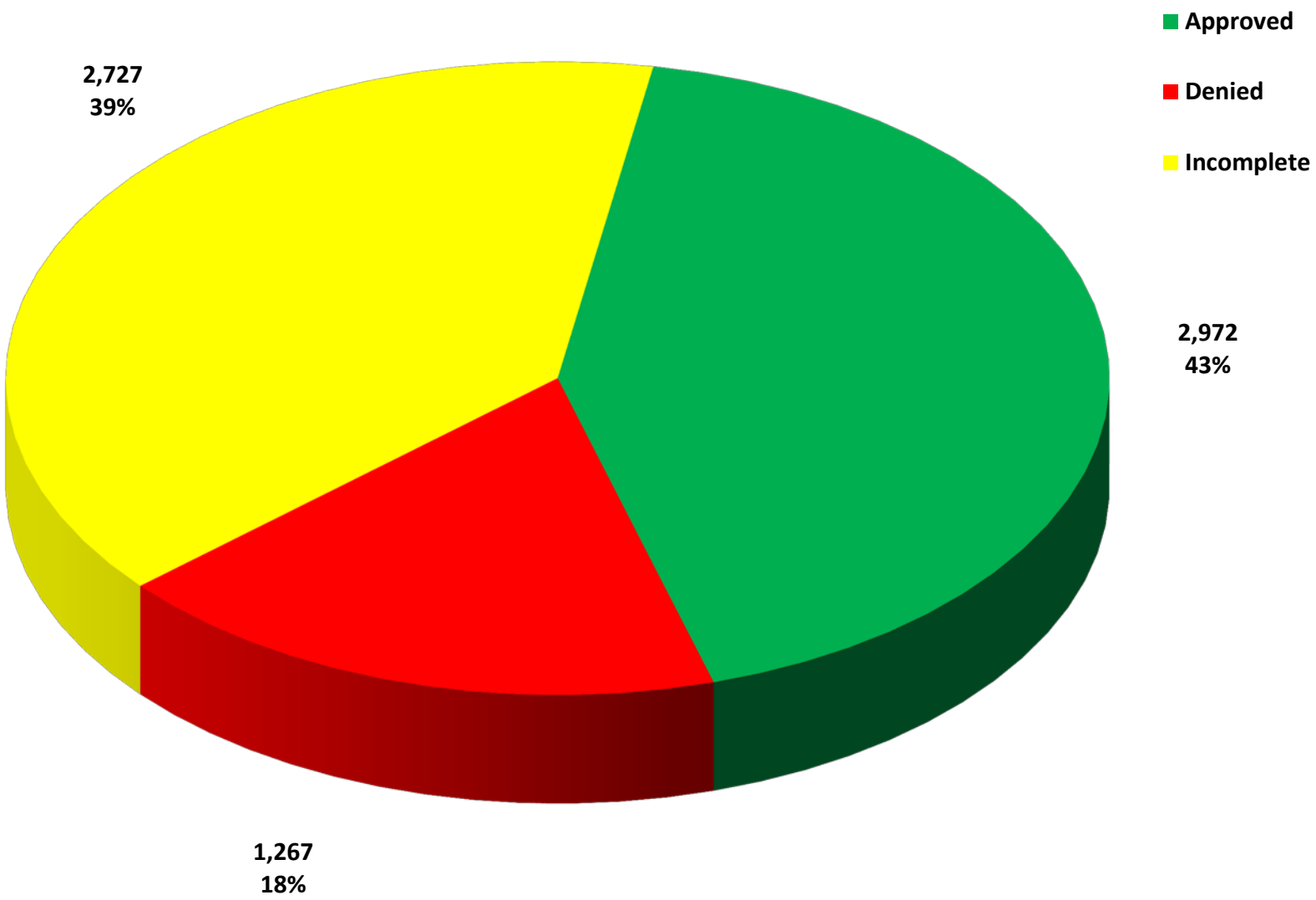
	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Suboxone/Subutex/Bunavail/Zubsolv	248	207	5	36	73
Testosterone	42	9	13	20	277
Topical Antifungal	43	1	7	35	90
Topical Corticosteroids	143	1	60	82	85
Vitamin	67	12	36	19	291
Pharmacotherapy	55	50	0	5	295
Emergency PAs	0	0	0	0	
Total	**7,439**	**3,146**	**1,327**	**2,966**	
Overrides					
Brand	51	30	9	12	281
Cumulative Early Refill	3	3	0	0	180
Diabetic Supplies	6	4	0	2	26
Dosage Change	340	322	2	16	12
High Dose	5	5	0	0	184
Ingredient Duplication	25	21	1	3	7
Lost/Broken Rx	83	71	5	7	9
NDC vs Age	31	31	0	0	255
Nursing Home Issue	65	62	1	2	10
Opioid Quantity	17	11	4	2	165
Other*	40	35	1	4	11
Quantity vs. Days Supply	600	416	45	139	251
STBS/STBSM	9	8	0	1	75
Stolen	12	11	1	0	9
Temporary Unlock	1	0	1	0	0
Third Brand Request	21	13	2	6	12
Overrides Total	**1,283**	**1,025**	**68**	**190**	
Total Regular PAs + Overrides	**8,722**	**4,171**	**1,395**	**3,156**	

Denial Reasons	
Unable to verify required trials.	2,679
Does not meet established criteria.	1,397
Lack required information to process request.	446

Other PA Activity	
Duplicate Requests	574
Letters	7,101
No Process	7
Changes to existing PAs	607
Helpdesk Initiated Prior Authorizations	755
PAs Missing Information	37

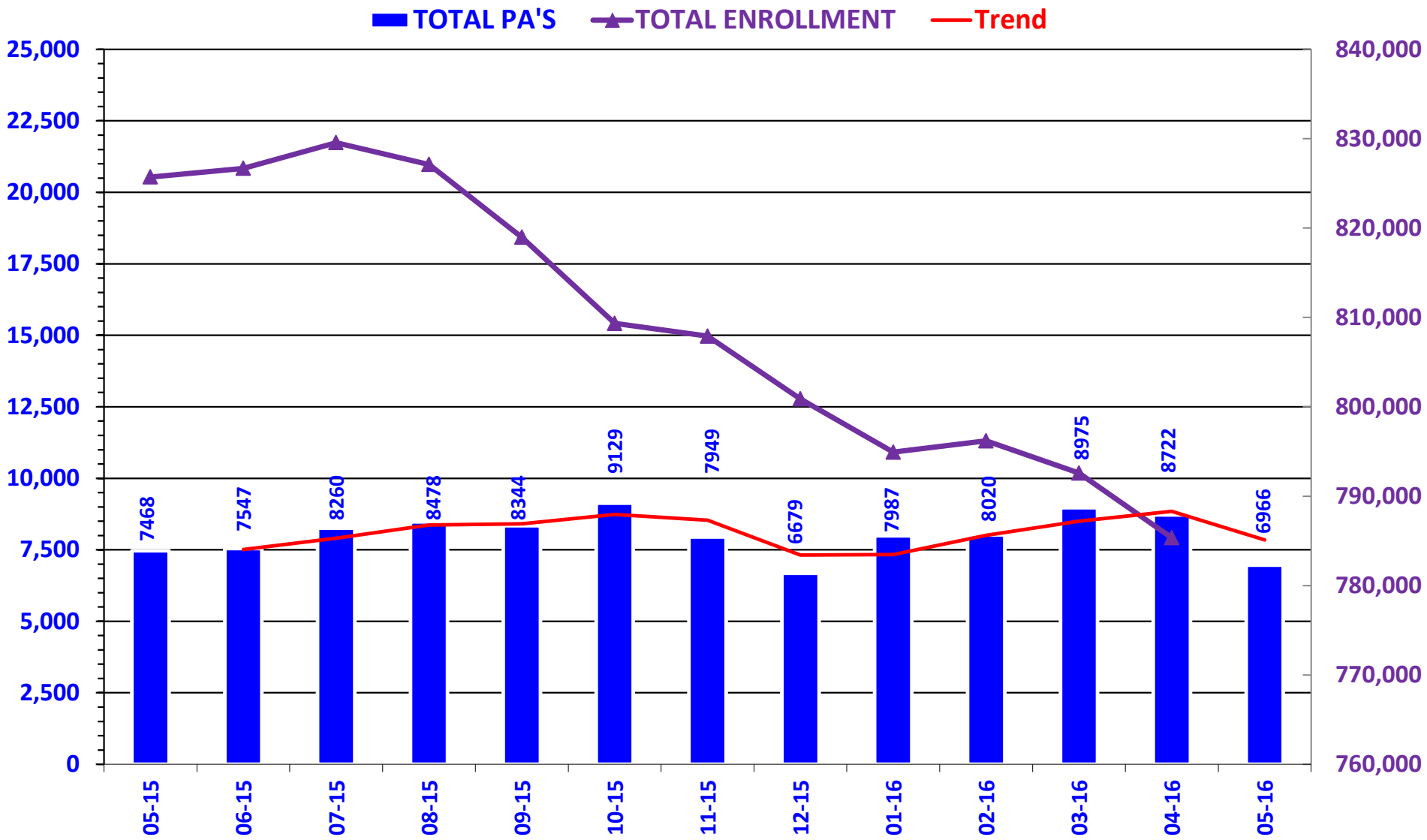
* Includes any therapeutic category with less than 10 prior authorizations for the month.

PRIOR AUTHORIZATION ACTIVITY REPORT: MAY 2016



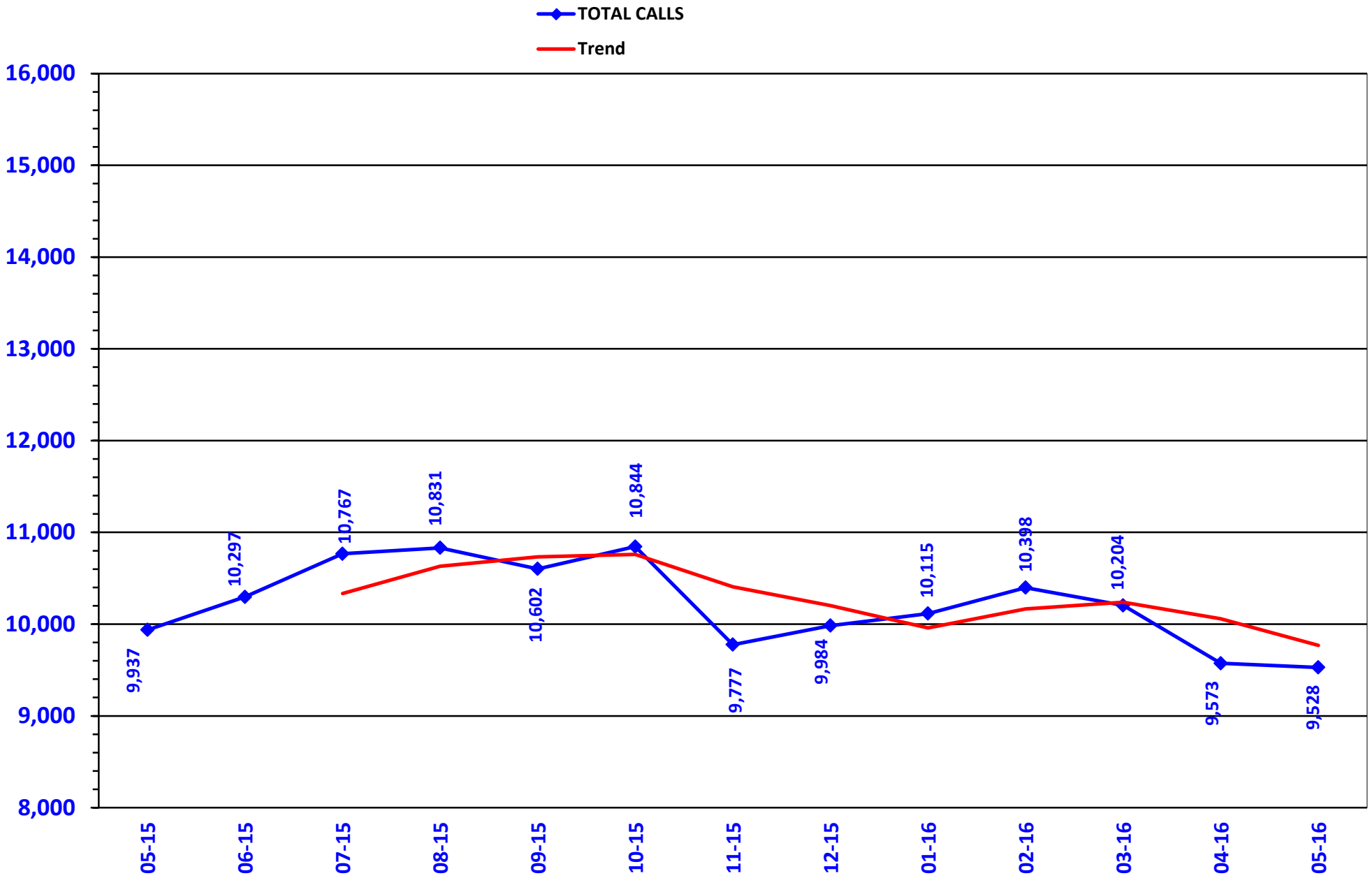
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MAY 2015 – MAY 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MAY 2015 – MAY 2016



Prior Authorization Activity

5/1/2016 Through 5/31/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	377	158	80	139	351
Analgesic - NonNarcotic	31	0	6	25	0
Analgesic, Narcotic	437	273	35	129	158
Angiotensin Receptor Antagonist	14	1	4	9	358
Antiasthma	76	25	16	35	338
Antibiotic	33	12	1	20	114
Anticoagulant	11	5	1	5	232
Anticonvulsant	83	26	17	40	319
Antidepressant	81	12	25	44	325
Antidiabetic	210	91	28	91	358
Antifungal	20	3	9	8	29
Antihistamine	220	179	14	27	356
Antimigraine	38	9	8	21	177
Antineoplastic	21	11	3	7	177
Antiplatelet	14	0	3	11	0
Antiulcers	159	39	60	60	166
Anxiolytic	72	41	6	25	221
Atypical Antipsychotics	479	267	38	174	336
Benign Prostatic Hypertrophy	11	1	7	3	360
Biologics	119	48	20	51	332
Bladder Control	80	24	19	37	343
Blood Thinners	172	116	7	49	338
Botox	36	26	6	4	344
Calcium Channel Blockers	13	1	2	10	34
Cardiovascular	69	34	9	26	289
Cephalosporins	14	6	1	7	9
Chronic Obstructive Pulmonary Disease	67	10	20	37	359
Contraceptive	18	16	0	2	308
Dermatological	81	13	45	23	128
Diabetic Supplies	577	323	24	230	224
Endocrine & Metabolic Drugs	80	59	5	16	128
Erythropoietin Stimulating Agents	23	16	2	5	102
Fibric Acid Derivatives	10	0	5	5	0
Fibromyalgia	200	25	99	76	335
Fish Oils	20	2	6	12	359
Gastrointestinal Agents	107	32	25	50	69
Genitourinary Agents	10	2	5	3	228
Growth Hormones	85	60	8	17	152
Hematopoietic Agents	59	22	14	23	110
Hepatitis C	155	86	23	46	7
HFA Rescue Inhalers	55	18	13	24	317
Insomnia	31	5	8	18	178
Insulin	60	5	23	32	358
Linzess/Amitiza/Relistor/Movantik	142	22	49	71	183
Miscellaneous Antibiotics	27	5	5	17	12
Multiple Sclerosis	52	26	6	20	185
Muscle Relaxant	59	10	22	27	63
Nasal Allergy	127	24	37	66	255
Neurological Agents	54	28	18	8	357
NSAIDs	164	24	50	90	302
Ocular Allergy	48	11	10	27	185
Ophthalmic Anti-infectives	11	3	4	4	11
Osteoporosis	25	8	7	10	335
Other*	271	47	64	160	237
Otic Antibiotic	10	3	1	6	19
Pediculicide	32	6	7	19	24

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Stimulant	742	384	84	274	320
Suboxone/Subutex/Bunavail/Zubsolv	241	184	14	43	78
Testosterone	57	18	15	24	283
Topical Antifungal	33	0	11	22	0
Topical Corticosteroids	178	3	62	113	247
Vitamin	78	16	38	24	295
Pharmacotherapy	38	34	0	4	235
Emergency PAs	0	0	0	0	
Total	**6,966**	**2,972**	**1,267**	**2,727**	
Overrides					
Brand	67	44	6	17	267
Cumulative Early Refill	3	3	0	0	180
Diabetic Supplies	2	2	0	0	54
Dosage Change	348	319	3	26	11
High Dose	6	3	0	3	250
Ingredient Duplication	28	22	0	6	11
Lost/Broken Rx	90	81	2	7	11
NDC vs Age	19	17	1	1	189
Nursing Home Issue	65	57	0	8	10
Opioid Quantity	13	11	2	0	171
Other*	31	26	1	4	13
Quantity vs. Days Supply	558	350	48	160	247
STBS/STBSM	14	13	0	1	80
Stolen	23	20	1	2	11
Temporary Unlock	1	1	0	0	28
Third	1	1	0	0	27
Third Brand Request	26	14	6	6	15
Wrong D.S. on Previous Rx	1	1	0	0	13
Overrides Total	**1,277**	**968**	**68**	**241**	
Total Regular PAs + Overrides	**8,243**	**3,940**	**1,335**	**2,968**	

Denial Reasons	
Unable to verify required trials.	2,519
Does not meet established criteria.	1,359
Lack required information to process request.	435

Other PA Activity	
Duplicate Requests	530
Letters	6,773
No Process	5
Changes to existing PAs	545
Helpdesk Initiated Prior Authorizations	709
PAs Missing Information	50

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

SoonerPsych Program Update

Oklahoma Health Care Authority
June 2016

Prescriber Mailing Summary

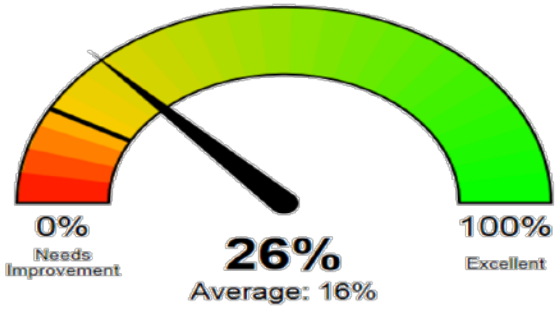
The SoonerPsych program is an educational quarterly mailing to prescribers with members on atypical antipsychotic medications. Each mailing includes a gauge showing prescribers how their prescriptions compare to those of other SoonerCare prescribers of atypical antipsychotic medications regarding potential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

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

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

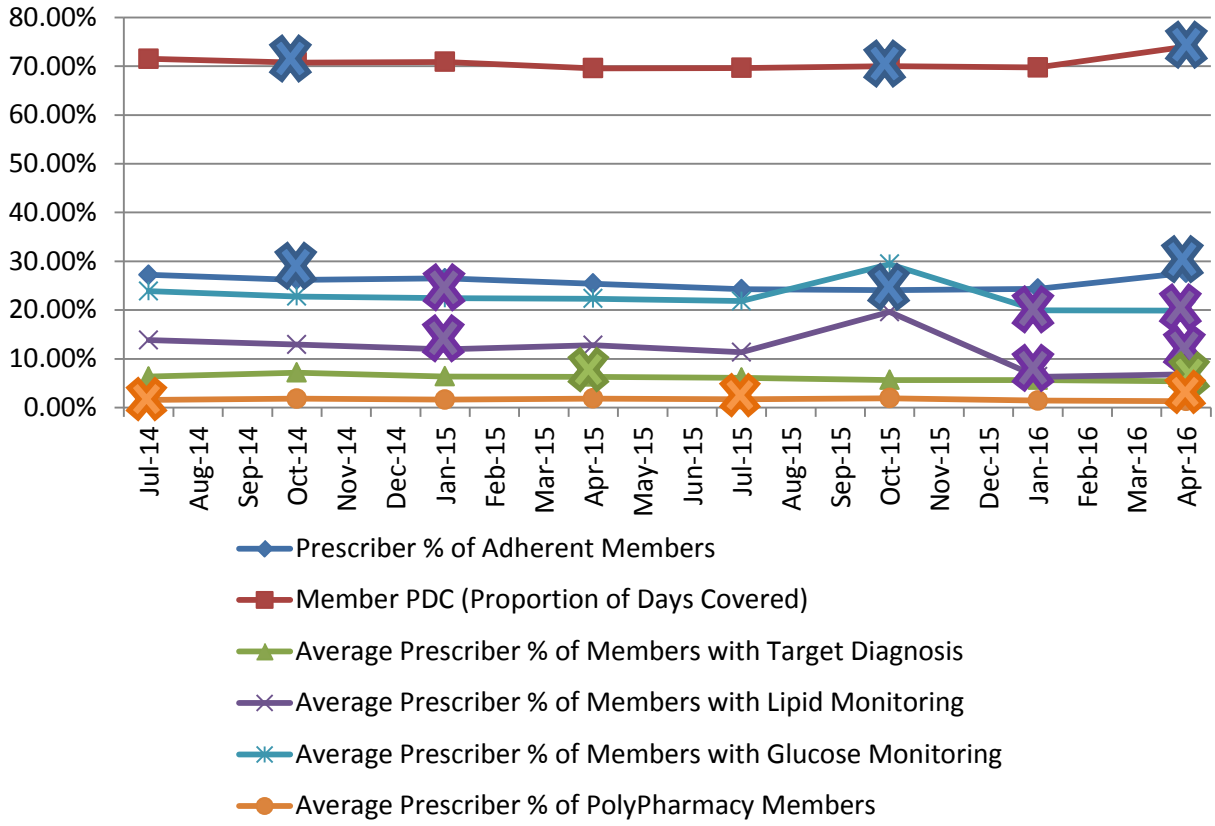
Example Gauge

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



SoonerPsych Trends: July 2014-April 2016

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



All modules were included in the April 2016 mailing. Future results of the combined mailing will be reviewed with the Drug Utilization Review (DUR) board as they become available. The list below summarizes changes in prescriber trends for each module depending on when the mailing was processed.

The prescriber percent of adherent members and the member PDC experienced a slight increase after the adherence mailing was processed in October 2014 and again in October 2015. A more substantial increase can be seen in April 2016.

The metabolic mailing was processed in January 2015 and again in January 2016. An increase was seen in the average prescriber percentage of members with lipid monitoring, however no increase was seen in the average prescriber percentage of members with glucose monitoring following the January 2015 mailing. A significant increase can be seen in both lipid and glucose monitoring as of October 2015 with a trend towards baseline in April 2016.

The diagnosis mailing was first processed in April 2014 and again in April 2015. The average prescriber percent of members with a target diagnosis increased slightly in October 2014, but has since trended towards baseline.

The polypharmacy mailing was processed in July 2014 and again in July 2015. The average prescriber percent of members with polypharmacy increased slightly in October 2014 and again in October 2015 following the polypharmacy mailings. As of April 2016 the average prescriber percent of members with polypharmacy was at an all-time low indicating fewer members are using multiple antipsychotics concomitantly.

Conclusions

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

Appendix C

Vote to Prior Authorize Zepatier™ (Elbasvir/Grazoprevir)

Oklahoma Health Care Authority
June 2016

Introduction[1]

Zepatier™ (elbasvir/grazoprevir) is a fixed-dose combination product containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor, indicated with or without ribavirin for the treatment of chronic HCV genotypes 1 or 4 infection in adults.

The recommended dosing of elbasvir/grazoprevir is one 50mg/100mg tablet by mouth once daily with or without food. The regimen and duration of therapy is dependent on host and viral factors including: genotype, prior treatment experience, and NS5A polymorphisms. The following table contains the recommended regimens and treatment durations:

Dosage Regimens for Zepatier™ in Patients With Genotype-1 or -4 HCV With or Without Cirrhosis		
Patient Population	**Treatment**	**Duration**
Genotype-1a: Treatment-naïve or PEG IFN/RBV experienced without baseline NS5A polymorphisms*	Zepatier™	12 weeks
Genotype-1a: Treatment-naïve or PEG IFN/RBV experienced with baseline NS5A polymorphisms*	Zepatier™ + RBV	16 weeks
Genotype-1b: Treatment-naïve or PEG IFN/RBV experienced	Zepatier™	12 weeks
Genotype-1a[+] or -1b: PEG IFN/RBV/PI experienced	Zepatier™ + RBV	12 weeks
Genotype-4: Treatment-naïve	Zepatier™	12 weeks
Genotype-4: PEG IFN/RBV experienced	Zepatier™ + RBV	16 weeks

*Polymorphisms at amino acid positions 28, 30, 31, or 93.
[+]The optimal elbasvir/grazoprevir-based treatment regimen and duration of therapy for PEG IFN/RBV/PI-experienced genotype-1a infected patients with baseline NS5A resistance-associated polymorphisms has not been established.
PEG IFN = Peginterferon Alfa, RBV = Ribavirin, PI = NS3/4A Protease Inhibitor
RBV dosing is weight-based, and administered orally in two divided doses with food.

Market News and Updates[2]

May 2016: Executive director of the National Association of Medicaid Directors (NAMD), Matt Salo, stated Medicaid budgets, which must be balanced each year, could find themselves in a "Death Star scenario" if states are required to cover hepatitis C treatments for all members without allowing states to set minimum criteria. Salo is also quoted as saying, "You spend an additional 5% of your program each year, which 5% do you want to cut? Who do you want to not cover because we're spending all this money here?"

NAMD sent a letter to Congress in 2014 with possible strategies for lowering the price of hepatitis C therapies. More recently in March 2016, NAMD sent a letter to the Senate Finance committee requesting Congress reconsider the matter.

Regimen Comparison[1,3,4,5,6,7,8,9]

The following table shows the current U.S. Food and Drug Administration (FDA) approved or American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) recommended regimens of direct-acting antivirals (DAAs) for the treatment of HCV infection in treatment-naïve patients with or without cirrhosis in genotypes 1 or 4. Specific regimens are used in particular patient populations depending on pre-treatment viral load, prior hepatitis C treatment experience, fibrosis stage, cirrhosis status, and baseline viral polymorphisms. Regimens marked with a star are not currently FDA approved, but are recommended by the AASLD/IDSA guidance. Most non-FDA approved regimens were studied in very small populations with limited sustained virologic response (SVR) or "cure" data. SVR rates found in clinical studies can be used as a measure of clinical efficacy for each regimen. SVR rates were obtained from studies cited in the AASLD/IDSA guidance or from an individual product's package labeling. Some SVR percentages in the following table may contain treatment-experienced patients if the study did not differentiate. Overall SVR percentages for genotypic subtypes may be reported together if the study did not differentiate.

Genotype	Host Factors	Treatment Regimen	Total Cost	SVR**
Genotype-1a	Treatment-naïve, Non-cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	98% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	$57,657.60-$77,400.96	92%-100%[+]
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	93% or 96%
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	97%
		SIM + **SOF** 12 wks	$158,780.16	95% (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	$99,605.04	92%[¥]
	Treatment-naïve, Cirrhotic	**DAC** + **SOF** 12 weeks	$155,232.00	91% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	$57,657.60-$77,400.96	92%-100%[+]
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 24 wks	$176,756.16	95%
		SIM + **SOF** +/- RBV 24 wks	$317,560.32-$318,346.56	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-92%[¥] (1a & 1b)
Genotype-1b	Treatment-naïve, Non-cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	98% (1a & 1b)
		EBR/GZR 12 wks	$57,657.60	98%
		LED/SOF 8 or 12 wks	$66,528.00-$99,792.00	98%
		PAR/RIT/OMB/DAS 12 wks	$87,984.96	100%
		SIM + **SOF** 12 wks	$158,780.16	95% (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	$99,605.04	83%[¥]
	Treatment-naïve, Cirrhotic	**DAC** + **SOF** 12 wks	$155,232.00	91% (1a & 1b)
		EBR/GZR 12 wks	$57,657.60	98%
		LED/SOF 12 wks	$99,792.00	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 12 wks	$88,378.08	100%
		SIM + **SOF** +/- RBV 24 wks	$317,560.32-$318,346.56	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-83%[¥] (1a & 1b)
Genotype-4	Treatment-naïve, Non-cirrhotic	**EBR/GZR** 12 wks	$57,657.60	97%
		LED/SOF 12 wks	$99,792.00	93%-100%
		PAR/RIT/OMB + RBV 12 wks	$81,338.88	100%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	96%[¥]
	Treatment-naïve, Cirrhotic	**EBR/GZR** 12 wks	$57,657.60	97%
		LED/SOF 12 wks	$99,792.00	93%
		***PAR/RIT/OMB** + RBV 12 wks	$81,338.88	96%-97%
		SOF + RBV + PEG IFN 12 wks	$99,605.04	79%-96%[¥]

*Not an FDA approved regimen, **SVR = Sustained virologic response 12 weeks after therapy completion in clinical studies

[¥]Percentage includes some cirrhotic and some non-cirrhotic patients. Lower percentage may include genotype-4 and both -1a and -1b subtypes.

[+]Lower percentage accounts for those with baseline RAVs and some cirrhotic patients; lower percentage shown is for 12 weeks without RBV.

Costs based on estimated acquisition cost (EAC).

Some SVR percentages may contain treatment-experienced or cirrhotic patients if the study did not differentiate.

If genotypic subtype not indicated then both GT1a and GT1b were included in the SVR results.

SIM = simeprevir SOF = sofosbuvir LED = ledipasvir PAR = paritaprevir RIT = ritonavir OMB = ombitasvir GT = genotype

DAS = dasabuvir DAC = daclatasvir EBR = elbasvir GZR = grazoprevir RBV = ribavirin PEG IFN = peginterferon alfa

RBV dosing based on >75kg patient (1,200mg).

Recommendations

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

Genotype	Patient Factors	Preferred Regimen(s)
2	Treatment-experienced, cirrhotic	Sovaldi® + RBV for 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
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.

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[2] Firth, Shannon. Medpage Today. "Covering Costly HCV Tx: Who Makes that Call". Available online at: http://www.medpagetoday.com/Gastroenterology/Hepatitis/57830?xid=nl_mpt_DHE_2016-05-11&eun=g720351d0r. Issued 05/2016. Last accessed 05/2016.

[3] American Association for the Study of Liver Diseases and Infectious Diseases Society of America HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. *Hepatol* 2015; 62(3): 932-954.

[4] Viekira Pak™ Product Information. AbbVie Inc. Available online at: http://www.rxabbvie.com/pdf/viekirapak_pi.pdf. Last revised 01/2016. Last accessed 05/2016.

[5] Harvoni® Product Information. Gilead Sciences, Inc. Available online at: www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf.last. Last revised 02/2016. Last accessed 05/2016.

[6] Olysio™ Product Information. Janssen Therapeutics, LP. Available online at: www.olysio.com/shared/product/olysio/prescribing-information.pdf. Last revised 02/2016. Last accessed 05/2016.

[7] Sovaldi™ Product Information. Gilead Sciences, Inc. Available online at: www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf. Last revised 08/2015. Last accessed 05/2016.

[8] Daklinza™ Product Information. Bristol-Myers Squibb Company. Available online at: http://packageinserts.bms.com/pi/pi_daklinza.pdf. Last revised 02/2016. Last accessed 05/2016.

[9] Technivie™ Product Information. AbbVie Inc. Available online at http://www.rxabbvie.com/pdf/technivie_pi.pdf. Last revised 01/2016. Last accessed 05/2016.

Appendix D

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

Oklahoma Health Care Authority
June 2016

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

- **Eloctate™ [antihemophilic factor (recombinant), Fc fusion protein]** was approved by the U.S. Food and Drug Administration (FDA) in June 2014 for adults and children with hemophilia A (congenital factor VIII deficiency). Eloctate™ has a prolonged half-life due to the Fc fusion protein of human immunoglobulin g1 (IgG1) which binds the neonatal Fc receptor(FcRn). The FcRn is part of a naturally occurring pathway that delays lysosomal degradation of immunoglobulins by cycling them back into circulation thereby prolonging their plasma half-life.
- **Adynovate® [antihemophilic factor (recombinant), PEGylated]** was approved by the FDA in November 2015 for adolescents (12 years and older) and adults with hemophilia A. Adynovate® exhibits an extended terminal half-life through pegylation of the parent molecule, Advate®, which reduces binding to the physiological factor VIII clearance receptor (LRP1).
- **Alprolix® [coagulation factor IX (recombinant), Fc fusion protein]** was approved by the FDA in March 2014 for adults and children with hemophilia B (factor IX deficiency). Alprolix® contains the Fc region of human IgG1, which binds to the neonatal FcRn. FcRn is part of a naturally occurring pathway that delays lysosomal degradation of immunoglobulins by cycling them back into circulation, and prolonging their plasma half-life.
- **Idelvion® [coagulation factor IX (recombinant), albumin fusion protein]** was approved by the FDA in March 2016 for children and adults with hemophilia B (congenital Factor IX deficiency). Idelvion® is comprised of genetically fused recombinant coagulation factor IX and recombinant albumin. Fusion with recombinant albumin extends the half-life of factor IX.
- **Obizur® [antihemophilic factor (recombinant), porcine sequence]** was approved by the FDA in October 2014 for adults with acquired hemophilia A (acquired factor XIII deficiency).
- **Corifact® [factor XIII concentrate (human)]** was approved by the FDA in February 2011 for adult and pediatric patients with congenital Factor XIII deficiency.

- **Tretten® [coagulation factor XIII A-subunit (recombinant)]** was approved by the FDA in December 2013 for routine prophylaxis for bleeding in patients with congenital factor XIII A-subunit deficiency.
- **Coagadex® [coagulation factor X (human)]** was approved by the FDA in October 2015 for adults and children (aged 12 years and above) with hereditary factor X deficiency.
- **Medical and Scientific Advisory Council (MASAC)** developed minimum standards of care for pharmacies providing factor products to patients with bleeding disorders for home use to ensure optimal service and quality care. When quality care is not provided, there is a potential for adverse events and an increase in costs.

Recommendations

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 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.

[1] Eloctate™ Prescribing Information. Biogen. Available online at: http://www.eloctate.com/pdfs/full-prescribing-information.pdf. Last revised 01/2016. Last accessed 04/2016.
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[3] Alprolix® Prescribing Information. Biogen. Available online at: http://www.alprolix.com/pdfs/PrescribingInformation.pdf. Last revised 02/2016. Last accessed 04/2016.
[4] Idelvion® Prescribing Information. U.S. Food and Drug Administration. Available online at: http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM489301.pdf. Last revised 03/2016. Last accessed 04/2016.
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[6] Corifact® Prescribing Information. CSL Behring. Available online at: http://labeling.cslbehring.com/PI/US/Corifact/EN/Corifact-Prescribing-Information.pdf. Last revised 01/2013. Last accessed 03/2016.
[7] Tretten® Prescribing Information. U.S. Food and Drug Administration. Available online at: http://www.novo-pi.com/tretten.pdf. Last revised 04/2014. Last accessed 03/2016.
[8] Coagadex® Prescribing Information. U.S. Food and Drug Administration. Available online at: http://www.coagadex.com/download/Coagadex_PI_10-2015.pdf. Last revised 10/2015. Last accessed 03/2016
[9] National Hemophilia Foundation. MASAC document #188. Available online at: https://www.hemophilia.org/Advocacy-Healthcare-Coverage/Payer-Education/MASAC. Issued 11/06/2008. Last accessed 03/2016.

SoonerCare
Oklahoma Health Care Authority

State of Oklahoma
Oklahoma Health Care Authority
Hemophilic Factor Replacement Dispensing

Pharmacy NPI:_____ ***Pharmacy Phone:*** _____ ***Pharmacy Fax:***_____

Pharmacy Name:_____ ***Pharmacist Name:***_____

Dispensing Information

Patient Name*	SoonerCare ID	Date Dispensed	Prescriber Name	Product	Prescribed Dose	Units per Vial	Number of Vials	Units per Dose[ŦŦ]	Type of Treatment[¥]	Proof of Delivery[+] (Y or N)

*Can be used for more than one patient

[ŦŦ] If more than 1 vial per dose please indicate vials to be given to make one dose (example: 1092 unit vial + 576 unit vial = 1668 units per dose) [¥] P=Prophylaxis, E=Episodic, B=Breakthrough, if breakthrough please specify date of last breakthrough bleed

[+] Proof of delivery should consist of member or caregiver's signature stating the product was received and should be dated

Pharmacist Signature: _____ **Date:** _____

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:

University of Oklahoma College of Pharmacy
Pharmacy Management Consultants
Product Based Prior Authorization Unit
Fax: 1-800-224-4014
Phone: 1-800-522-0114 Option 4

State of Oklahoma
Oklahoma Health Care Authority

Hemophilia and Other Rare Bleeding Disorders
Patient In-Home Assessment

Member Name: _____ ***Date of Birth:*** _____ ***Member ID#:*** _____

Pharmacy NPI: _____ ***Pharmacy Name:*** _____ ***PIC:*** _____

Pharmacy Phone: _____ ***Pharmacy Fax:*** _____

To be completed by member during yearly in-home assessment.
Please Initial after each line and sign at the bottom. Please complete all applicable blanks.

1. I agree to allow an in-home assessment on a yearly basis to verify the below items. **Initials_____**
2. I have been counseled and understand how to properly store my factor replacement product(s). **Initials_____**
3. I have been counseled and understand how to properly store the supplies that go with my factor replacement product(s). **Initials _____**
4. I have been counseled and understand how to rotate my factor stock so factor does not expire before using it. (In some patients with mild hemophilia, it may not be possi-ble to avoid factor expiring.) **Initials _____**
5. I have been taught and understand how to properly dispose of sharps and biohazard-ous materials. **Initials _____**
6. I have been instructed on how to properly dispose of a full sharps/biohazardous con-tainer and obtain a new one. **Initials _____**
7. I will use the factor exactly how my doctor instructed. **Initials_____**
8. I agree to keep a record/log of my factor infusions and send the infusion log to my doctor on a regular basis. **Initials _____**
9. I understand the benefits of being seen at a comprehensive hemophilia treatment cen-ter such as the Oklahoma Center for Bleeding and Clotting Disorders. **Initials_____**
10. I understand I may be contacted by an OHCA care management nurse to discuss my treatment. **Initials_____**
11. I understand the information given to me on the following additional topics:
    _____ **Initials _____**
    _____ **Initials _____**
    _____ **Initials _____**
    _____ **Initials _____**

I have read, understand, and agree to the above statements.
Member Signature: _____ Date: _____
Pharmacy Staff Signature: _____ Date: _____

PLEASE PROVIDE THE INFORMATION REQUESTED AND RETURN TO:

University of Oklahoma College of Pharmacy
Pharmacy Management Consultants
Product Based Prior Authorization Unit

Fax: 1-800-224-4014
Phone: 1-800-522-0114 Option 4

SoonerCare
Oklahoma Health Care Authority

Appendix E

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

Oklahoma Health Care Authority
June 2016

Introduction[1,2,3,4]

- **Makena® (hydroxyprogesterone caproate injection)** is approved by the U.S. Food and Drug Administration (FDA) to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth, and is indicated to begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation, and continue via once weekly administration until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first.
- **Vaginal progesterone** is recommended by the American College of Obstetricians and Gynecologists (ACOG) as a management option to reduce the risk of preterm birth in asymptomatic women with a short cervix identified with transvaginal ultrasonography (cervical length of 20mm or less before or at 24 weeks of gestation), singleton gestation, and no prior spontaneous preterm birth. **Crinone® (progesterone vaginal gel) and Endometrin® (progesterone vaginal insert)** are the two available vaginal progesterone products, and after taking into account federal and supplemental rebate participation, the net cost of the management of short cervix using Endometrin® is significantly less costly than using Crinone®.
- Based on fiscal year 2015 data, the Oklahoma Health Care Authority (OHCA) Finance Department has estimated the combined total annual savings in neonatal intensive care unit (NICU) costs of extending the start window for Makena® to 26 weeks, 6 days of gestation and of covering Endometrin® for pregnant women with a short cervix to be approximately $1 million. This estimated cost savings does not take into account federal or supplemental rebate participation, which could contribute to even more savings.

Recommendations

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.

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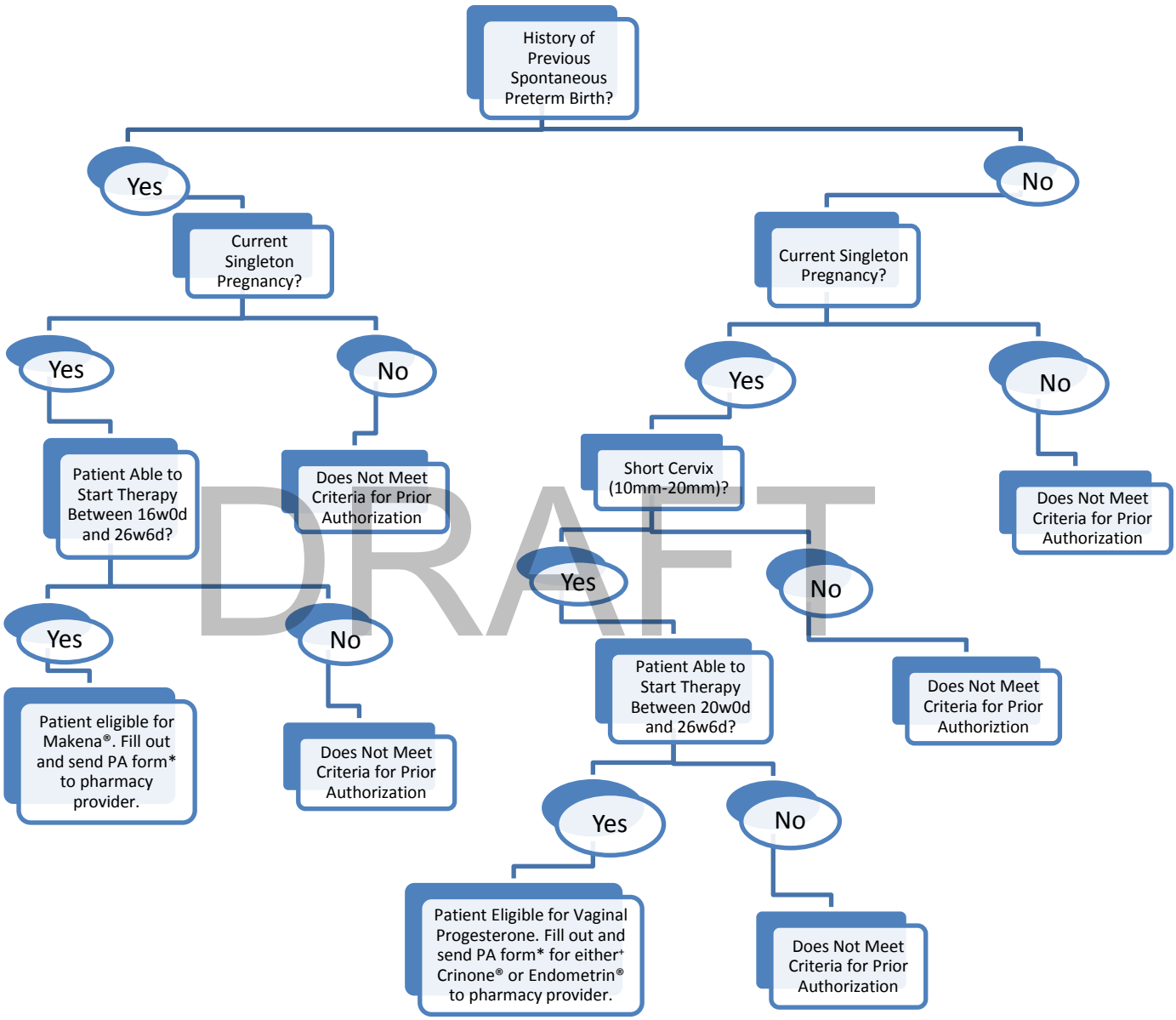
[1] Makena® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/makena/. Last revised 03/04/2016. Last accessed 03/18/2016.

[2] Practice Bulletin No. 130: Prediction and Prevention of Preterm Birth. American College of Obstetricians and Gynecologists. *Obstetrics & Gynecology,* 120(4): 964-73, October 2012.

[3] Crinone® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/crinone-2/. Last revised 11/19/2013. Last accessed 03/18/2016.

[4] Endometrin® Package Insert. Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/endometrin/. Last revised 06/16/2014. Last accessed 03/18/2016.

SoonerCare Coverage of Makena®, Crinone®, and Endometrin® for the Prevention of Spontaneous Preterm Birth



*Makena® PA form (**PHARM-23**) and Endometrin®/Crinone® PA form (**PHARM-04**) for SoonerCare can be found at www.okhca.org/forms.

+Endometrin® is the SoonerCare preferred vaginal progesterone product, authorization of Crinone® requires a patient-specific, clinically significant reason the member cannot use Endometrin®.

This information may be subject to change and is accurate as of 9/16/2015.

SoonerCare
Oklahoma Health Care Authority

SoonerCare Coverage of Progesterone Products for the Prevention of Spontaneous Preterm Birth (SPTB)

Product	SoonerCare Coverage	PA required	Prior Authorization requirements*# and Comments
Makena®	Pharmacy Benefit	Y	**1**. Documented history of previous singleton SPTB prior to 37 weeks gestation **2**. Current singleton pregnancy **3**. Gestational age at start of therapy between 16w0d and 26w6d **4.** Weekly injections via healthcare professional through 36w6d **5.** Use PA form specific for Makena (PHARM-23)
Compounded 17 alpha-hydroxprogesterone caproate	Medical Benefit (S5000)	N	In June 2012 the FDA issued a statement on compounded versions of hydroxyprogesterone caproate.[Ŧ] Also, the Oklahoma State Board of Pharmacy rules prohibit compounding medications that are essentially a copy of an available FDA approved product.
Progesterone oral	Pharmacy Benefit	N	
Progesterone vaginal gel (Crinone® only)	Pharmacy Benefit	Y	**1.** No history of previous singleton SPTB **2.** Current singleton pregnancy **3.** Gestational age at start of therapy between 20w0d and 26w6d **4.** Short Cervix (10mm-20mm) **5.** Reason why member cannot use Endometrin® **6.** Daily dosing through week 36w6d **7.** Use universal PA form (PHARM-04)
Progesterone vaginal insert (Endometrin® only)	Pharmacy Benefit	Y	**1.** No history of previous singleton SPTB **2.** Current singleton pregnancy **3.** Gestational age at start of therapy between 20w0d and 26w6d **4.** Short Cervix (10mm-20mm) **5.** Daily dosing through week 36w6d **6.** Use universal PA form (PHARM-04)
Compounded Progesterone	Pharmacy Benefit	N	The Oklahoma State Board of Pharmacy rules prohibit compounding medications that are essentially a copy of an available FDA approved product.

* PA criteria can be found in the Endocrine Therapeutic Category at www.okhca.org/pa

PA forms can be found at www.okhca.org/forms

Ŧ The FDA statement can be found at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308546.htm

This information is subject to change and is accurate as of 9/16/2015

SoonerCare
Oklahoma Health Care Authority

Appendix F

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)

Oklahoma Health Care Authority
June 2016

Indication(s)[1,2,3,4,5]

- Humalog® (insulin lispro) is a rapid-acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.
- Tresiba® (insulin degludec) is a long-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus. Tresiba® is not recommended for treating diabetic ketoacidosis.
- Ryzodeg® 70/30 mix (insulin degludec/insulin aspart) is an insulin analog indicated to improve glycemic control in adults with diabetes mellitus. Ryzodeg® is not recommended for treating diabetic ketoacidosis.
- Basaglar® (insulin glargine) is a long-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with type-1 diabetes mellitus and in adults with type-2 diabetes mellitus. Basaglar® is not recommended for treating diabetic ketoacidosis.
- Synjardy® (empagliflozin/metformin) is a combination of empagliflozin, a sodium-glucose co-transporter-2 (SGLT2) inhibitor, and metformin, a biguanide, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes mellitus who are not adequately controlled on a regimen containing empagliflozin or metformin, or in patients already being treated with both empagliflozin and metformin. Synjardy® is not for the treatment of type-1 diabetes mellitus or diabetic ketoacidosis.

Recommendations

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. An updated diabetic medications tier chart can be found on the following page.

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

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).

DPP-4 = dipeptidyl peptidase-4, GLP-1 = glucagon-like peptide-1, SGLT2 = sodium-glucose cotransporter-2

[1] Humalog® Kwikpen® Prescribing Information. Eli Lilly and Company. Available online at: http://uspl.lilly.com/humalog/humalog.html#section-1. Last revised 05/2015. Last accessed 03/2016.
[2] Tresiba® Prescribing Information. Novo Nordisk. Available online at: http://www.novo-pi.com/tresiba.pdf. Last revised 09/2015. Last accessed 03/2016.
[3] Ryzodeg® Prescribing Information. Novo Nordisk. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/203313lbl.pdf. Last revised 09/2015. Last accessed 03/2016.
[4] Basaglar® Prescribing Information. Eli Lilly and Company. Available online at: http://uspl.lilly.com/basaglar/basaglar.html#pi. Last revised 12/2015. Last accessed 03/2016.
[5] Synjardy® Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc. Available online at: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Synjardy/Synjardy.pdf. Last revised 12/2015. Last accessed 03/2016.

Appendix G

Vote to Prior Authorize Entresto™ (Sacubitril/Valsartan)

Oklahoma Health Care Authority
June 2016

Introduction[1]

Entresto™ (sacubitril/valsartan) is a combination of a neprilysin inhibitor and an angiotensin II receptor blocker indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with reduced ejection fraction (HFrEF) and chronic heart failure (NYHA Class II-IV). Entresto™ is available as an oral tablet in the following strengths: 24/26mg, 49/51mg, and 97/103mg. The recommended starting dose is 49/51mg twice daily. After two to four weeks, the dose should be doubled to the target maintenance dose of 97/103mg twice daily, as tolerated by the patient.

Cost Comparison:

Medication Name	Strength	Cost/ Tablet	Cost/ Month	Cost/ Year
Entresto™ (sacubitril/valsartan)	**24/26mg, 49/51mg, 97/103mg**	**$6.60***	**$396.00**	**$4,752.00**
enalapril	10mg	$0.35[+]	$21.00	$252.00
valsartan	160mg[◊]	$0.37[+]	$22.20	$266.40

*Cost based on estimated acquisition cost (EAC).
[+]Cost based on state maximum allowable cost (SMAC).
[◊]103mg of valsartan in Entresto™ (sacubitril/valsartan) is equivalent to 160mg of valsartan in Diovan® due to the fact that they are different salts

Market News and Updates[2]

- **May 2016:** The American College of Cardiology, the American Heart Association, and the Heart Failure Society of America published an update to the heart failure guidelines in the *Journal of the American College of Cardiology*. The updated guidelines give a "Class I" recommendation to angiotensin-converting enzyme (ACE) inhibitors, or angiotensin-receptor blockers (ARBs), or angiotensin receptor-neprilysin inhibitors (ARNI) in conjunction with evidence-based beta-blockers and aldosterone antagonists in selected patients to reduce morbidity and mortality. The societies gave ARNIs a "Class I" recommendation to replace an ACE inhibitor or ARB in selected patients with chronic symptomatic HFrEF NYHA class II or III with adequate blood pressure who are already tolerating an ACE inhibitor or an ARB.

Recommendations

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

[1]Entresto™ Product Information. Novartis Pharmaceuticals. Available online at: https://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf. Last revised 08/2015. Last accessed 03/2016.

[2] Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol.* 2016;():. doi:10.1016/j.jacc.2016.05.011.

Appendix H

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

Oklahoma Health Care Authority
June 2016

Introduction[1,2,3]

According to the National Cancer Institute, in 2016 an estimated 180,890 men will be diagnosed with prostate cancer, making prostate cancer 10.7% of all new cancer cases in the United States.[1] Prostate cancer is the second leading cause of cancer death in men. The incidence of prostate cancer is closely correlated with trends in screening practices. Prostate specific antigen (PSA) is a protein produced by cells of the prostate gland and elevations in its levels may indicate prostate cancer. PSA has been used as a screening marker for prostate cancer over the last 3 decades with its peak utilization occurring in the early 1990s and has gradually declined since that time.[1] Following the same trend, the incidence rates of prostate cancer were highest in 1992 and have slowly decreased from that date. Physicians have gone away from recommending generalized PSA screening for the average-risk male for several reasons. The main reason is that the mortality associated with prostate cancer is very low with an estimated 98% survival at 5 years. Early detection of prostate cancer can lead to overtreatment of cancers that do not impact life expectancy, which may result in unwarranted side effects, reduced quality of life, and increased cost. Prostate cancer detection and progression models estimate that 23% to 42% of all screen-detected cancers are overtreated.[2]

The most common type of prostate cancer is adenocarcinoma which accounts for 99% of tumors in the prostate.[3] Sarcomas, transitional, small and squamous cell carcinomas are rare. The treatment principles for prostate cancer have largely remained the same over the past 50 years with surgery, radiation, and androgen deprivation therapy making up the main components of therapy.[3] Androgens, the most common of which is testosterone, promote the growth of prostate cancers. Androgen deprivation therapy (ADT) involves medications that reduce the body's level of androgens or surgery to remove the testicles which ultimately can decrease and slow the growth of prostate cancers. Early stage (stage I and II localized) prostate cancer is typically treated with either surgery, radiation therapy, or active surveillance. Stage III cancer treatment often involves a combination of radiation therapy with androgen deprivation therapy and surgery. ADT is usually recommended for initial treatment of men with metastatic (stage IV) prostate cancer and it is often combined with chemotherapy. Other treatment strategies for advanced cancers include immunotherapy and radiation. Advanced prostate cancer is incurable but treatment can help to control the tumor burden for long periods of time.

Utilization of Prostate Cancer Medications: Calendar Year 2015[◊]

Comparison of Calendar Years: Prostate Cancer Medications (Pharmacy Claims)

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	6	21	$172,980.08	$8,237.15	$274.57	2,520	630
2015	3	22	$198,091.56	$9,004.16	$300.14	2,640	660
% Change	**-50.00%**	**4.80%**	**14.50%**	**9.30%**	**9.30%**	**4.80%**	**4.80%**
Change	**-3**	**1**	**$25,111.48**	**$767.01**	**$25.57**	**120**	**30**

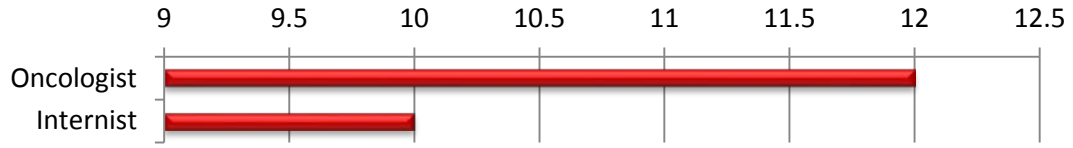
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- There were no medical claims for Zytiga® (abiraterone), Jevtana® (cabazitaxel), Xtandi® (enzalutamide), Xofigo® (radium Ra 223 dichloride), and Provenge® (sipuleucel-T) during calendar year 2015.

Demographics of Members Utilizing Prostate Cancer Medications

- Due to the small number of members utilizing prostate cancer medications during calendar year 2015, detailed demographic information could not be provided. All members were male and age 50 years or older.

Top Prescriber Specialties of Prostate Cancer Medications By Number of Claims



Market News and Updates[4]

National Comprehensive Cancer Network (NCCN) guidelines for the treatment of prostate cancer are continually updated, but the major indications are reflected in the product summaries.

The U.S. Food and Drug Administration (FDA) Orange Book indicates the following patent expiration dates for each of the products:

- Provenge® (sipuleucel-T): 2019
- Xofigo® (radium Ra 223 dichloride): January 2020
- Zytiga® (abiraterone): August 2027
- Xtandi® (enzalutamide): August 2027
- Jevtana® (cabazitaxel): October 2030

[◊] Utilization data includes Zytiga® (abiraterone) and Xtandi® (enzalutamide). Other medications included in this review did not have utilization by SoonerCare members during calendar year 2015.

Product Summaries[3]

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 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 castration-resistant prostate cancer

Xofigo® (Radium Ra 223 Dichloride)

- Radium Ra 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 castration-resistant prostate cancer (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 castration-resistant (hormone-refractory) prostate cancer

Summary of Clinical Studies[5,6,7,8,9]

Medication/ Study Participants	Dosing	Cost[+]	Study Outcomes*
Zytiga® (abiraterone) *Patients with metastatic castration-resistant prostate cancer who had received prior docetaxel chemotherapy*	1,000mg (four 250mg tablets) once daily	$9,110.40 per month	• Percentage of deaths compared to placebo (42% vs 55%) • Median survival (months) compared to placebo (14.8 vs 10.9) • p-value: <0.0001, HR: 0.646 (0.543, 0.768)
Jevtana® (cabazitaxel) *Patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen*	50mg every 3 weeks *(25mg/m^2 every 3 weeks; based on 2m^2 person)*	$33,611.85 per dose	• Percentage of deaths compared to mitoxantrone (61.9% vs 74%) • Median survival (months) compared to mitoxantrone (15.1 vs 12.7) • p-value: <0.0001, HR: 0.70 (0.59, 0.83)
Xtandi® (enzalutamide) *Patients with metastatic castration-resistant prostate cancer who had received prior docetaxel chemotherapy*	160mg (four 40mg capsules) once daily	$9,343.20 per month	• Percentage of deaths compared to placebo (38.5% vs 53.1%) • Median survival (months) compared to placebo (18.4 vs 13.6) • p-value: <0.0001, HR: 0.63 (0.53, 0.75)
Xofigo® (radium Ra 223 dichloride) *Patients with castration-resistant prostate cancer with symptomatic bone metastases (58% had received prior docetaxel chemotherapy)*	3,850kBq every 4 weeks *(55kBq/kg every 4 weeks for 6 injections; based on 70kg person; dose could be less after factoring in decay correction factor)*	$90,961.48 per dose	• Percentage of deaths compared to placebo (38.3% vs 45.9%) • Median survival (months) compared to placebo (14.0 vs 11.2) • p-value: <0.00185, HR: 0.695 (0.552, 0.875)
Provenge® (Sipuleucel-T) *Patients with hormone-refractory metastatic prostate cancer (18% had received prior chemotherapy)*	3 doses, given at 2-week intervals	$42,760.00 per dose	• Median survival (months) compared to placebo (25.8 vs 21.7) • p-value: <0.032, HR: 0.775 (0.614, 0.979)

Studies included are from package labeling for each drug.
[+]Costs based on estimated acquisition cost (EAC).
*Most of the studies compared standard of care plus placebo or the study drug.

Recommendations

Zytiga® (Abiraterone) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer; and
2. Zytiga® 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. Jevtana® 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 Ra 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 Xofigo® 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.

Utilization Details of Prostate Cancer Medications: Calendar Year 2015

Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ABIRATERONE PRODUCTS					
ZYTIGA TAB 250MG	6	1	$50,674.92	6	$8,445.82
SUBTOTAL	**6**	**1**	**$50,674.92**	**6**	**$8,445.82**
ENZALUTAMIDE PRODUCTS					
XTANDI CAP 40MG	16	3	$147,416.64	5.33	$9,213.54
SUBTOTAL	**16**	**3**	**$147,416.64**	**5.33**	**$9,213.54**
TOTAL	**22**	**3***	**$198,091.56**	**7.33**	**$9,004.16**

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

[1] National Cancer Institute. SEER Cancer Statistics. Available online at: http://www.cancer.gov/about-cancer/what-is-cancer/statistics. Accessed 05/16/2016.
[2] Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. *J Natl Cancer Inst*. 2009 Mar 18; 101(6):374-83.
[3] NCCN. *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.
[4] 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 04/22/2016. Accessed 05/16/2016.
[5] Zytiga® Product Information. Janssen Biotech Inc. Available online at: https://www.zytigahcp.com/shared/product/zytiga/zytiga-prescribing-information.pdf. Last revised 05/2016. Last accessed 05/2016.
[6] Jevtana® Product Information. Sanofi Oncology. Available online at: http://products.sanofi.us/jevtana/jevtana.html. Last revised 06/2015. Last accessed 05/2016.
[7] Xtandi® Product Information. Astellas Pharma US, Inc. Available online at: https://www.astellas.us/docs/us/12A005-ENZ-WPI.pdf?v=1. Last revised 10/2015. Last accessed 05/2016.
[8] Xofigo® Product Information. Bayer HealthCare Pharmaceuticals Inc. Available online at: http://labeling.bayerhealthcare.com/html/products/pi/Xofigo_PI.pdf. Last revised 03/2016. Last accessed 05/2016.
[9] Provenge® Product Information. Dendreon Corporation. Available online at: http://www.provenge.com/pdf/prescribing-information.pdf. Last revised 10/2014. Last accessed 05/2016.

Appendix I

Calendar Year 2015 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)

Oklahoma Health Care Authority
June 2016

Current Prior Authorization Criteria

ADHD & Narcolepsy Medications Tier-2 Approval Criteria:

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

ADHD & Narcolepsy Medications Tier-3 Approval Criteria:

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

ADHD & Narcolepsy Medications Special Prior Authorization Approval Criteria:

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

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior authorization is required for all tiers for members greater than 20 years of age and for members 0 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 a diagnosis of weight loss. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
    e. A quantity limit of 30 capsules per 30 days will apply; and
    f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

ADHD & Narcolepsy Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			Daytrana™ (methylphenidate ER) Desoxyn® (methamphetamine) Dexedrine® (dextroamphetamine) Dexedrine Spansules® (dextroamphetamine ER) Evekeo™ (amphetamine) Methylin® (methylphenidate soln & chew tabs) Nuvigil® (armodafinil) Provigil® (modafinil) 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
Soln = Solution

Utilization of ADHD & Narcolepsy Medications: Calendar Year 2015

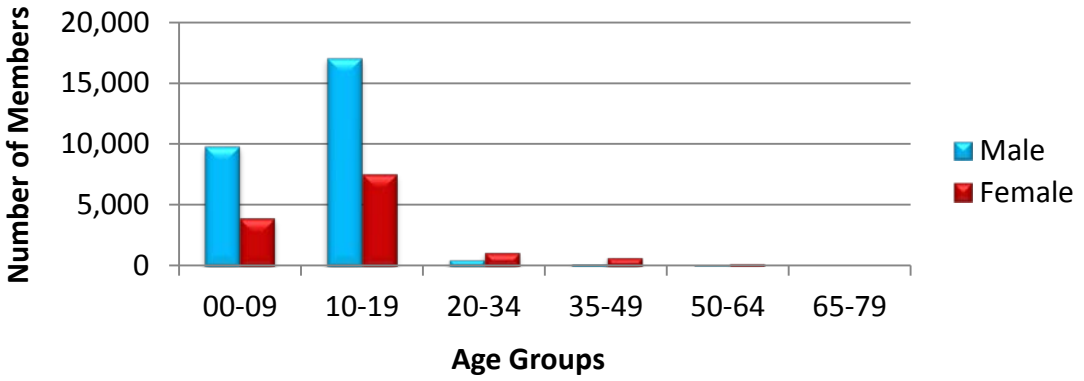
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	40,444	328,070	$60,142,831.16	$183.32	$6.17	11,469,956	9,753,093
2015	41,236	333,974	$61,156,523.18	$183.12	$6.16	11,781,872	9,925,777
% Change	**2.00%**	**1.80%**	**1.70%**	**-0.10%**	**-0.20%**	**2.70%**	**1.80%**
Change	**792**	**5,904**	**$1,013,692.02**	**-$0.20**	**-$0.01**	**311,916**	**172,684**

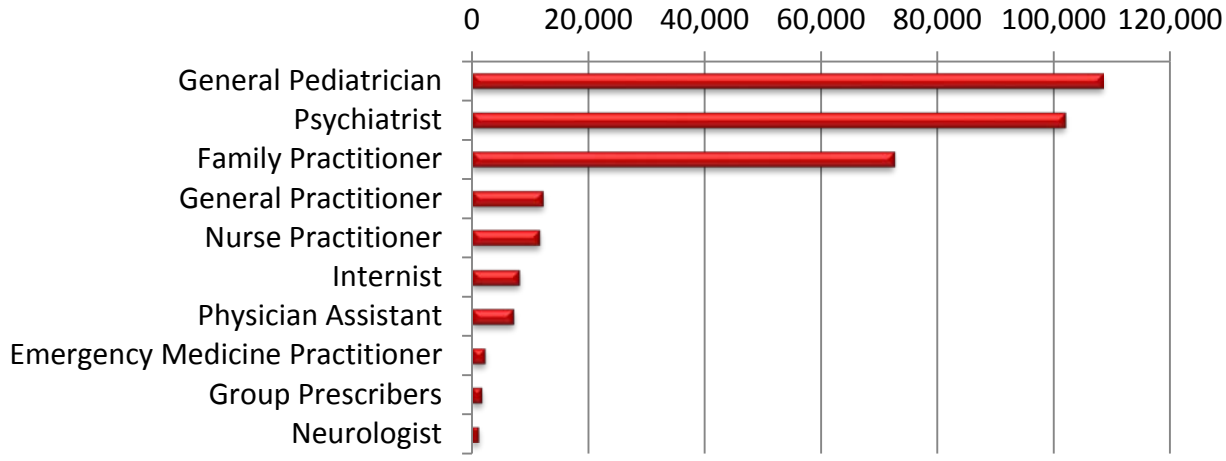
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Aggregate drug rebates collected during calendar year 2015 for ADHD and narcolepsy medications: $43,937,564.80[1]

Demographics of Members Utilizing ADHD & Narcolepsy Medications



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

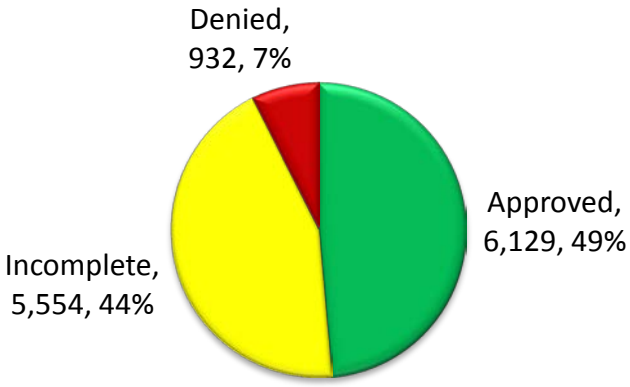


[1] Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed. Claims data includes Indian Health Service providers; aggregated drug rebates do not.

Prior Authorization of ADHD & Narcolepsy Medications

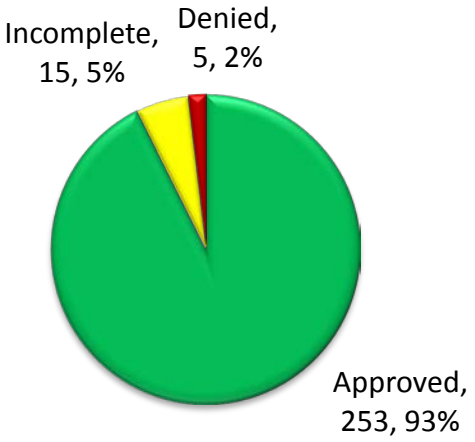
There were 12,615 prior authorization requests submitted for ADHD & narcolepsy medications during calendar year 2015. Computer edits are in place to detect Tier-1 medications in the member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



There were 273 prior authorization requests submitted for a total of 221 unique members for ADHD & narcolepsy medications during calendar year 2015 that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations



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

Anticipated Patent Expirations:

- Strattera® (atomoxetine capsules): May 2017
- Focalin XR® (dexmethylphenidate ER capsules): November 2019
- Aptensio XR™ (methylphenidate ER capsules): December 2019
- Vyvanse® (lisdexamfetamine capsules): February 2023

- Nuvigil® (armodafinil tablets): June 2024
- Daytrana™ (methylphenidate ER patches): October 2025
- Quillivant XR® (methylphenidate ER suspension): February 2031
- Xyrem® (sodium oxybate solution): March 2033

New FDA Approvals:

- **October 2015:** The U.S. Food and Drug Administration (FDA) approved Dyanavel™ XR (amphetamine ER) for the treatment of ADHD in pediatric patients 6 to 17 years of age. With this approval, Dyanavel™ XR becomes the only once-daily, extended-release amphetamine oral suspension approved for the treatment of ADHD.
- **December 2015:** The FDA approved QuilliChew ER™ (methylphenidate ER) for the treatment of ADHD in patients six years of age and older. With this approval, QuilliChew ER™ becomes the first and only once-daily, extended-release chewable methylphenidate tablet approved for the treatment of ADHD.
- **January 2016:** The FDA approved Adzenys XR-ODT™ (amphetamine ER) for the treatment of ADHD in patients six years of age and older. With this approval, Adzenys XR-ODT™ becomes the first and only once-daily, extended-release orally disintegrating tablet (ODT) approved for the treatment of ADHD.

Medications in the Pipeline:

- **Proprietary Drug Delivery Platform:** Highland Therapeutics has developed a novel oral, once-daily, drug delivery technology, Delexis®, which allows drugs to be dosed at night, targeting the onset of action prior to awakening. Two Phase 3 studies for a novel formulation of methylphenidate (Benjorna™, formally HLD-200) based on Delexis® technology for the treatment of ADHD were initiated in 2015 with data results expected in early 2016. Submission of a New Drug Application (NDA) for Benjorna™ to the FDA is expected in mid-2016. Additionally, a Phase 3 study for a novel formulation of amphetamine (HLD-900) based on Delexis® technology for the treatment of binge eating disorder (BED) is planned in 2016.
- **Methylphenidate Product:** Neos Therapeutics received a Complete Response Letter (CRL) from the FDA in November 2015 regarding the NDA for Cotempla XR-ODT™ (methylphenidate extended-release ODT), citing unspecified deficiencies that preclude discussion of labeling and post-marketing requirements/commitments. Neos Therapeutics remains committed to Cotempla XR-ODT™ and plans to work closely with the FDA to address the deficiencies identified in the CRL.

News:

- **Quillivant XR® Study in Children with ADHD and Autism:** A clinical study to determine whether low to moderate doses of Quillivant XR® are effective in the treatment of ADHD in children (ages 6 to 16 years) with ADHD and Autism Spectrum Disorder (ASD) is currently ongoing and is being conducted through Seattle Children's Hospital in collaboration with Pfizer. The study is anticipated to be completed in December 2016.

Dyanavel™ XR (Amphetamine Extended-Release) Product Summary[11,12]

Indications: Dyanavel™ XR (amphetamine ER) is indicated for the treatment of ADHD in pediatric patients 6 to 17 years of age.

Dosing:

- Dyanavel™ XR is available as an extended-release, bubblegum-flavored oral suspension that contains 2.5mg amphetamine base per milliliter (2.5mg/mL). The ratio of extended-release components to immediate-release components is unknown.
- Dyanavel™ XR should be administered orally once daily in the morning with or without food. The dose should be individualized according to the needs and responses of the patient.
- The recommended starting dose of Dyanavel™ XR is 2.5mg or 5mg once daily in the morning. The dose may be increased in increments of 2.5mg to 10mg per day every four to seven days up to a maximum dose of 20mg per day.
- If switching from other amphetamine products, treatment with the other product should be discontinued, and the patient should be titrated with Dyanavel™ XR using the recommended dosing and titration schedule (*see above*). Dyanavel™ XR should not be substituted for other amphetamine products on a milligram-per-milligram basis, due to different amphetamine base compositions and differing pharmacokinetic profiles.
- The safety and effectiveness of Dyanavel™ XR in pediatric patients younger than six years of age with ADHD have not been established.
- Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of Dyanavel™ XR, and adjust the dosage as needed.

Estimated Acquisition Cost: The estimated acquisition cost (EAC) of Dyanavel™ XR is $2.08/mL, which results in a monthly cost of $499.20, based on the maximum dose of 20mg per day (8mL per day).

QuilliChew ER™ (Methylphenidate Extended-Release) Product Summary[13,14]

Indications: QuilliChew ER™ (methylphenidate ER) is indicated for the treatment of ADHD. QuilliChew ER™ was studied in patients 6 to 12 years of age.

Dosing:

- QuilliChew ER™ is available as 20mg, 30mg, and 40mg methylphenidate extended-release, cherry-flavored chewable tablets.
- QuilliChew ER™ should be administered orally once daily in the morning with or without food. The dose should be individualized according to the treatment needs and responses of the patient.
- The recommended starting dose of QuilliChew ER™ is 20mg once daily in the morning. The dose may be titrated up or down weekly in increments of 10mg, 15mg, or 20mg. The 10mg and 15mg doses can be achieved by breaking in half the functionally scored 20mg and 30mg tablets, respectively. Daily doses above 60mg have not been studied and are not recommended.

- If switching from other methylphenidate products, treatment with the other product should be discontinued, and the patient should be titrated with QuilliChew ER™ using the recommended dosing and titration schedule (*see above*). QuilliChew ER™ should not be substituted for other methylphenidate products on a milligram-per-milligram basis, due to different methylphenidate base compositions and differing pharmacokinetic profiles.
- The safety and effectiveness of QuilliChew ER™ in pediatric patients younger than six years of age have not been evaluated.
- Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of QuilliChew ER™, and adjust the dosage as needed.

Estimated Acquisition Cost: The EAC of QuilliChew ER™ is $9.50 per tablet, regardless of strength, which results in a monthly cost of $570.00, based on the maximum dose of 60mg per day (two 30mg tablets per day).

Adzenys XR-ODT™ (Amphetamine Extended-Release) Product Summary[15,16]

Indications: Adzenys XR-ODT™ (amphetamine ER) is indicated for the treatment of ADHD in patients 6 years of age and older.

Dosing:

- Adzenys XR-ODT™ is available as 3.1mg, 6.3mg, 9.4mg, 12.5mg, 15.7mg, and 18.8mg amphetamine extended-release, orange-flavored orally disintegrating tablets (ODTs).
- Adzenys XR-ODT™ should be administered orally once daily with or without food. The entire ODT should be placed on the tongue and allowed to disintegrate without chewing or crushing, and then swallowed. The dose should be individualized according to the therapeutic needs and response of the patient.
- The recommended starting dose of Adzenys XR-ODT™ for pediatric patients is 6.3mg once daily in the morning. The dose may be increased in increments of 3.1mg or 6.3mg at weekly intervals. The maximum recommended dose is 18.8mg per day for patients 6 to 12 years of age, and 12.5mg per day for patients 13 to 17 years of age.
- The recommended dose of Adzenys XR-ODT™ for adults is 12.5mg once daily.
- The safety and effectiveness of Adzenys XR-ODT™ in pediatric patients younger than six years of age with ADHD have not been established.
- Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of Adzenys XR-ODT™, and adjust the dosage as needed.
- If switching from any other amphetamine products (except for Adderall XR®), treatment with the other product should be discontinued, and the patient should be titrated with Adzenys XR-ODT™ using the recommended dosing and titration schedule (*see above*). Adzenys XR-ODT™ should not be substituted for other amphetamine products on a milligram-per-milligram basis, due to different amphetamine base compositions and differing pharmacokinetic profiles.

- Patients taking Adderall XR® may be switched to Adzenys XR-ODT™ at the equivalent dose taken once daily (*see following table for equivalent doses of Adzenys XR-ODT™ and Adderall XR®).*

Equivalent Doses of Adzenys XR-ODT™ and Adderall XR®						
Adzenys XR-ODT™	3.1mg	6.3mg	9.4mg	12.5mg	15.7mg	18.8mg
Adderall XR®	5mg	10mg	15mg	20mg	25mg	30mg

Estimated Acquisition Cost: The EAC of Adzenys XR-ODT™ is $9.50 per ODT, regardless of strength, which results in a monthly cost of $285.00, based on once daily dosing.

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 PA category based on estimated acquisition cost.
    a. The existing criteria for methylphenidate 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.
2. Place QuilliChew ER™ (methylphenidate ER) into the Special PA category based on estimated acquisition cost.
    a. The existing criteria for other methylphenidate 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.
3. Place Adzenys XR-ODT™ (amphetamine ER) into the Special PA category based on estimated acquisition cost.
    a. The existing criteria for methylphenidate products in the Special PA category will apply.
    b. A quantity limit of 30 ODTs per 30 days will apply.

ADHD & Narcolepsy Medications Tier-2 Approval Criteria:

1. A covered diagnosis; and
2. A trial with at least one long-acting Tier-1 stimulant:
    a. Trials should have been within the last 180 days; and

b. Trials should have been dosed up to maximum recommended dose or documented adverse effects at higher doses should be included; and
c. If trials are not in member's claim history, the pharmacy profile should be submitted or detailed information regarding dates and doses should be included along with the signature from the physician.

ADHD & Narcolepsy Medications Tier-3 Approval Criteria:

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

ADHD & Narcolepsy Medications Special Prior Authorization Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, 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.
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 recent trials with Tier-1 and Tier-2 stimulants from different chemical categories, and trials with both Provigil® and Nuvigil® within the past six months, unless contraindicated, that did not yield adequate results.
d. The diagnosis of obstructive sleep apnea requires concurrent treatment for the obstructive sleep apnea.
e. The diagnosis of shift work sleep disorder requires the member's work schedule to be included with the prior authorization request.

ADHD & Narcolepsy Medications Additional Criteria:

1. Doses exceeding 1.5 times the FDA maximum are not covered.
2. Prior Authorization is required for all tiers for members greater than 20 years of age and for members 0 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 a diagnosis of weight loss. The safety and effectiveness of Vyvanse® for the treatment of obesity have not been established; and
    e. A quantity limit of 30 capsules per 30 days will apply; and
    f. Initial approvals will be for the duration of three months. Continued authorization will require prescriber documentation of improved response/effectiveness of Vyvanse®.

ADHD & Narcolepsy Medications			
Tier-1*	**Tier-2***	**Tier-3***	**Special PA**
Amphetamine			**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, Soln = Solution, Susp = Suspension

Utilization Details of ADHD & Narcolepsy Medications: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
LISDEXAMFETAMINE PRODUCTS						
VYVANSE CAP 30MG	22,868	6,328	$5,092,221.38	$7.50	$222.68	8.33%
VYVANSE CAP 20MG	16,802	5,468	$3,711,616.64	$7.48	$220.90	6.07%
VYVANSE CAP 40MG	16,141	4,092	$3,602,733.14	$7.51	$223.20	5.89%
VYVANSE CAP 50MG	11,544	2,693	$2,574,543.51	$7.49	$223.02	4.21%
VYVANSE CAP 70MG	7,762	1,296	$1,728,953.30	$7.46	$222.75	2.83%
VYVANSE CAP 60MG	7,013	1,463	$1,539,554.20	$7.39	$219.53	2.52%
VYVANSE CAP 10MG	2,552	1,386	$565,989.77	$7.63	$221.78	0.93%
SUBTOTAL	**84,682**	**22,726**	**$18,815,611.94**	**$7.49**	**$222.19**	**30.77%**
METHYLPHENIDATE PRODUCTS						
METHYLPHENID TAB 10MG	9,963	2,445	$341,822.23	$1.15	$34.31	0.56%
METHYLPHENID TAB 36MG	8,867	1,736	$2,040,378.67	$7.71	$230.11	3.34%
METHYLPHENID TAB 5MG	7,720	2,271	$211,321.71	$0.92	$27.37	0.35%
METHYLPHENID TAB 54MG	7,601	1,403	$1,435,240.54	$6.31	$188.82	2.35%
METADATE CD CAP 20MG	6,202	2,134	$1,323,419.05	$7.23	$213.39	2.16%
METHYLPHENID TAB 36MG	4,978	1,087	$1,111,182.53	$7.46	$223.22	1.82%
METHYLPHENID TAB 54MG	4,809	894	$875,738.63	$6.10	$182.10	1.43%
METADATE CD CAP 30MG	4,632	1,429	$985,711.91	$7.20	$212.80	1.61%
METHYLPHENID TAB 27MG	3,930	841	$650,737.39	$5.55	$165.58	1.06%
METHYLPHENID TAB 20MG	3,897	808	$226,296.04	$1.94	$58.07	0.37%
METADATE CD CAP 10MG	3,377	1,386	$715,949.89	$7.22	$212.01	1.17%
METADATE CD CAP 40MG	2,892	807	$837,492.12	$9.75	$289.59	1.37%
METHYLPHENID TAB 18MG	2,468	551	$424,723.11	$5.77	$172.09	0.69%
METHYLPHENID TAB 20MG	2,416	711	$428,772.19	$5.96	$177.47	0.70%
METHYLPHENID TAB 27MG	1,490	423	$244,276.22	$5.48	$163.94	0.40%
METADATE CD CAP 60MG	1,007	226	$346,498.34	$11.53	$344.09	0.57%
METADATE CD CAP 50MG	986	271	$345,636.37	$11.85	$350.54	0.57%
METHYLPHENID TAB 18MG	852	226	$133,948.05	$5.25	$157.22	0.22%
METHYLPHENID TAB 10MG	701	281	$94,389.33	$4.45	$134.65	0.15%
METHYLPHENID SOL 5MG/5ML	484	129	$111,704.41	$7.82	$230.79	0.18%
DAYTRANA DIS 30MG/9HR	475	79	$121,302.49	$8.51	$255.37	0.20%
METADATE TAB 20MG ER	444	157	$31,762.28	$2.39	$71.54	0.05%
RITALIN LA CAP 30MG	301	76	$76,094.46	$8.47	$252.81	0.12%
RITALIN LA CAP 20MG	292	86	$64,212.19	$7.45	$219.90	0.10%
QUILLIVANT SUS 25MG/5ML	278	49	$74,472.32	$8.54	$267.89	0.12%
METHYLPHENID SOL	278	69	$83,498.93	$9.83	$300.36	0.14%
RITALIN LA CAP 40MG	248	54	$58,031.41	$7.83	$234.00	0.09%
DAYTRANA DIS 20MG/9HR	232	59	$68,342.86	$9.82	$294.58	0.11%
DAYTRANA DIS 15MG/9HR	206	48	$59,791.30	$9.67	$290.25	0.10%
DAYTRANA DIS 10MG/9HR	145	43	$40,857.16	$9.39	$281.77	0.07%
RITALIN LA CAP 10MG	102	38	$21,694.86	$7.11	$212.69	0.04%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
METHYLPHENID TAB 20MG	87	56	$5,590.52	$2.16	$64.26	0.01%
METHYLPHENID CAP 40MG	46	7	$5,507.89	$3.99	$119.74	0.01%
CONCERTA TAB 36MG	32	5	$7,153.15	$7.45	$223.54	0.01%
CONCERTA TAB 54MG	26	3	$5,791.11	$7.42	$222.74	0.01%
RITALIN TAB 20MG	24	7	$2,434.37	$3.61	$101.43	0.00%
METHYLPHENID CAP 30MG	23	6	$3,268.67	$4.74	$142.12	0.01%
METHLPHENIDA CHW 2.5MG	20	13	$2,023.86	$3.46	$101.19	0.00%
METHYLPHENID CHW 5MG	18	13	$2,976.45	$5.47	$165.36	0.00%
METHYLPHENID CHW 10MG	16	6	$5,706.25	$11.91	$356.64	0.01%
RITALIN TAB 10MG	14	10	$608.14	$1.50	$43.44	0.00%
METHYLPHENID CAP 20MG	12	4	$1,680.07	$4.67	$140.01	0.00%
METHYLIN SOL 10MG/5ML	12	5	$3,273.40	$9.63	$272.78	0.01%
METHYLPHENID CAP 20MG	10	5	$3,396.21	$12.44	$339.62	0.01%
METHYLPHENID CAP 30MG	10	5	$1,450.94	$4.84	$145.09	0.00%
METHYLIN SOL 5MG/5ML	9	7	$3,869.04	$13.20	$429.89	0.01%
METHYLPHENID CAP 10MG	7	4	$1,161.81	$5.53	$165.97	0.00%
METHYLPHENID CAP 20MG	6	3	$2,550.92	$14.17	$425.15	0.00%
CONCERTA TAB 18MG	3	1	$466.34	$5.18	$155.45	0.00%
APTENSIO XR CAP 40MG	2	1	$419.26	$6.99	$209.63	0.00%
METHYLPHENID CAP 40MG	1	1	$334.79	$13.39	$334.79	0.00%
APTENSIO XR CAP 30MG	1	1	$209.63	$6.99	$209.63	0.00%
APTENSIO XR CAP 20MG	1	1	$209.63	$6.99	$209.63	0.00%
METHYLPHENID CAP 10MG	1	1	$139.49	$4.65	$139.49	0.00%
SUBTOTAL	**82,654**	**20,982**	**$13,645,520.93**	**$5.54**	**$165.09**	**22.31%**
AMPHETAMINE/DEXTROAMPHETAMINE COMBINATION PRODUCTS						
AMPHET/DEXTR TAB 10MG	13,020	3,130	$579,946.36	$1.50	$44.54	0.95%
AMPHET/DEXTR TAB 20MG	8,256	1,671	$410,749.09	$1.66	$49.75	0.67%
AMPHET/DEXTR TAB 5MG	8,173	2,281	$373,540.01	$1.55	$45.70	0.61%
ADDERALL XR CAP 30MG	6,052	927	$1,349,937.91	$7.46	$223.06	2.21%
ADDERALL XR CAP 20MG	5,405	1,102	$1,245,561.07	$7.71	$230.45	2.04%
AMPHET/DEXTR TAB 30MG	3,443	668	$182,330.18	$1.78	$52.96	0.30%
AMPHET/DEXTR TAB 15MG	3,055	764	$142,948.68	$1.57	$46.79	0.23%
ADDERALL XR CAP 15MG	3,053	677	$678,614.58	$7.45	$222.28	1.11%
ADDERALL XR CAP 10MG	2,807	684	$619,791.25	$7.42	$220.80	1.01%
ADDERALL XR CAP 25MG	2,180	409	$474,941.26	$7.30	$217.86	0.78%
AMPHET/DEXTR TAB 7.5MG	676	180	$32,086.21	$1.60	$47.46	0.05%
ADDERALL XR CAP 5MG	556	158	$126,754.64	$7.66	$227.98	0.21%
AMPHETAMINE TAB 30MG	356	82	$19,082.05	$1.79	$53.60	0.03%
AMPHET/DEXTR TAB 12.5MG	312	65	$19,149.16	$2.04	$61.38	0.03%
AMPHETAMINE CAP 20MG	196	53	$34,571.18	$5.92	$176.38	0.06%
AMPHETAMINE CAP 30MG	141	36	$15,541.72	$3.71	$110.22	0.03%
AMPHETAMINE CAP 10MG	91	28	$10,679.22	$4.02	$117.35	0.02%
AMPHETAMINE CAP 15MG	88	23	$10,802.01	$4.09	$122.75	0.02%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
AMPHETAMINE CAP 25MG	51	14	$5,746.33	$3.89	$112.67	0.01%
AMPHETAMINE CAP 5MG	35	17	$5,014.82	$4.85	$143.28	0.01%
ADDERALL TAB 10MG	22	15	$3,258.01	$4.94	$148.09	0.01%
ADDERALL TAB 15MG	16	9	$4,483.89	$9.54	$280.24	0.01%
ADDERALL TAB 5MG	15	11	$1,398.00	$3.11	$93.20	0.00%
ADDERALL TAB 30MG	13	3	$1,682.81	$4.31	$129.45	0.00%
ADDERALL TAB 20MG	10	4	$1,605.80	$5.43	$160.58	0.00%
ADDERALL TAB 7.5MG	4	2	$1,107.96	$9.23	$276.99	0.00%
SUBTOTAL	**58,026**	**13,013**	**$6,351,324.20**	**$3.67**	**$109.46**	**10.39%**
DEXMETHYLPHENIDATE PRODUCTS						
DEXMETHYLPH TAB 10MG	7,959	1,598	$377,055.53	$1.58	$47.37	0.62%
DEXMETHYLPH TAB 5MG	6,279	1,514	$220,552.20	$1.18	$35.13	0.36%
FOCALIN XR CAP 20MG	4,534	979	$1,205,056.51	$8.91	$265.78	1.97%
DEXMETHYLPH CAP 15MG	3,878	886	$673,340.64	$5.82	$173.63	1.10%
DEXMETHYLPH CAP 30MG	3,234	562	$504,712.97	$5.22	$156.06	0.83%
FOCALIN XR CAP 10MG	2,130	707	$547,852.41	$8.61	$257.21	0.90%
FOCALIN XR CAP 25MG	2,071	379	$583,301.71	$9.44	$281.65	0.95%
DEXMETHYLPHE CAP 10MG	1,841	558	$383,951.27	$7.00	$208.56	0.63%
DEXMETHYLPHE CAP 20MG	1,150	456	$252,507.00	$7.33	$219.57	0.41%
FOCALIN XR CAP 15MG	931	353	$253,209.12	$9.13	$271.98	0.41%
DEXMETHYLPH CAP 40MG	868	141	$166,408.49	$6.41	$191.71	0.27%
DEXMETHYLPH TAB 2.5MG	860	295	$24,647.41	$0.97	$28.66	0.04%
FOCALIN XR CAP 5MG	526	171	$130,414.30	$8.33	$247.94	0.21%
DEXMETHYLPHE CAP 5MG	501	172	$92,628.72	$6.23	$184.89	0.15%
FOCALIN XR CAP 35MG	488	88	$146,999.78	$10.08	$301.23	0.24%
FOCALIN TAB 5MG	134	46	$6,428.67	$1.60	$47.98	0.01%
FOCALIN TAB 2.5MG	119	41	$3,292.32	$0.93	$27.67	0.01%
FOCALIN TAB 10MG	109	32	$7,502.21	$2.30	$68.83	0.01%
FOCALIN XR CAP 30MG	76	43	$20,644.16	$9.12	$271.63	0.03%
FOCALIN XR CAP 40MG	57	30	$16,802.84	$10.03	$294.79	0.03%
SUBTOTAL	**37,745**	**9,051**	**$5,617,308.26**	**$4.99**	**$148.82**	**9.19%**
GUANFACINE PRODUCTS						
GUANFACINE TAB 2MG ER	7,122	2,204	$189,419.64	$0.89	$26.60	0.31%
INTUNIV TAB 2MG	5,529	1,879	$1,643,454.91	$10.04	$297.24	2.69%
GUANFACINE TAB 3MG ER	5,397	1,434	$148,681.86	$0.92	$27.55	0.24%
GUANFACINE TAB 1MG ER	4,453	1,853	$115,009.25	$0.89	$25.83	0.19%
INTUNIV TAB 3MG	4,429	1,287	$1,317,646.05	$10.00	$297.50	2.15%
GUANFACINE TAB 4MG ER	4,192	955	$115,591.80	$0.92	$27.57	0.19%
INTUNIV TAB 4MG	3,354	870	$991,208.48	$9.92	$295.53	1.62%
INTUNIV TAB 1MG	2,892	1,382	$818,183.89	$10.05	$282.91	1.34%
SUBTOTAL	**37,368**	**11,864**	**$5,339,195.88**	**$4.84**	**$142.88**	**8.73%**
ATOMOXETINE PRODUCTS						
STRATTERA CAP 40MG	8,755	2,350	$2,980,888.31	$11.44	$340.48	4.87%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
STRATTERA CAP 25MG	7,292	2,139	$2,410,070.43	$11.20	$330.51	3.94%
STRATTERA CAP 60MG	5,380	1,255	$1,745,826.26	$10.88	$324.50	2.85%
STRATTERA CAP 80MG	3,585	873	$1,281,521.50	$11.66	$357.47	2.10%
STRATTERA CAP 18MG	3,178	1,157	$1,048,266.95	$11.53	$329.85	1.71%
STRATTERA CAP 10MG	2,229	908	$728,966.45	$11.64	$327.04	1.19%
STRATTERA CAP 100MG	968	206	$359,707.22	$11.57	$371.60	0.59%
SUBTOTAL	**31,387**	**8,888**	**$10,555,247.12**	**$11.34**	**$336.29**	**17.26%**
CLONIDINE PRODUCTS						
CLONIDINE TAB 0.1MG ER	1,427	214	$344,756.30	$8.00	$241.60	0.56%
KAPVAY TAB 0.1 MG	39	6	$18,974.65	$16.36	$486.53	0.03%
SUBTOTAL	**1,466**	**220**	**$363,730.95**	**$8.22**	**$248.11**	**0.59%**
MODAFINIL PRODUCTS						
MODAFINIL TAB 200MG	300	39	$94,153.91	$10.51	$313.85	0.15%
MODAFINIL TAB 100MG	32	7	$5,328.63	$5.39	$166.52	0.01%
SUBTOTAL	**332**	**46**	**$99,482.54**	**$10.00**	**$299.65**	**0.16%**
ARMODAFINIL PRODUCTS						
NUVIGIL TAB 250MG	104	14	$58,315.37	$18.69	$560.72	0.10%
NUVIGIL TAB 150MG	67	8	$39,489.75	$19.99	$589.40	0.06%
NUVIGIL TAB 50MG	2	1	$396.02	$6.60	$198.01	0.00%
NUVIGIL TAB 200MG	1	1	$587.68	$19.59	$587.68	0.00%
SUBTOTAL	**174**	**24**	**$98,788.82**	**$19.05**	**$567.75**	**0.16%**
DEXTROAMPHETAMINE PRODUCTS						
DEXTROAMPHET CAP 15MG	35	5	$13,003.00	$12.56	$371.51	0.02%
DEXTROAMPHET TAB 10MG	32	6	$3,940.49	$4.41	$123.14	0.01%
DEXTROAMPHET CAP 10MG	24	2	$2,976.26	$4.13	$124.01	0.00%
DEXTROAMPHET CAP 5MG	13	2	$1,218.53	$3.12	$93.73	0.00%
ZENZEDI TAB 2.5MG	3	1	$851.21	$9.46	$283.74	0.00%
DEXTROAMPHET TAB 5MG	3	2	$273.67	$3.04	$91.22	0.00%
SUBTOTAL	**110**	**18**	**$22,263.16**	**$6.92**	**$202.39**	**0.04%**
SODIUM OXYBATE PRODUCTS						
XYREM SOL 500MG/ML	29	3	$247,731.40	$284.75	$8,542.46	0.41%
SUBTOTAL	**29**	**3**	**$247,731.40**	**$284.75**	**$8,542.46**	**0.41%**
AMPHETAMINE PRODUCTS						
EVEKEO TAB 5MG	1	1	$317.98	$10.60	$317.98	0.00%
SUBTOTAL	**1**	**1**	**$317.98**	**$10.60**	**$317.98**	**0.00%**
TOTAL	**333,974**	**41,236***	**$61,156,523.18**	**$6.16**	**$183.12**	**100.00%**

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

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[4] Medscape: FDA Okays First Orally Disintegrating Tablet for ADHD in Kids. Available online at: http://www.medscape.com/viewarticle/857892. Issued 01/28/2016. Last accessed 05/13/2016.
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[6] Micromedex 2.0: Methylphenidate Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 05/04/2016. Last accessed 05/13/2016.
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Appendix J

Calendar Year 2015 Annual Review of Cholbam® (Cholic Acid)

Oklahoma Health Care Authority
June 2016

Introduction[1,2,3]

Bile acid synthesis disorders (BASDs) are a group of rare metabolic disorders characterized by defects in the synthesis of bile acids. Bile acids are chemical compounds found in the liver that have several roles in the body including promoting the flow and excretion of bile and assisting in the intestinal absorption of fat and fat-soluble vitamins (vitamins A, D, E, and K). Bile acids are synthesized from cholesterol and, therefore, bile acid synthesis serves as the main pathway in cholesterol degradation.

The failure to produce normal or functional bile acids results in the accumulation of abnormal bile acids, intermediary metabolites, and cholesterol within the body, which can damage certain organ systems. The main symptom of most BASDs is cholestasis (interruption or suppression of the flow of bile from the liver) and fat-soluble vitamin malabsorption. Malabsorption leads to vitamin deficiency and can result in various symptoms including rickets (vitamin D deficiency), vision problems (vitamin A deficiency), poor coordination and developmental delays (vitamin E deficiency), and blood clotting problems leading to easy bleeding and bruising (vitamin K deficiency). Additional symptoms such as progressive neurological disease may develop in certain cases of BASDs. If untreated, the more severe forms of these disorders can eventually progress to cause life-threatening complications, such as cirrhosis and liver failure. Many of these disorders can be successfully treated by replacing the missing bile acids (bile acid replacement therapy).

Cholic acid is a primary bile acid synthesized from cholesterol, and treatment with oral cholic acid therapy increases the bile acid concentration in the digestive system to facilitate the absorption of fats and fat-soluble vitamins leading to a normal growth rate. Oral bile acid also blocks the affected bile production pathway so the abnormal bile acids and intermediary metabolites cannot be produced, and improves bile flow to prevent cholestasis. Cholbam® (cholic acid) is an oral bile acid approved by the U.S. Food and Drug Administration (FDA) as an orphan drug in March 2015 for treatment in patients three weeks of age and older, and is the first FDA approved treatment for BASDs.

Current Prior Authorization Criteria

Cholbam® (Cholic Acid) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Treatment of bile acid disorders due to single enzyme defects (SEDs); or
    b. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat-soluble vitamin absorption; and

2. Treatment with Cholbam® should be initiated and monitored by a hepatologist or pediatric gastroenterologist; and
3. The prescriber must verify that AST, ALT, GGT, alkaline phosphatase, bilirubin, and INR will be monitored every month for the first three months, every three months for the next nine months, every six months during the next three years and annually thereafter; and
4. Cholbam® should be discontinued if liver function does not improve within three months of starting treatment, if complete biliary obstruction develops, or if there are persistent clinical or laboratory indicators of worsening liver function or cholestasis; and
5. Initial approvals will be for the duration of three months to monitor for compliance and liver function tests.
6. Continuation approvals will be granted for the duration of one year.
7. A quantity limit of 120 capsules per 30 days will apply. Quantity limit requests will be based on the member's recent weight taken within the last 30 days.

Utilization of Cholbam® (Cholic Acid)

There has been no utilization of Cholbam® in the SoonerCare population since its FDA approval in March 2015.

Prior Authorization of Cholbam® (Cholic Acid)

There were no prior authorization requests submitted for Cholbam® during calendar year 2015.

Market News and Updates[4]

Anticipated Exclusivity Expiration:

- Cholbam® (cholic acid): March 2022

Recommendations

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

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Appendix K

Calendar Year 2015 Annual Review of Atypical Antipsychotic Medications and 30-Day Notice to Prior Authorize Rexulti® (Brexpiprazole), Vraylar™ (Cariprazine), and Aristada™ (Aripiprazole Lauroxil)

Oklahoma Health Care Authority
June 2016

Current Prior Authorization Criteria

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

Atypical Antipsychotic Tier-2 Approval Criteria:

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

Atypical Antipsychotic Tier-3 Approval Criteria:

1. Trials of two Tier-1 products at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects; and
    a. *Pending aripiprazole move to Tier-1:* One of the Tier-1 trials must include a trial with aripiprazole unless member has a patient-specific, clinically significant reason why aripiprazole is not appropriate or an FDA approved diagnosis not covered by aripiprazole.
    b. Clozapine does not count towards a Tier-1 trial.
2. Trials of two Tier-2 medications, at least 14 days in duration each, titrated to recommended dose, that did not yield adequate response or resulted in intolerable adverse effects.
3. A manual prior authorization may be submitted for consideration of a Tier-3 medication when the member has had at least four trials of Tier-1 and Tier-2 products (two trials must be from Tier-1) that did not yield an adequate response or resulted in intolerable adverse effects.
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), or Symbyax® (olanzapine/fluoxetine) for a diagnosis of major depressive disorder requires current use of an antidepressant, and previous trials with at least two other antidepressants from both categories (an SSRI and duloxetine) and a trial of aripiprazole tablets (*pending aripiprazole move to Tier-1*) that did not yield adequate response. Tier structure applies.

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

Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).
ER = extended-release

* Mandatory generic plan applies

¥ Does not count toward a Tier-1 trial

∞ In addition to tier trials, use of Invega Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.

Utilization of Atypical Antipsychotic Medications: Calendar Year 2015

Comparison of Calendar Years

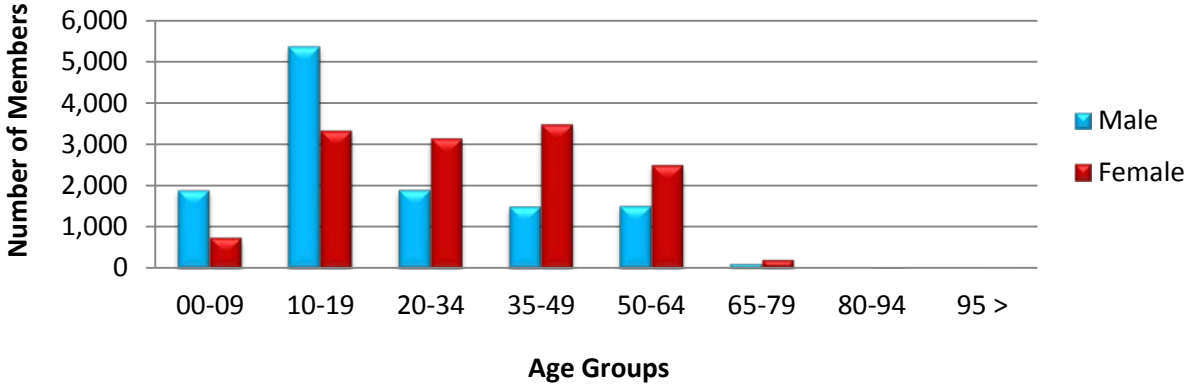
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	26,049	182,740	$51,840,540.61	$283.68	$9.35	7,563,534	5,544,641
2015	25,862	181,076	$56,932,621.67	$314.41	$10.31	7,463,886	5,520,363
% Change	**-0.70%**	**-0.90%**	**9.80%**	**10.80%**	**10.30%**	**-1.30%**	**-0.40%**
Change	**-187**	**-1,664**	**$5,092,081.06**	**$30.73**	**$0.96**	**-99,648**	**-24,278**

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

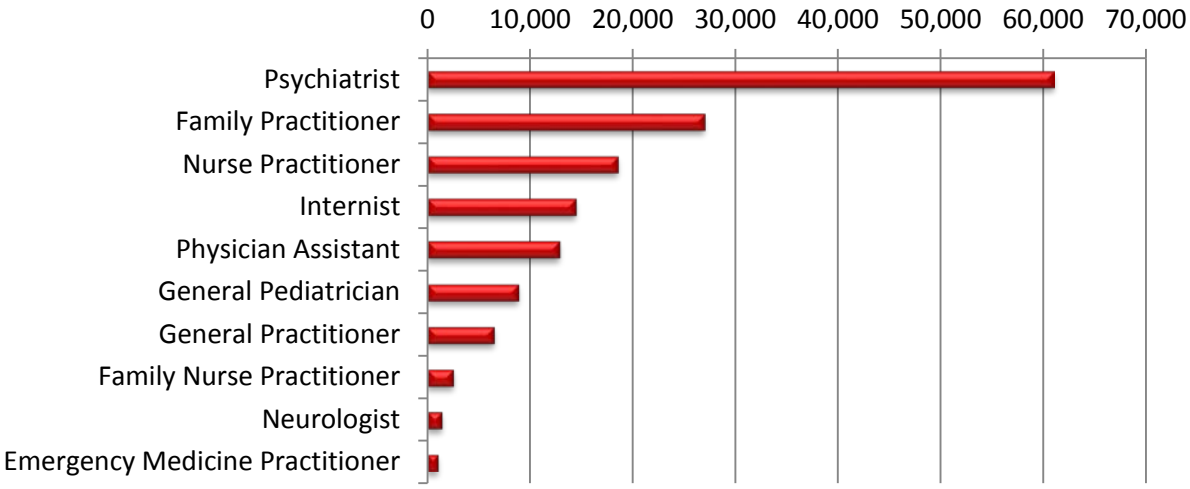
- Aggregate drug rebates collected during calendar year 2015 for atypical antipsychotic medications: $38,220,344.65[†]

[†] Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed. Claims data includes Indian Health Service providers; aggregated drug rebates do not.

Demographics of Members Utilizing Atypical Antipsychotic Medications



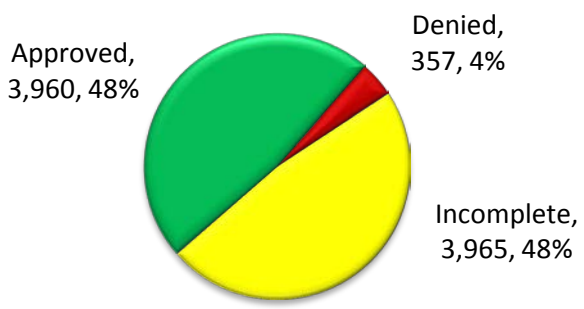
Top Prescriber Specialties of Atypical Antipsychotic Medications By Number of Claims



Prior Authorization of Atypical Antipsychotic Medications

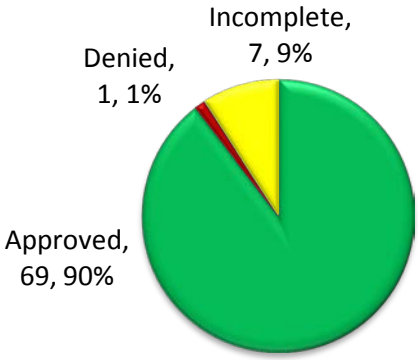
There were 8,282 prior authorization requests submitted for atypical antipsychotic medications during calendar year 2015. Computer edits are in place to detect Tier-1 medications in members' recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions.

Status of Petitions



There were 77 prior authorization requests submitted for a total of 62 unique members for atypical antipsychotics medications during calendar year 2015 that were referred for a psychiatric consultation. Most requests were for children between the ages of 0 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations



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

Anticipated Patent Expiration(s):

- Seroquel XR® (quetiapine extended-release tablets): November 2017
- Invega® Sustenna® (paliperidone injection): May 2019
- Saphris® (asenapine sublingual tablets): October 2026
- Latuda® (lurasidone tablets): May 2031
- Fanapt® (iloperidone tablets): December 2031

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

- Rexulti® (brexpiprazole): July 2015
- Vraylar™ (cariprazine): September 2015
- Aristada® (aripiprazole lauroxil): October 2015

Safety Update(s):

- **September 2015:** The FDA issued a drug safety communication regarding changes in monitoring for neutropenia caused by clozapine treatment. The FDA is requiring changes to clozapine prescribing information and Risk Evaluation and Mitigation Strategy (REMS) program stating neutropenia will be monitored by the absolute neutrophil count (ANC) only, rather than in conjunction with the white blood cell count. Moreover, in the Clozapine REMS Program, the requirements for ANC are being modified so that patients will be able to continue on clozapine treatment with a lower ANC, a change that will allow continued treatment for a greater number of patients.
- **May 2016:** The FDA issued a drug safety communication regarding impulse-control problems associated with aripiprazole. The communication warns that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify®, Abilify Maintena®, Aristada™, and generics). These uncontrollable urges were reported to have stopped when the medicine was discontinued or the dose was reduced. Cases of impulse control have

been reported to the FDA or in medical literature 184 times since aripiprazole was approved in the U.S. in November 2002.

- **May 2016:** The FDA issued a warning that the antipsychotic medication olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. The FDA announced they are adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). A search of the FDA Adverse Event Reporting System (FAERS) database identified 23 cases of DRESS reported with olanzapine worldwide since 1996, when the first olanzapine-product was approved.

Market News:

- **March 2016:** Results from two Phase 3 clinical trials of encenicline, a novel, orally administered alpha 7 receptor agonist, in patients with cognitive impairment in schizophrenia (CIS) were announced. Neither of the two Phase 3 studies met its co-primary endpoints based on effect on cognitive function and patient function. The FDA placed Phase 3 clinical trials for encenicline to treat Alzheimer's disease on hold in September 2015 following reports of gastrointestinal side effects. FORUM Pharmaceuticals is implementing a significant restructuring of its organization to appropriately scale its spending and resources and to evaluate a potential path forward, if any.
- **April 2016:** The FDA issued a Complete Response Letter (CRL) regarding a drug/device combination product, which combines Abilify® with the FDA-approved Proteus ingestible sensor, embedded in a single tablet at point of manufacture. The NDA was submitted for an indication to measure medication adherence to aripiprazole in adults as a treatment for schizophrenia, as an acute treatment for manic or mixed episodes of bipolar I disorder, and as an adjunctive treatment for major depression. The CRL requested additional information, including data regarding the performance of the product under the conditions in which it is likely to be used, and further human factors investigations. The goal of human factors testing is to evaluate use-related risks and confirm that users can use the device safely and effectively.

Rexulti® (Brexpiprazole) Product Summary[12]

Indications: Rexulti® (brexpiprazole) is an atypical antipsychotic indicated for the following:

- Use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD).
- Treatment of schizophrenia.

Dosing:

- Rexulti® (brexpiprazole) is available as an oral tablet in six strengths: 0.25mg, 0.5mg, 1mg, 2mg, 3mg, and 4mg.
- Brexpiprazole should be administered by mouth once daily with or without food.
- The starting dose of brexpiprazole for MDD is 0.5mg or 1mg per day. The recommended dose for MDD is 2mg per day with a maximum dose of 3mg per day.

- The starting dose of brexpiprazole for schizophrenia is 1mg per day. The recommended dose for schizophrenia is 2mg to 4mg per day with a maximum dose of 4mg per day.
- For moderate-to-severe hepatic impairment (Child-Pugh score ≥7) and moderate, severe, or end-stage renal impairment (creatinine clearance <60 mL/minute) the maximum recommended dosage is 2mg once daily for patients with MDD and 3mg once daily for patients with schizophrenia.
- Patients who are known CYP2D6 poor metabolizers should reduce the usual dosage by half.

Mechanism of Action:

- The mechanism of action of brexpiprazole in the treatment of MDD or schizophrenia is unknown. However, the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D_2 receptors, and antagonist activity at serotonin 5-HT_{2A} receptors.

Contraindications:

- Known hypersensitivity to brexpiprazole or any of its components.

Safety:

- Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: In placebo-controlled trials with risperidone, aripiprazole, and olanzapine in elderly patients with dementia, there was a higher incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack) compared to placebo-treated patients. Brexpiprazole is not FDA approved for the treatment of patients with dementia-related psychosis.
- Neuroleptic Malignant Syndrome: Patients with neuroleptic malignant syndrome should be managed with immediate discontinuation of brexpiprazole and close monitoring.
- Tardive Dyskinesia: A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Brexpiprazole should be discontinued if clinically appropriate.
- Metabolic Changes: Patients should be monitored for hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain.
- Leukopenia, Neutropenia, and Agranulocytosis: Complete blood counts (CBC) should be performed in patients with pre-existing low white blood cell count (WBC) or history of leukopenia or neutropenia. Consideration should be given to discontinuing brexpiprazole if a clinically significant decline in WBC occurs in absence of other causative factors.
- Orthostatic Hypotension and Syncope: Heart rate and blood pressure should be monitored and patients with known cardiovascular or cerebrovascular disease and risk of dehydration or syncope should be warned.
- Seizures: Brexpiprazole should be used cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.

Adverse Reactions:

- MDD: Weight increased and akathisia (≥5% and at least twice the rate for placebo)
- Schizophrenia: Weight increased (≥4% and at least twice the rate of placebo)

Efficacy:

- MDD: The efficacy of brexpiprazole in the adjunctive treatment of MDD was evaluated in two 6-week, double-blind, placebo-controlled, fixed-dose trials of adult patients meeting DSM-IV-TR criteria for MDD who had an inadequate response to prior antidepressant therapy (one to three courses) and who had also demonstrated an inadequate response throughout the eight weeks of prospective antidepressant treatment (with escitalopram, fluoxetine, paroxetine controlled-release, sertraline, duloxetine delayed-release, or venlafaxine extended-release). The primary endpoint was change from baseline to Week 6 in the Montgomery-Asberg Depression Rating Scale (MADRS), a 10-item clinician-related scale used to assess the degree of depressive symptomatology, with 0 representing no symptoms, and 60 representing the worst symptoms. At randomization the mean MADRS total score was 27. In Studies 1 and 2, brexpiprazole plus an antidepressant were superior to placebo plus an antidepressant in reducing mean MADRS total scores. Study 1 which was specific to brexpiprazole 2mg showed a difference of -3.2 (-4.9,-1.5; 95% CI) compared to placebo.
- Schizophrenia: The efficacy of brexpiprazole in the treatment of adults with schizophrenia was evaluated in two 6-week, double-blind, placebo-controlled, fixed-dose trials of adult patients meeting DSM-IV-TR criteria for schizophrenia. The primary endpoint was change from baseline to Week 6 in the Positive and Negative Syndrome Scale (PANSS) total score. PANSS is a 30-item scale that measures positive (7 items) and negative (7 items) symptoms of schizophrenia, and general psychopathology (16 items), each rated on a scale of 1 (absent) to 7 (extreme); the total PANSS score ranges from 30 (best) to 210 (worst). In Study 3, Rexulti® at both 2mg and 4mg per day was superior to placebo on the PANSS total score. In Study 4, brexpiprazole 4mg per day was superior to placebo on the PANSS total score, -6.5 (-10.6, -2.4; 95% CI).

Cost Comparison:

Drug	Strength	Cost per Tablet	Cost per Month**
Rexulti® (brexpiprazole)	**All Strengths**	**$32.90**	**$987.00**
aripiprazole tablets	All Strengths	$5.79-$8.63*	$173.70-$258.90
Seroquel XR® (quetiapine XR)	All Strengths	$15.57-$26.41	$467.10-$1,584.60
risperidone tablets	4mg	$0.21*	$12.60

Costs listed are based on maximum recommended dose at estimated acquisition cost (EAC) unless otherwise noted.
* SMAC = state maximum allowable cost
** Costs do not reflect rebated prices or net costs.

Vraylar™ (Cariprazine) Product Summary[13]

Indications: Vraylar™ (cariprazine) is an atypical antipsychotic indicated for the following:

- Treatment of schizophrenia.
- Acute treatment of manic or mixed episodes associated with bipolar I disorder.

Dosing:

- Vraylar™ (cariprazine) is available as an oral capsule in the following strengths: 1.5mg, 3mg, 4.5mg, and 6mg.
- Cariprazine should be administered once daily with or without food.
- The starting dose of cariprazine for a diagnosis of schizophrenia is 1.5mg per day and the recommended daily dose is 1.5mg to 6mg per day.
- The starting dose of cariprazine for bipolar mania is 1.5mg per day and the recommended daily dose is 3mg to 6mg per day.
- Doses of cariprazine above 6mg per day do not confer significant benefit but increased the risk of dose-related adverse events.

Mechanism of Action: The mechanism of action of cariprazine in schizophrenia and bipolar I disorder is unknown. However, the efficacy of cariprazine could be mediated through a combination of partial agonist activity at central dopamine D_2 and serotonin 5-HT_{1A} receptors and antagonist activity at serotonin 5-HT_{1A} receptors. Cariprazine forms two major metabolites, desmethyl cariprazine (DCAR) and didesmethyl cariprazine (DDCAR) that have *in vitro* receptor binding profiles similar to the parent drug.

Contraindications:

- Known hypersensitivity to cariprazine or any of its components.

Safety:

- Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: In placebo-controlled trials in elderly subjects with dementia, patients randomized to risperidone, aripiprazole, and olanzapine had a higher incidence of stroke and transient ischemic attack, including fatal stroke. Cariprazine is not FDA approved for the treatment of patients with dementia-related psychosis.
- Neuroleptic Malignant Syndrome: Patients with neuroleptic malignant syndrome should be managed with immediate discontinuation and close monitoring.
- Tardive Dyskinesia: A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Cariprazine should be discontinued if clinically appropriate.
- Late-Occurring Adverse Reactions: Because of cariprazine's long half-life, patients should be monitored for adverse reactions and patient response for several weeks after starting cariprazine and with each dosage change.
- Metabolic Changes: Patients should be monitored for hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain.
- Orthostatic Hypotension and Syncope: Heart rate and blood pressure should be monitored and patients with known cardiovascular or cerebrovascular disease, and risk of dehydration or syncope should be warned.

Adverse Reactions: The most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) were:

- Schizophrenia: extrapyramidal symptoms and akathisia
- Bipolar Mania: extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness

Efficacy:

- Schizophrenia: The efficacy of cariprazine in the treatment of schizophrenia was evaluated in three 6-week, randomized, double-blind, placebo-controlled trials in patients (aged 18 to 60 years) meeting DSM-IV-TR criteria for schizophrenia. An active control arm (risperidone or aripiprazole) was included in two trials to assess assay sensitivity. The primary endpoint was change from baseline to Week 6 in the PANSS total score. In all three studies, cariprazine was superior to placebo. In Study 3, cariprazine 3mg to 6mg per day was superior to placebo on the PANSS total score, -6.8 (-11.3, -2.4; 95% CI) and cariprazine 6mg to 9mg per day was superior to placebo on the PANSS total score, -9.9 (-14.5,-5.3; 95% CI). The efficacy of cariprazine was demonstrated at doses ranging from 1.5mg to 9mg per day compared to placebo; however, the maximum recommended dose is 6mg per day due to dose-related increases in certain adverse reactions, particularly above 6mg per day.
- Manic or Mixed Episodes Associated with Bipolar I Disorder: The efficacy of cariprazine in the acute treatment of bipolar mania was established in three, 3-week placebo-controlled trials in patients (18 to 65 years old) who met DSM-IV-TR criteria for bipolar I disorder with manic or mixed episodes with or without psychotic features. The primary endpoint was decrease from baseline in Young Mania Rating Scale (YMRS) total score at the end of Week 3. The YMRS is an 11-item clinician-rated scale traditionally used to assess the degree of manic symptomatology. YMRS total score may range from 0 to 60 with a higher score reflecting greater severity. In all three trials cariprazine was superior to placebo. In Study 3, cariprazine dosed 3mg to 12mg per day was superior to placebo on the YMRS total score, -4.3 (-6.7, -1.9; 95% CI). The efficacy of cariprazine was established at doses from 3mg to 12mg per day; however, doses above 6mg per day did not appear to have additional benefit over lower doses and there was a dose-related increase in certain adverse reactions.

Cost Comparison:

Drug	Strength	Cost per Tablet	Cost per Month**
Vraylar™ (cariprazine)	**All Strengths**	**$35.41**	**$1,062.30**
aripiprazole tablets	All Strengths	$5.79-8.63*	$173.70-$258.90
Seroquel XR® (quetiapine XR)	All Strengths	$15.57-26.41	$467.10-$1,584.60
risperidone tablets	4mg	$0.21*	$12.60

Costs listed are based on maximum recommended dose at estimated acquisition cost (EAC) unless otherwise noted.

* SMAC = state maximum allowable cost

** Costs do not reflect rebated prices or net costs.

Aristada™ (Aripiprazole Lauroxil) Product Summary[14]

Indications: Aristada™ (aripiprazole lauroxil) is an atypical antipsychotic indicated for the treatment of schizophrenia.

Dosing:

- Aristada™ (aripiprazole lauroxil) is available as an extended-release injectable suspension in single-use, pre-filled syringes in the following strengths: 441mg, 662mg, and 882mg.
- Aripiprazole lauroxil is to be administered by intramuscular injection in the deltoid (441mg dose only) or gluteal (all doses) muscle by a healthcare professional.
- For patients naïve to aripiprazole, tolerability should be established with oral aripiprazole prior to initiating treatment with aripiprazole lauroxil.
- Aripiprazole lauroxil can be initiated at a dose of 441mg, 662mg, or 882mg administered monthly, or 882mg administered every six weeks.
- In conjunction with the first aripiprazole lauroxil injection, patients should also receive treatment with oral aripiprazole for 21 consecutive days.
- Dosing regimen adjustments may be required for missed doses.
- Dose adjustments are required for:
    - Known CYP2D6 poor metabolizers
    - Patients taking CYP3A4 inhibitors, CYP2D6 inhibitors, or CYP3A4 inducers for more than two weeks

Mechanism of Action: Aripiprazole lauroxil is a prodrug of aripiprazole. Following intramuscular injection, aripiprazole lauroxil is likely converted by enzyme-mediated hydrolysis to N-hydroxymethyl aripiprazole, which is then hydrolyzed to aripiprazole. The mechanism of action of aripiprazole in the body is unknown. However, efficacy could be mediated through a combination of partial agonist activity at D_2 and 5-HT_{1A} receptors and antagonist activity at 5-HT_{2A} receptors. Actions at receptors other than D_2, 5-HT_{1A}, and 5-HT_{2A} could explain some of the adverse reactions of aripiprazole (e.g., the orthostatic hypotension observed with aripiprazole may be explained by its antagonist activity at adrenergic alpha-1 receptors).

Contraindications:

- Known hypersensitivity to aripiprazole lauroxil or any of its components.

Safety:

- <u>Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis:</u> In placebo-controlled trials with risperidone, aripiprazole, and olanzapine in elderly patients with dementia, there was a higher incidence of cerebrovascular adverse reactions (cerebrovascular accidents and transient ischemic attacks) including fatalities compared to placebo-treated patients. Aripiprazole lauroxil is not FDA approved for the treatment of patients with dementia-related psychosis.
- <u>Neuroleptic Malignant Syndrome:</u> Patients with neuroleptic malignant syndrome should be managed with immediate discontinuation and close monitoring.

- Tardive Dyskinesia: A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Aripiprazole lauroxil should be discontinued if clinically appropriate.
- Metabolic Changes: Patients should be monitored for hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain.
- Orthostatic Hypotension: Heart rate and blood pressure should be monitored and patients with known cardiovascular or cerebrovascular disease, and risk of dehydration or syncope should be warned.
- Leukopenia, Neutropenia, and Agranulocytosis: Complete blood counts in patients with a history of clinically significant low WBC count should be performed. Consideration should be given to discontinuation if a clinically significant decline in WBC occurs in the absence of other causative factors.
- Seizures: Aripiprazole lauroxil should be used cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.
- Potential for Cognitive and Motor Impairment: Aripiprazole lauroxil has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with aripiprazole lauroxil does not affect them adversely.

Adverse Reactions: The most common adverse reaction with aripiprazole lauroxil (incidence ≥5% and at least twice the rate of placebo) was akathisia.

Efficacy: The efficacy of aripiprazole lauroxil in the treatment of schizophrenia was established in part, on the basis of efficacy data from trials with the oral formulation of aripiprazole. In addition, aripiprazole lauroxil efficacy was also established in a 12-week, randomized, double-blind, placebo-controlled, fixed-dose study in adult patients with schizophrenia meeting DSM-IV-TR criteria. After establishing tolerability to oral aripiprazole, patients received oral aripiprazole or placebo daily for the first three weeks. The intramuscular (IM) injections were administered on Days 1, 29, and 57. The primary endpoint was change from baseline to endpoint (Day 85) in PANSS total score. The aripiprazole lauroxil group achieved statistically significant separation from placebo in the change of total PANSS score from baseline. Aripiprazole lauroxil 441mg PANSS total score difference from placebo was -10.9 (-14.5,-7.3; 95% CI) and aripiprazole lauroxil 882mg PANSS total score difference from placebo was -11.9 (-15.4,-8.3; 95% CI).

Cost Comparison:

Drug	Strength	Cost per Unit	Cost per Month**
Aristada™ (aripiprazole lauroxil)	**441mg/1.6mL**	**$696.30/mL**	**$1,114.08**
Aristada™ (aripiprazole lauroxil)	**662mg/2.4mL**	**$696.52/mL**	**$1,671.65**
Aristada™ (aripiprazole lauroxil)	**882mg/3.2mL**	**$695.97/mL**	**$2,227.10**
Abilify Maintena® (aripiprazole)	400mg/syringe	$1,806.24/syringe	$1,806.27
Risperdal® Consta® (risperidone)	50mg/2mL	$767.20/syringe*	$1,534.40
Invega® Sustenna® (paliperidone)	234mg/1.5mL	$1,484.02/mL	$2,226.03

Costs listed are based on maximum recommended dose at estimated acquisition cost (EAC) unless otherwise noted.
*SMAC = state maximum allowable cost
**Costs do not reflect rebated prices or net costs.

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 category. Current Tier-3 criteria 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 Maintena®)	**brexpiprazole (Rexulti®)**
olanzapine (Zyprexa®)	**aripiprazole lauroxil (Aristada®)**	**cariprazine (Vraylar™)**
quetiapine (Seroquel®)	aripiprazole (Abilify®)	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®)	

Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC).

* Mandatory generic plan applies

¥ Does not count toward a Tier-1 trial

ER = extended-release

∞ In addition to tier trials, use of Invega Trinza™ requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.

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.

Utilization Details of Atypical Antipsychotic Medications: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 UTILIZATION						
RISPERIDONE ORAL PRODUCTS						
RISPERIDONE TAB 1MG	16,863	4,036	$160,504.20	$0.31	$9.52	0.28%
RISPERIDONE TAB 0.5MG	12,462	3,194	$117,736.13	$0.31	$9.45	0.21%
RISPERIDONE TAB 2MG	8,606	1,950	$85,122.87	$0.32	$9.89	0.15%
RISPERIDONE TAB 0.25MG	6,123	1,664	$61,275.78	$0.33	$10.01	0.11%
RISPERIDONE TAB 3MG	4,447	854	$48,106.29	$0.35	$10.82	0.08%
RISPERIDONE TAB 4MG	2,404	431	$30,613.08	$0.39	$12.73	0.05%
RISPERIDONE SOL 1MG/ML	1,003	178	$41,946.25	$1.32	$41.82	0.07%
RISPERIDONE TAB 0.5MG OD	273	64	$13,758.62	$1.68	$50.40	0.02%
RISPERIDONE TAB 2MG ODT	146	40	$16,150.09	$2.92	$110.62	0.03%
RISPERIDONE TAB 1MG ODT	128	48	$7,366.79	$1.97	$57.55	0.01%
RISPERIDONE TAB 0.25 ODT	107	34	$18,815.52	$5.96	$175.85	0.03%
RISPERIDONE TAB 3MG ODT	61	12	$17,970.50	$9.11	$294.60	0.03%
RISPERDAL TAB 0.25MG	43	8	$417.73	$0.33	$9.71	0.00%
RISPERDAL SOL 1MG/ML	21	2	$13,969.36	$22.17	$665.21	0.02%
RISPERIDONE TAB 4MG ODT	20	4	$6,156.61	$11.91	$307.83	0.01%
RISPERDAL TAB 3MG	16	2	$16,348.96	$34.06	$1,021.81	0.03%
RISPERDAL TAB 1MG	15	2	$11,771.70	$26.16	$784.78	0.02%
RISPERDAL TAB 4MG	13	2	$21,806.71	$55.91	$1,677.44	0.04%
RISPERDAL TAB 2MG	8	3	$5,266.58	$21.94	$658.32	0.01%
SUBTOTAL	**52,759**	**12,528**	**$695,103.77**	**$10.39**	**$311.49**	**1.20%**
QUETIAPINE PRODUCTS						
QUETIAPINE TAB 100MG	9,878	2,979	$107,051.56	$0.35	$10.84	0.19%
QUETIAPINE TAB 50MG	7,466	2,361	$78,284.06	$0.34	$10.49	0.14%
QUETIAPINE TAB 200MG	7,174	1,981	$111,459.56	$0.50	$15.54	0.20%
QUETIAPINE TAB 300MG	6,850	1,621	$145,496.63	$0.67	$21.24	0.26%
QUETIAPINE TAB 400MG	5,753	1,129	$132,983.35	$0.73	$23.12	0.23%
QUETIAPINE TAB 25MG	4,465	1,477	$40,371.61	$0.29	$9.04	0.07%
QUETIAPINE TAB 200MG	209	78	$3,626.86	$0.56	$17.35	0.01%
SEROQUEL TAB 400MG	13	1	$15,959.97	$40.92	$1,227.69	0.03%
SEROQUEL TAB 300MG	10	1	$15,670.50	$52.23	$1,567.05	0.03%
SEROQUEL TAB 200MG	1	1	$4.57	$0.33	$4.57	0.00%
SUBTOTAL	**41,819**	**11,629**	**$650,908.67**	**$9.69**	**$290.69**	**1.16%**
CLOZAPINE PRODUCTS						
CLOZAPINE TAB 100MG	5,869	438	$383,936.03	$3.49	$65.42	0.67%
CLOZAPINE TAB 200MG	1,327	110	$108,728.45	$5.21	$81.94	0.19%
CLOZAPINE TAB 50MG	1,067	96	$39,860.99	$2.33	$37.36	0.07%
CLOZAPINE TAB 25MG	983	104	$29,613.70	$1.67	$30.13	0.05%
CLOZARIL TAB 100MG	56	5	$104,254.57	$67.09	$1,861.69	0.18%
SUBTOTAL	**9,302**	**753**	**$666,393.74**	**$15.96**	**$415.31**	**1.16%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
OLANZAPINE PRODUCTS						
OLANZAPINE TAB 10MG	4,648	1,404	$52,413.48	$0.36	$11.28	0.09%
OLANZAPINE TAB 20MG	4,307	886	$79,015.37	$0.57	$18.35	0.14%
OLANZAPINE TAB 5MG	3,507	1,333	$33,706.86	$0.31	$9.61	0.06%
OLANZAPINE TAB 15MG	2,008	531	$31,537.26	$0.50	$15.71	0.06%
OLANZAPINE TAB 2.5MG	912	370	$8,225.66	$0.30	$9.02	0.01%
OLANZAPINE TAB 20MG	794	156	$15,053.03	$0.60	$18.96	0.03%
OLANZAPINE TAB 20MG ODT	593	256	$161,212.84	$4.42	$271.86	0.28%
OLANZAPINE TAB 10MG ODT	537	205	$58,972.54	$2.55	$109.82	0.10%
OLANZAPINE TAB 10MG	492	165	$5,043.92	$0.35	$10.25	0.01%
OLANZAPINE TAB 7.5MG	401	138	$4,727.74	$0.37	$11.79	0.01%
OLANZAPINE TAB 15MG ODT	302	134	$54,158.93	$3.48	$179.33	0.10%
OLANZAPINE TAB 5MG ODT	202	96	$12,454.36	$1.88	$61.66	0.02%
OLANZAPINE TAB 10MG	70	33	$840.32	$0.39	$12.00	0.00%
OLANZAPINE TAB 15 MG	58	21	$1,027.70	$0.56	$17.72	0.00%
OLANZAPINE TAB 15MG	58	21	$805.49	$0.46	$13.89	0.00%
OLANZAPINE 5MG TAB	49	14	$488.10	$0.32	$9.96	0.00%
ZYPREXA TAB 20MG	29	3	$33,894.03	$38.96	$1,168.76	0.06%
ZYPREXA TAB 5MG	13	2	$5,047.94	$12.94	$388.30	0.01%
ZYPREXA TAB 15MG	12	1	$10,511.76	$29.20	$875.98	0.02%
ZYPREXA TAB 10MG	11	1	$6,422.79	$19.46	$583.89	0.01%
OLANZAPINE TAB 15MG	10	3	$179.51	$0.57	$17.95	0.00%
OLANZAPINE TAB 15MG	7	3	$105.41	$0.53	$15.06	0.00%
ZYPREXA TAB 2.5MG	2	1	$656.34	$10.94	$328.17	0.00%
OLANZAPINE INJ 10MG	1	1	$108.89	$36.30	$108.89	0.00%
ZYPREXA TAB 7.5MG	1	1	$12.32	$0.41	$12.32	0.00%
SUBTOTAL	**19,024**	**5,779**	**$576,622.59**	**$6.67**	**$171.22**	**1.01%**
ZIPRASIDONE PRODUCTS						
ZIPRASIDONE CAP 80MG	2,883	561	$232,745.97	$2.58	$80.73	0.41%
ZIPRASIDONE CAP 40MG	2,421	827	$143,988.46	$1.96	$59.47	0.25%
ZIPRASIDONE CAP 20MG	2,391	897	$160,057.75	$2.27	$66.94	0.28%
ZIPRASIDONE CAP 60MG	1,758	454	$127,382.02	$2.33	$72.46	0.22%
GEODON CAP 80MG	28	9	$6,825.52	$8.13	$243.77	0.01%
GEODON CAP 40MG	16	4	$7,911.69	$16.48	$494.48	0.01%
GEODON INJ 20MG	4	4	$567.91	$81.13	$141.98	0.00%
GEODON CAP 20MG	3	3	$264.84	$2.94	$88.28	0.00%
SUBTOTAL	**9,504**	**2,759**	**$679,744.16**	**$14.73**	**$156.01**	**1.18%**
RISPERIDONE INJECTABLE PRODUCTS						
RISPERDAL INJ 50MG	570	70	$724,351.51	$48.61	$1,270.79	1.27%
RISPERDAL INJ 25MG	333	62	$158,622.72	$23.68	$476.34	0.28%
RISPERDAL INJ 37.5MG	192	41	$184,115.33	$35.81	$958.93	0.32%
RISPERDAL INJ 12.5MG	37	5	$12,305.84	$12.16	$332.59	0.02%
SUBTOTAL	**1,132**	**178**	**$1,079,395.40**	**$30.07**	**$759.66**	**1.89%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
TIER-1 SUBTOTAL	**133,540**	**33,626**	**$4,348,168.33**	**$14.59**	**$350.73**	**7.60%**
TIER-2 UTILIZATION						
ARIPIPRAZOLE ORAL PRODUCTS						
ABILIFY TAB 10MG	5,993	1,646	$5,649,813.07	$29.99	$942.74	9.92%
ABILIFY TAB 5MG	5,474	1,600	$5,001,466.39	$29.69	$913.68	8.78%
ABILIFY TAB 15MG	4,130	1,056	$3,723,303.66	$28.62	$901.53	6.54%
ABILIFY TAB 20MG	3,246	743	$4,367,195.54	$42.38	$1,345.41	7.67%
ABILIFY TAB 30MG	2,409	471	$3,340,944.27	$42.65	$1,386.86	5.87%
ABILIFY TAB 2MG	1,681	468	$1,566,549.52	$30.22	$931.92	2.75%
ARIPIPRAZOLE TAB 10MG	482	421	$336,196.94	$21.26	$697.50	0.59%
ARIPIPRAZOLE TAB 5MG	443	376	$285,123.76	$20.32	$643.62	0.50%
ARIPIPRAZOLE TAB 15MG	301	259	$196,242.79	$20.07	$651.97	0.34%
ARIPIPRAZOLE TAB 20MG	225	205	$232,731.85	$29.86	$1,034.36	0.41%
ARIPIPRAZOLE TAB 30MG	167	138	$160,920.29	$29.61	$963.59	0.28%
ARIPIPRAZOLE TAB 2MG	144	108	$92,683.40	$21.10	$643.63	0.16%
ABILIFY SOL 1MG/ML	84	22	$123,596.10	$52.35	$1,471.38	0.22%
ARIPIPRAZOLE SOL 1MG/ML	11	4	$17,219.80	$52.18	$1,565.44	0.03%
ABILIFY DISC TAB 10MG	9	2	$10,123.11	$37.49	$1,124.79	0.02%
ABILIFY DISC TAB 15MG	6	1	$6,143.61	$36.57	$1,023.94	0.01%
ARIPIPRAZOLE 10MG ODT	1	1	$974.23	$32.47	$974.23	0.00%
ARIPIPRAZOLE 15MG ODT	1	1	$974.23	$32.47	$974.23	0.00%
SUBTOTAL	**24,807**	**7,522**	**$25,112,202.56**	**$32.74**	**$1,010.60**	**44.09%**
PALIPERIDONE INJECTABLE PRODUCTS						
INVEGA SUST INJ 234/1.5	3,260	534	$6,751,979.45	$72.13	$2,071.16	11.86%
INVEGA SUST INJ 156MG/ML	1,745	398	$2,426,777.64	$48.66	$1,390.70	4.26%
INVEGA SUST INJ 117/0.75	449	96	$460,572.91	$35.90	$1,025.77	0.81%
INVEGA TRINZ INJ 819MG	76	54	$479,977.16	$71.55	$6,315.49	0.84%
INVEGA TRINZ INJ 546MG	48	30	$203,752.44	$48.65	$4,244.84	0.36%
INVEGA SUST INJ 78/0.5ML	25	8	$17,357.99	$23.71	$694.32	0.03%
INVEGA TRINZ INJ 410MG	6	4	$19,096.44	$36.58	$3,182.74	0.03%
INVEGA TRINZ INJ 273MG	3	2	$6,365.22	$24.11	$2,121.74	0.01%
INVEGA SUST INJ 39/0.25	2	1	$714.70	$12.76	$357.35	0.00%
SUBTOTAL	**5,614**	**1,127**	**$10,366,593.95**	**$41.56**	**$2,378.23**	**18.20%**
LURASIDONE PRODUCTS						
LATUDA TAB 40MG	2,111	629	$1,946,581.81	$28.18	$922.11	3.42%
LATUDA TAB 80MG	1,599	397	$1,698,542.66	$31.64	$1,062.25	2.98%
LATUDA TAB 20MG	970	330	$785,922.70	$27.59	$810.23	1.38%
LATUDA TAB 120MG	847	180	$1,116,415.49	$41.49	$1,318.08	1.96%
LATUDA TAB 60MG	758	240	$684,316.68	$28.44	$902.79	1.20%
SUBTOTAL	**6,285**	**1776**	**$6,231,779.34**	**$31.47**	**$1,003.09**	**10.94%**
QUETIAPINE EXTENDED-RELEASE PRODUCTS						
SEROQUEL XR TAB 400MG	1,123	182	$1,223,923.08	$33.40	$1,089.87	2.15%
SEROQUEL XR TAB 300MG	1,011	198	$889,559.52	$27.52	$879.88	1.56%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
SEROQUEL XR TAB 200MG	395	101	$198,960.64	$15.63	$503.70	0.35%
SEROQUEL XR TAB 150MG	326	90	$148,315.75	$14.98	$454.96	0.26%
SEROQUEL XR TAB 50MG	270	66	$101,885.11	$12.29	$377.35	0.18%
SUBTOTAL	**3,125**	**637**	**$2,562,644.10**	**$20.76**	**$661.15**	**4.50%**
ARIPIPRAZOLE LAROXIL PRODUCTS						
ARISTADA INJ 441MG	1	1	$1,117.79	$39.92	$1,117.79	0.00%
SUBTOTAL	**1**	**1**	**$1,117.79**	**$39.92**	**$1,117.79**	**0.00%**
ASENAPINE PRODUCTS						
SAPHRIS SUB 10MG	831	223	$608,525.41	$24.18	$732.28	1.07%
SAPHRIS SUB 5MG	499	147	$332,949.12	$22.18	$667.23	0.58%
SAPHRIS SUB 2.5MG	37	21	$24,282.27	$21.04	$656.28	0.04%
SUBTOTAL	**1,367**	**391**	**$965,756.80**	**$22.47**	**$685.26**	**1.69%**
ARIPIPRAZOLE INJECTABLE PRODUCTS						
ABILIFY MAIN INJ 400MG	991	167	$1,691,436.81	$59.49	$1,706.80	2.97%
ABILIFY MAIN INJ 300MG	141	31	$180,526.23	$44.42	$1,280.33	0.32%
SUBTOTAL	**1,132**	**198**	**$1,871,963.04**	**$51.96**	**$1,493.57**	**3.29%**
TIER-2 SUBTOTAL	**42,331**	**11,652**	**$47,112,057.58**	**$34.41**	**$1,192.81**	**82.71%**
TIER-3 UTILIZATION						
PALIPERIDONE ORAL PRODUCTS						
INVEGA TAB 6MG	1,117	247	$1,297,254.57	$39.24	$1,161.37	2.28%
INVEGA TAB 9MG	586	124	$805,093.01	$42.65	$1,373.88	1.41%
INVEGA TAB 3MG	523	152	$488,602.96	$30.49	$934.23	0.86%
PALIPERIDONE TAB ER 6MG	214	121	$192,856.36	$29.66	$901.20	0.34%
PALIPERIDONE TAB ER 3MG	124	67	$86,378.33	$22.40	$696.60	0.15%
PALIPERIDONE TAB ER 9MG	121	63	$129,236.47	$33.59	$1,068.07	0.23%
INVEGA TAB 1.5MG	60	17	$45,566.14	$28.59	$759.44	0.08%
PALIPERIDONE ER 1.5MG	30	14	$16,442.04	$19.55	$548.07	0.03%
SUBTOTAL	**2,775**	**805**	**$3,061,429.88**	**$30.77**	**$930.36**	**5.38%**
ILOPERIDONE PRODUCTS						
FANAPT TAB 8MG	352	50	$309,493.38	$30.08	$879.24	0.54%
FANAPT TAB 6MG	302	58	$269,119.33	$30.71	$891.12	0.47%
FANAPT TAB 12MG	297	43	$407,615.72	$47.00	$1,372.44	0.72%
FANAPT TAB 4MG	198	34	$150,814.43	$25.01	$761.69	0.26%
FANAPT TAB 10MG	106	16	$155,463.74	$51.65	$1,466.64	0.27%
FANAPT TAB 2MG	61	12	$45,997.54	$26.06	$754.06	0.08%
FANAPT TAB 1MG	4	4	$3,325.94	$27.72	$831.49	0.01%
FANAPT PAK	1	1	$122.22	$30.55	$122.22	0.00%
SUBTOTAL	**1,321**	**218**	**$1,341,952.30**	**$33.60**	**$884.86**	**2.35%**
CLOZAPINE ORALLY DISINTEGRATING PRODUCTS						
FAZACLO TAB 100 ODT	311	37	$396,836.08	$49.20	$1,276.00	0.70%
CLOZAPINE TAB 100/ODT	233	27	$172,062.26	$29.76	$738.46	0.30%
FAZACLO TAB 150 ODT	131	11	$123,910.98	$42.13	$945.89	0.22%
FAZACLO TAB 200 ODT	96	15	$172,336.45	$68.85	$1,795.17	0.30%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
FAZACLO TAB 25MG ODT	92	12	$29,439.98	$12.89	$320.00	0.05%
CLOZAPINE TAB 25MG ODT	66	7	$13,799.98	$10.92	$209.09	0.02%
CLOZAPINE TAB 200/ODT	25	6	$43,108.13	$57.40	$1,724.33	0.08%
CLOZAPINE TAB 150/ODT	16	3	$15,901.25	$48.33	$993.83	0.03%
SUBTOTAL	**970**	**118**	**$967,395.11**	**$39.94**	**$1,000.35**	**1.70%**
OLANZAPINE/FLUOXETINE COMBINATION PRODUCTS						
OLANZA/FLUOX CAP 6-25MG	36	5	$13,626.83	$10.48	$378.52	0.02%
OLANZA/FLUOX 12-50MG	32	6	$28,541.41	$21.14	$891.92	0.05%
OLANZA/FLUOX 12-25MG	12	4	$12,570.27	$16.12	$1,047.52	0.02%
OLANZA/FLUOX CAP 6-50MG	12	3	$6,129.30	$11.35	$510.78	0.01%
OLANZA/FLUOX CAP 3-25MG	11	1	$1,870.00	$5.67	$170.00	0.00%
SUBTOTAL	**103**	**19**	**$62,737.81**	**$12.95**	**$599.75**	**0.10%**
CLOZAPINE ORAL SOLUTION PRODUCTS						
VERSACLOZ SUS 50MG/ML	15	2	$20,967.40	$46.59	$1,397.83	0.04%
SUBTOTAL	**15**	**2**	**$20,967.40**	**$46.59**	**$1,397.83**	**0.04%**
BREXPIPRAZOLE PRODUCTS						
REXULTI TAB 2MG	10	6	$9,144.80	$30.48	$914.48	0.02%
REXULTI TAB 1MG	6	3	$4,892.77	$30.58	$815.46	0.01%
REXULTI TAB 0.5MG	2	2	$1,134.65	$25.79	$567.33	0.00%
REXULTI TAB 4MG	2	1	$1,827.36	$30.46	$913.68	0.00%
REXULTI TAB 3MG	1	1	$913.68	$30.46	$913.68	0.00%
SUBTOTAL	**21**	**13**	**$17,913.26**	**$29.55**	**$824.93**	**0.03%**
TIER-3 SUBTOTAL	**5,205**	**1175**	**$5,472,395.76**	**$32.23**	**$939.68**	**9.60%**
TOTAL	**181,076**	**25,862***	**$56,932,621.67**	**$10.31**	**$701.96**	**100%**

*Total number of unduplicated members.

Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

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Appendix L

Fiscal Year 2015 Annual Review of Anthelmintic Medications and 30-Day Notice to Prior Authorize Albenza® (Albendazole) and Emverm™ (Mebendazole)

Oklahoma Health Care Authority
June 2016

Background Information[1,2,3,4,5,6,7]

The anthelmintics are approved for the treatment of nematode (roundworms), cestode (tapeworms), and trematode (flukes) infections. Soil-transmitted helminth infections are among the most common infections worldwide. The most common helminthic infections in the United States are pinworm infections (*Enterobius vermicularis*).

Morbidity due to helminth infections is associated with worm burden: the greater the number of worms, the greater the severity of disease. Most infections are asymptomatic as few worms are present. However, patients infected with a large number of worms can present with a range of symptoms, including abdominal pain, diarrhea, blood and protein loss, rectal prolapse, and physical and cognitive growth retardation. The diagnosis of most helminth infections is based on stool microscopy.

The anthelmintic therapies differ in their mechanism of action. Ivermectin opens glutamate-sensitive chloride channel currents in helminths, resulting in paralysis and death of the parasite. The benzimidazoles (i.e., thiabendazole, mebendazole, albendazole, and triclabendazole) bind to free beta-tubulin and inhibit the polymerization of tubulin and microtubule-dependent glucose uptake. Praziquantel's mechanism of action is unknown; however, in schistosomes, it causes paralysis and tegumental disruption. Pyrantel is a pyrimidine derivative that acts against intestinal nematodes by inducing neuromuscular paralysis.

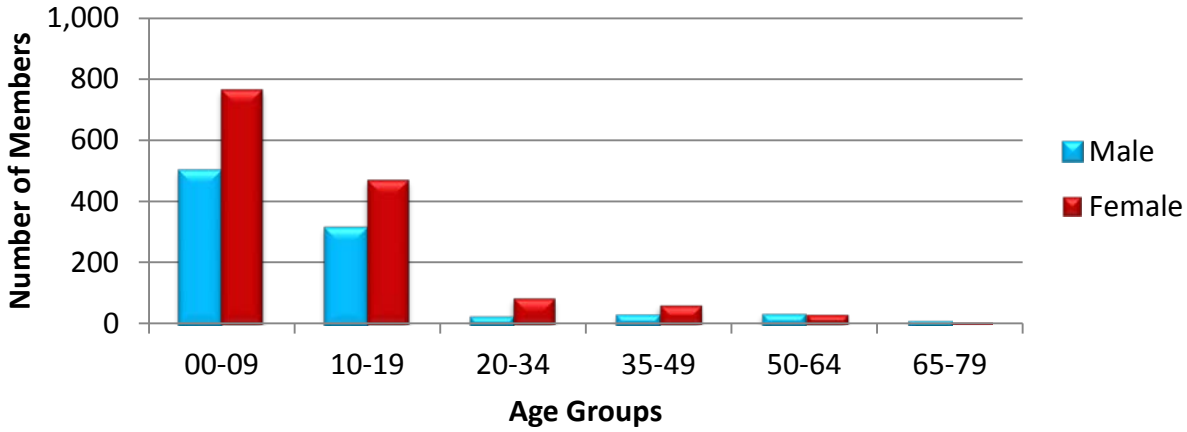
Utilization of Anthelmintic Medications: Fiscal Year 2015

Comparison of Fiscal Years

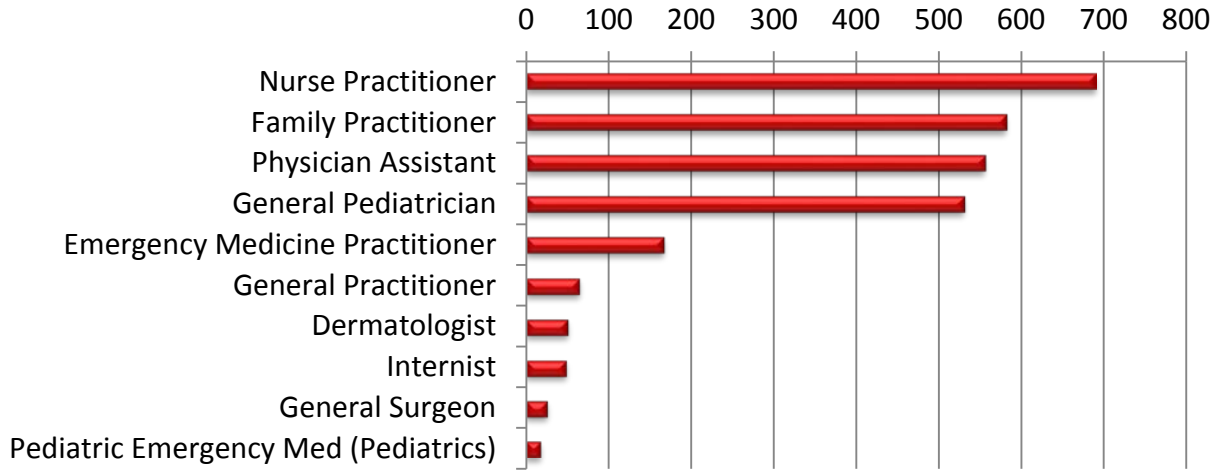
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	2,333	2,693	$570,474.17	$211.84	$25.70	12,551	22,200
2015	2,335	2,814	$920,688.38	$327.18	$40.46	13,325	22,754
% Change	**0.10%**	**4.50%**	**61.40%**	**54.40%**	**57.40%**	**6.20%**	**2.50%**
Change	**2**	**121**	**$350,214.21**	**$115.34**	**$14.76**	**774**	**554**

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

Demographics of Members Utilizing Anthelmintic Medications



Top Prescriber Specialties of Anthelmintic Medications by Number of Claims



Market News and Updates[8]

FDA Approvals:

- In January 2016, the FDA approved Emverm™ (mebendazole), an anthelmintic 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.

Regimen Comparison[9,10,11,12,13,14]

The following table shows 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 1 g as a single dose[+]	<$10[¥]	Approximately 90%
Hookworm (Ancylostoma)	**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

[+]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) unless otherwise noted. 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

Cure rates vary based on source of information. Cure rates in above table found in *Uptodate*.

Albenza® (Albendazole) Product Summary[15]

FDA Approved: June 1996

Indications:

- Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*.
- Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

Dosing:

- Albendazole is available as a 200mg tablet.
- The recommended dosing is listed in the following table:

Indication	Dose	Duration of Therapy
Hydatid disease	• Patients weighing 60kg or greater: 400mg twice a day • Patients weighing less than 60 kg: 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

Mechanism of Action: Albendazole is a synthetic, anthelmintic drug of the benzimidazole class. Albendazole binds to the colchicine-sensitive side of β-tubulin inhibiting their polymerization into microtubules. The decrease in microtubules in the intestinal cells of the parasites decreases their absorptive function. This decreases the uptake of glucose and also depletes glycogen storage. The parasite eventually dies due to insufficient energy for the production of adenosine trisphosphate as a result of insufficient glucose.

Contraindications: Known hypersensitivity to the benzimidazole class of compounds or any components of Albenza®.

Warnings and Precautions:

- Bone marrow suppression
- Teratogenic effects
- Risk of neurologic symptoms in neurocysticercosis
- Risk of retinal damage in patients with retinal neurocysticercosis
- Hepatic effects
- Unmasking of neurocysticercosis in hydatid patients

Adverse Reactions: The adverse reaction profile differs between hydatid disease and neurocysticercosis.

- Hydatid Disease: Adverse reactions occurring in 1% or greater in hydatid disease include abnormal liver function, pain, nausea/vomiting, reversible alopecia, headache, dizziness/vertigo, and fever.
- Neurocysticercosis: Adverse reactions occurring in 1% or greater in neurocysticercosis include headache, nausea/vomiting, raised intracranial pressure, and meningeal signs.

Special Populations:

- Pregnancy: Albendazole is Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women and albendazole should only be used in pregnancy if the potential benefit outweighs the potential risk to the fetus.
- Nursing Mothers: It is not known if albendazole is excreted in human milk; it is excreted in animal milk. Caution should be exercised when albendazole is administered to a nursing woman.
- Pediatric Use: In neurocysticercosis, the efficacy of albendazole in children appears to be similar to in adults. Hydatid disease is uncommon in infants and young children.
- Geriatric Use: There was insufficient data to determine whether the safety and effectiveness of albendazole was different for patients aged 65 and older from that of younger patients.
- Renal Impairment: Albendazole's pharmacokinetics have not been studied in patients with impaired renal function.
- Extra-Hepatic Obstruction: The systemic availability of albendazole was increased in patients with evidence of extra-hepatic obstruction.

Efficacy:

- Albenza® is indicated for the treatment of parenchymal neurocysticercosis due to active lesions of the pork tapework, *Taenia solium.* Lesions considered responsive to therapy with albendazole appear as nonenhancing cysts with no surrounding edema on contrast-enhanced computerized tomography. A 74% to 88% reduction in number of cysts was demonstrated in clinical studies in patients with lesions of this type. A total of 40% to 70% of albendazole treated patients showed resolution of all active cysts.
- Albenza® is also indicated for the treatment of cystic hydatid disease caused by the dog tapeworm, *Echinococcus granulosus*. Combined clinical studies demonstrated non-infectious cysts in approximately 80% to 90% of patients given albendazole for three cycles of therapy of 28 days each. Disappearance of cysts (clinical cure) was seen in approximately 30% of patients and improvement (reduction in cyst diameter of ≥25%) was seen in an additional 40%.

Utilization: During fiscal year 2015, there were 1,780 claims for albendazole.

Emverm™ (Mebendazole) Product Summary[16]

FDA Approved: January 2016

Indications: 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.

Dosing:

- Emverm™ (mebendazole) is available as a 100mg chewable tablet.
- The recommended dosing for mebendazole can be found in the following table:

	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

- If the patient is not cured, a second course of treatment is advised three weeks after initial treatment.

Mechanism of Action: Mebendazole is a broad-spectrum anthelmintic. It inhibits the formation of the worms' microtubules and causes the worms' glucose depletion.

Contraindications: Known hypersensitivity to Emverm™ or any of its components.

Warnings and Precautions:

- Hydatid Disease: There is no evidence that mebendazole is effective for hydatid disease. There have been rare reports of agranulocytosis and neutropenia when mebendazole was taken for prolonged periods and at dosages substantially above those recommended.
- Organ System Functions: During prolonged therapy, periodic assessment of organ system functions, including hematopoietic and hepatic, is advisable.

Adverse Reactions:

- Gastrointestinal: Transient symptoms of abdominal pain and diarrhea have occurred.
- Hypersensitivity: Rash, urticaria, and angioedema have been observed on rare occasions.
- Central Nervous System: Very rare cases of convulsions have been reported.
- Liver: Liver function test elevations and rare reports of hepatitis have occurred when mebendazole was taken for prolonged periods and at dosages substantially above those recommended.
- Hematologic: Neutropenia and agranulocytosis have occurred.

Special Populations:

- Pregnancy: Mebendazole is Pregnancy Category C. In pregnant rats at single doses as low as 10 mg/kg, mebendazole has shown embryotoxic and teratogenic activity. Therefore, mebendazole is not recommended in pregnant women.
- Nursing Mothers: It is not known whether mebendazole is excreted in human milk. Caution should be exercised when mebendazole is administered to a nursing woman, as many drugs are excreted in human milk.
- Pediatric Use: Mebendazole has not been extensively studied in children under two years of age. The relative benefit/risk should be considered in the treatment of children younger than two years of age.

Efficacy: The efficacy of mebendazole varies due to factors such as preexisting diarrhea and gastrointestinal transit time, degree of infection, and helminth strains. The table below shows efficacy rates from various studies.

	Pinworm *(enterobiasis)*	Whipworm *(trichuriasis)*	Common Roundworm *(ascariasis)*	Hookworm
Cure rates mean	95%	68%	98%	96%
Egg reduction mean	-	93%	99%	99%

Cure rates vary based on source of information. Cure rates in above table found in product prescribing information.

Utilization: There has been one paid claim for Emverm™ in the SoonerCare population since its FDA approval in January 2016.

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

Utilization Details of Anthelmintic Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	UNITS/MEMBER	COST/CLAIM
ALBENZA TAB 200MG	1,780	1,501	$893,325.03	5.40	$501.87
STROMECTOL TAB 3MG	671	565	$17,538.59	5.64	$26.14
IVERMECTIN TAB 3MG	352	306	$8,725.46	6.49	$24.79
BILTRICIDE TAB 600MG	10	9	$1,094.56	2.22	$109.46
MEBENDAZOLE POW	1	1	$4.74	30.00	$4.74
GRAND TOTAL	**2,814**	**2,335***	**$920,688.38**	**5.59**	**$327.18**

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

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Appendix M

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

Oklahoma Health Care Authority
June 2016

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

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. The increase in price has led to questions regarding the therapeutic value of H.P. Acthar® Gel, especially in comparison to other potentially therapeutically equivalent and lower-priced alternatives, such as corticosteroids. 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.

Infantile spasms (IS), also known as West syndrome, is a rare epileptic disorder that typically presents in infants between three and seven months of age. The incidence ranges from two to 3.5 per 10,000 live births and occurs more often in boys than girls. The majority of cases occur during the first year of life, but can affect children up to the age of four. In 2010, the Infantile Spasms Working Group (ISWG) established guidelines for the treatment of infantile spasms. There was consensus in the group that use of ACTH is effective as first-line therapy for IS. However, there was insufficient evidence to precisely define the optimum ACTH dose and duration of treatment of IS. Generally, short duration was preferred (i.e., approximately two weeks followed by taper). The group also agreed on the efficacy of vigabatrin (Sabril®) as a first-line treatment option.

H.P. Acthar® Gel was approved in 1978 by the FDA as a short-term treatment for acute exacerbations of MS. Corticosteroids (e.g., methylprednisolone or dexamethasone) are considered treatment of choice for acute exacerbations. H.P. Acthar® Gel is available for those individuals who cannot tolerate the side effects of high dose corticosteroids, have been treated unsuccessfully with corticosteroids in the past, or have difficulty receiving intravenous medication because of poor venous access.

Nephrotic syndrome (NS) is defined by the presence of heavy proteinuria, hypoalbuminemia, and peripheral edema. A variety of diseases damage the kidneys and cause proteinuria in patients with NS. Proteinuria is one of the most important adverse prognostic factors in patients with glomerular disease for progression to end stage renal disease. The goal of treatment includes reducing or eliminating proteinuria. H.P. Acthar® Gel is currently FDA approved for the treatment of inducing diuresis or remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus. The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for glomerulonephritis do not recommend use of ACTH as a steroid-like option for children as there is insufficient data in this population and it is very expensive. For the treatment of membranous nephropathy in adults, the group states that further study is required and the guidelines do not recommend use of ACTH for initial treatment of idiopathic membranous nephropathy.

Utilization of H.P. Acthar® Gel (Corticotropin Injection)

Comparison of Fiscal Years

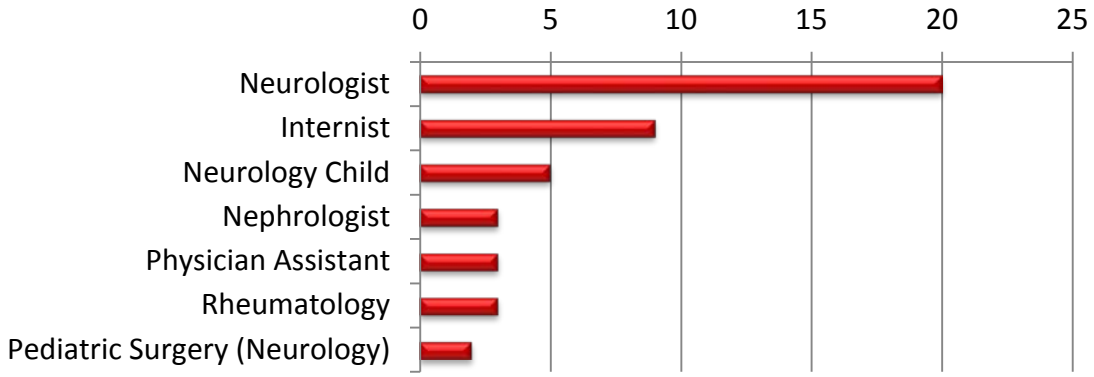
Fiscal Year	Total Members*	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	28	60	$3,826,740.18	$63,779.00	$2,418.93	620	1,582
2015	24	45	$2,949,049.31	$65,534.43	$3,284.02	450	898
% Change	**-14.30%**	**-25.00%**	**-22.90%**	**2.80%**	**35.80%**	**-27.40%**	**-43.20%**
Change	**-4**	**-15**	**-$877,690.87**	**$1,755.43**	**$865.09**	**-170**	**-684**

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

Demographics of Members Utilizing H.P. Acthar® Gel (Corticotropin Injection)

- Detailed demographic information could not be provided due to the small number of SoonerCare members utilizing H.P. Acthar® Gel.

Top Prescriber Specialties of H.P. Acthar® Gel (Corticotropin Injection) By Number of Claims



H.P. Acthar® Gel (Corticotropin Injection) Product Summary[1,8,9,10,11]

FDA Approved: 1952

Indications: H.P. Acthar® Gel is an adrenocorticotropic hormone (ACTH) analogue indicated for the following:

- Treatment of infantile spasms in infants and children under 2 years of age
- Treatment of exacerbations of multiple sclerosis in adults over 18 years of age
- Treatment of nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus to induce diuresis or remission
- May be used for the following disorders and diseases: rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, and edematous states

Dosing:

- H.P. Acthar® Gel is supplied as a 5mL multi-dose vial containing 80 units per mL.
- H.P. Acthar® Gel is a self-injection. It can be injected subcutaneously or intramuscularly.
- In the treatment of infantile spasms, the recommended dose is twice daily intramuscular injections of 75 units/m^2. After two weeks of treatment, the dosing should be gradually tapered and discontinued over a two week period.
- In the treatment of acute exacerbations of multiple sclerosis, daily intramuscular or subcutaneous doses of 80 units to 120 units for two to three weeks may be administered. The dose may need to be tapered.
- In the treatment of other disorders or diseases, dosing will need to be individualized depending on the disease that is being treated and the patient's medical condition. It may be necessary to taper the dose.

Mechanism of Action: The mechanism of action in the treatment of infantile spasms is unknown.

- H.P. Acthar® Gel stimulates the adrenal cortex to secrete cortisol, corticosterone, aldosterone, and a number of weakly androgenic substances. The prolonged administration of large doses of H.P. Acthar® Gel induces hyperplasia and hypertrophy of the adrenal cortex and continuous high output of cortisol, corticosterone, and weak androgens.

Contraindications:

- Intravenous administration
- Patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, uncontrolled hypertension, or sensitivity to proteins of porcine origin.
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of H.P. Acthar® Gel.
- Children under 2 years of age with suspected congenital infections.
- Treatment of conditions listed within the indications section is contraindicated when they are accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction.

Warnings and Precautions:

- Infections: H.P. Acthar® Gel may cause increased susceptibility to new infections and increase risk of exacerbation, dissemination, or reactivation of latent infections. H.P. Acthar® Gel may also mask signs and symptoms of infection.
- Adrenal Insufficiency After Prolonged Therapy: After stopping treatment, the patient should be monitored for effects of hypothalamic-pituitary-axis suppression.
- Cushing's Syndrome: Patients should be monitored for signs and symptoms of Cushing's syndrome which may occur after prolonged therapy.
- Elevated Blood Pressure, Salt and Water Retention, and Hypokalemia: Blood pressure and sodium and potassium levels should be monitored.
- Vaccination: Patients should not receive live or live attenuated vaccines while on immunosuppressive doses.
- Masking of Symptoms of Other Underlying Disease/Disorders: Patients should be monitored for signs of other underlying disease/disorders that may be masked.
- Gastrointestinal Perforation and Bleeding: There is a risk for gastric ulcers and bleeding. Patients should be monitored for signs of perforation and bleeding.
- Behavioral and Mood Disturbances: Behavioral and mood disturbances may include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis.
- Comorbid Diseases: Symptoms of diabetes and myasthenia gravis may be worsened with treatment.
- Ophthalmic Effects: Patients should be monitored for cataracts, infections, and glaucoma.
- Immunogenicity Potential: Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH activity.
- Use in Patients with Hypothyroidism or Liver Cirrhosis: Use in patients with hypothyroidism or liver cirrhosis may result in an enhanced effect.
- Negative Effects on Growth and Physical Development: H.P. Acthar® Gel may have negative effects on growth and physical development. Pediatric patients on long-term therapy should be monitored.
- Decrease in Bone Density: Patients on long-term therapy should be monitored for osteoporosis.
- Use in Pregnancy: H.P. Acthar® Gel has been shown to have an embryocidal effect.

Adverse Reactions:

- The most common adverse effects with H.P. Acthar® Gel are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain.
- In children younger than 2 years of age using the medication, specific adverse reactions include increased risk of infections, hypertension, irritability, Cushingoid symptoms, cardiac hypertrophy, and weight gain.

Special Populations:

- Pregnancy: H.P. Acthar® Gel has been shown to have an embryocidal effect and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Nursing Mothers: It is not known whether H.P. Acthar® Gel is excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the medication, considering the risk and benefit to the mother.
- Pediatric Use: H.P. Acthar® Gel is indicated as monotherapy for the treatment of infantile spasms in infants and children less than 2 years of age. The types of adverse reactions seen in infants and children younger than 2 years of age are similar to those seen in older patients; however, their frequency and severity may be different due to the very young age of the infant, underlying disorders, duration of therapy, and dosage regimen. The effects on growth are of particular concern.

Efficacy:

- Infantile Spasms: For the treatment of infantile spasms, the effectiveness of H.P. Acthar® Gel was demonstrated in a single blinded clinical trial. Patients were randomized to receive either a two week course of treatment with H.P. Acthar® Gel or prednisone (1 mg/kg by mouth twice daily). The primary outcome was a comparison of the number of patients in each group who were treatment responders, defined as having complete suppression of both clinical spasms and hypsarrhythmia on a full sleep cycle video electroencephalogram (EEG) performed two weeks following treatment initiation, rated by an investigator blinded to treatment. Thirteen of the fifteen patients responded to H.P. Acthar® Gel as compared to four of fourteen patients given prednisone ($p<0.002$).
- Acute Exacerbations of MS: For the treatment for acute exacerbations of MS, the effectiveness has been demonstrated in clinical trials. In one study, the efficacy of H.P. Acthar® Gel was compared to intravenous methylprednisolone (IVMP). Both ACTH and IVMP were shown to be effective in MS relapses; however, there was no difference between groups in the final outcome in acute relapse or in the rate of recovery.
- Glomerular Diseases: For the treatment glomerular diseases, a prospective, non-blinded, open-label trial of 15 patients was conducted to assess the safety and efficacy of H.P. Acthar® Gel. Patients were treated with H.P. Acthar® Gel for 24 weeks, doses at 40 units twice-weekly for two weeks, then 80 units twice-weekly thereafter. A total of 8 of 15 patients with various nephrotic syndrome etiologies saw a reduction in proteinuria. The authors reported study limitations including the small sample size, lack of control group, and most patients were on multiple therapies, therefore clinical outcomes may not be solely attributable to H.P. Acthar® Gel.
- Corticosteroid-Responsive Conditions: In corticosteroid-responsive conditions, there are a lack of clinical studies comparing the effectiveness of H.P. Acthar® Gel to corticosteroids. There is also no reliable evidence of the effectiveness of H.P. Acthar® Gel in persons who have failed to respond to corticosteroids.

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[¥]

[+]EAC = estimated acquisition cost

*State Maximum Allowable Cost (SMAC)

[◊]Dosing regimen based on 80units 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.

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[11] Gettig J, Cummings JP, Matuszewski K. H.P. Acthar Gel and Cosyntropin Review: Clinical and Financial Implications. *Pharmacy and Therapeutics*. 2009; 34(5):250-257.

Appendix N

Calendar Year 2015 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)

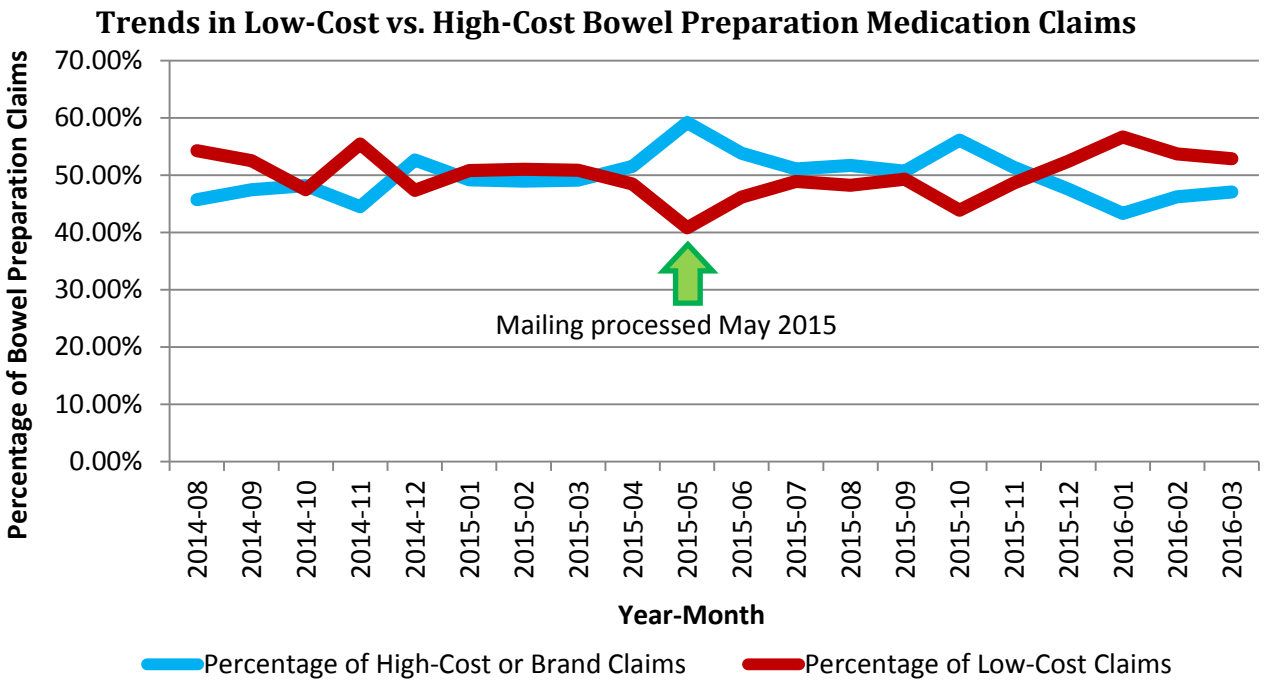
Oklahoma Health Care Authority
June 2016

Introduction

In May 2015, an educational letter was sent to prescribers of bowel preparation medications in the previous six months. The mailing included general cost information for brand products in comparison to generic products and suggestions to maximize the pharmacy benefit through generic and over-the-counter utilization. Prescribers were eligible for inclusion in the mailing if they had prescribed a bowel preparation medication for a SoonerCare member from October 1, 2014 to March 31, 2015. A total of 369 prescribers were flagged for having at least one patient with a paid claim for a bowel preparation medication. These prescribers accounted for 1,547 flagged patients. All flagged prescribers were included in the mailing.

The following chart shows the trends in percentage of claims comparing higher cost bowel preparation medication utilization to lower cost medications. Higher cost bowel preparation medications include MoviPrep®, OsmoPrep®, Prepopik®, Suclear®, and SUPREP®. Following the mailing, an immediate decline in higher cost bowel preparation medications was seen in June and July 2015 as well as a corresponding increase in utilization of lower cost bowel preparation medications. The effect of the mailing declined in subsequent months. More recently, since October of 2015 an increase in percentage of lower cost bowel preparation medications can be seen indicating more cost-effective prescribing.

While an encouraging trend in lower cost bowel preparation medication utilization was seen following the educational mailing, further review in the bowel preparation medication class is necessary. 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.



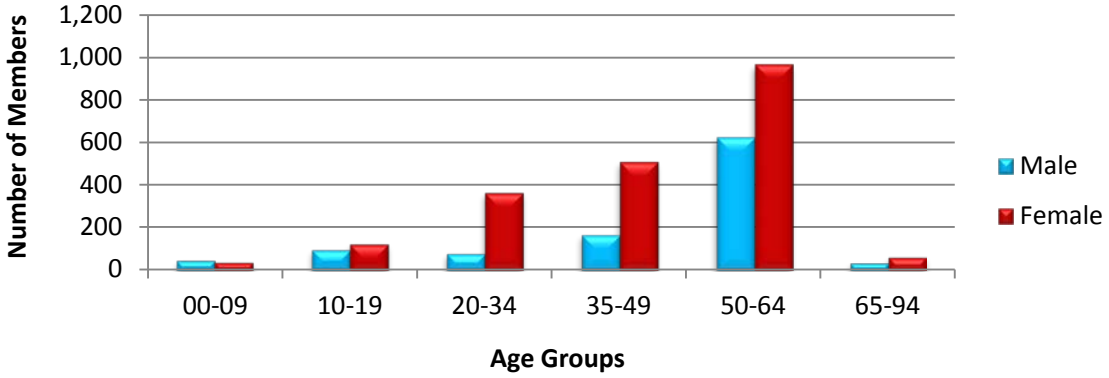
Utilization of Bowel Preparation Medications: Calendar Year 2015

Comparison of Calendar Years

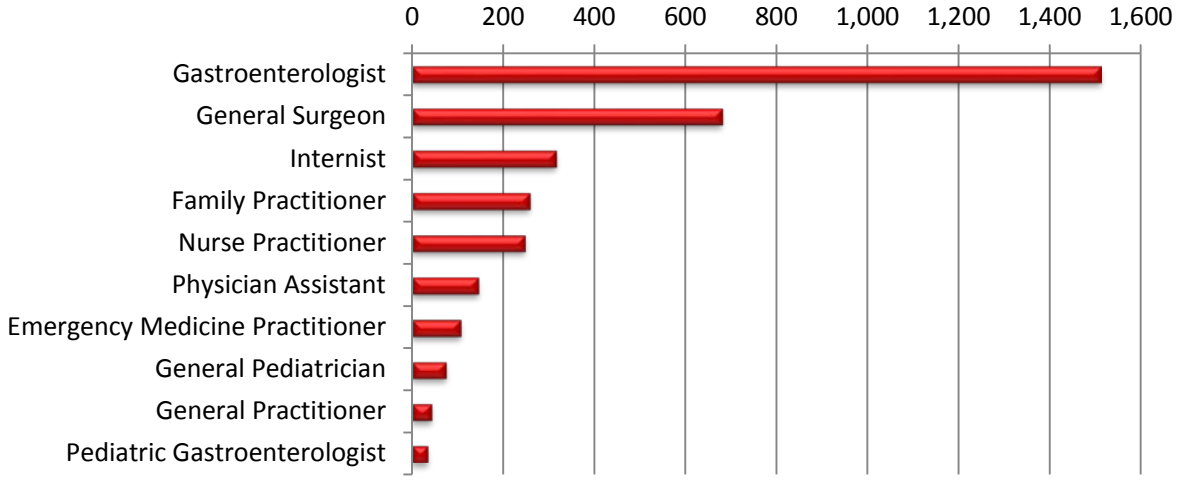
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	3,270	3,770	$179,393.23	$47.58	$13.55	8,612,446	13,241
2015	3,110	3,493	$188,449.92	$53.95	$15.03	6,983,403	12,536
% Change	**-4.90%**	**-7.30%**	**5.00%**	**13.40%**	**10.90%**	**-18.90%**	**-5.30%**
Change	**-160**	**-277**	**$9,056.69**	**$6.37**	**$1.48**	**-1,629,043**	**-705**

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

Demographics of Members Utilizing Bowel Preparation Medications



Top Prescriber Specialties of Bowel Preparation Medications by Number of Claims



Market News and Updates[1]

Anticipated Patent Expirations:

- SUPREP® (sodium sulfate/potassium sulfate/magnesium sulfate): March 2023
- MoviPrep® (PEG-3350/sodium sulfate/sodium chloride/potassium chloride/sodium ascorbate/ascorbic acid): September 2024
- OsmoPrep® (sodium phosphate monobasic/sodium phosphate dibasic): June 2028
- Prepopik® (sodium picosulfate/magnesium oxide/citric acid): October 2028

Bowel Preparation Medications Summary[2,3,4,5]

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

Guideline Recommendations:

- The success of the colonoscopy procedure is linked closely to the adequacy of the preprocedure bowel cleansing. The diagnostic accuracy and therapeutic safety of colonoscopy depends, in part, on the quality of the colonic cleansing or preparation.
- Patient education significantly improves the quality of bowel preparation.
- Split-dose regimens result in higher-quality colonoscopy examination compared with single-dose, one day regimens. In addition, split-dose regimens improve patient tolerance.
- A split-dose regimen of 4-liters of polyethylene glycol electrolyte lavage solution provides high quality bowel cleansing.
- Sodium phosphate and magnesium citrate preparations should not be used in the elderly or patients with renal disease.

OsmoPrep® (Sodium Phosphate Monobasic/Sodium Phosphate Dibasic) Product Summary[6]

Indications: OsmoPrep® (sodium phosphate monobasic/sodium phosphate dibasic) is an osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults 18 years of age or older.

Boxed Warning: There have been rare, but serious reports of acute phosphate nephropathy in patients who received oral sodium phosphate products for colon cleansing prior to colonoscopy. Some cases have resulted in permanent impairment of renal function and some patients required long-term dialysis. While some cases have occurred in patients without identifiable risk factors, patients at increased risk of acute phosphate nephropathy may include those with increased age, hypovolemia, increased bowel transit time (such as bowel obstruction), active colitis, or baseline kidney disease, and those using medicines that affect renal perfusion or function (such as diuretics, angiotensin converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and possibly nonsteroidal anti-inflammatory drugs [NSAIDs]). It is important to use the dose and dosing regimen as recommended (pm/am split dose).

Dosing:

- OsmoPrep® is available as oral tablets contacting 1.5g of sodium phosphate.
- The recommended dose of OsmoPrep® is 32 tablets (48 grams of sodium phosphate) taken by mouth with a total of two quarts of clear liquids. The 32 tablet regimen should be administered two separate dosing times:
    - The evening before the colonoscopy: Take four tablets with eight ounces of clear liquids every fifteen minutes for a total of twenty tablets.
    - On the day of the colonoscopy: Starting three to five hours before the procedure, take four tablets with eight ounces of clear liquids every fifteen minutes for a total of 12 tablets.
- Patients should not use OsmoPrep® for colon cleansing within seven days of previous administration.

Prepopik® (Sodium Picosulfate/Magnesium Oxide/Citric Acid) Product Summary[7]

Indications: Prepopik® (sodium picosulfate/magnesium oxide/citric acid) is a combination of sodium picosulfate, a stimulant laxative, and magnesium oxide and anhydrous citric acid which form magnesium citrate, an osmotic laxative, indicated for cleansing of the colon as a preparation for colonoscopy in adults.

Dosing:

- Prepopik® is available as an oral powder that must be reconstituted with cold water right before its use. The powder is supplied in a kit containing two packets (orange or cranberry flavored), along with a pre-marked dosing cup. Each packet contains 10mg sodium, picosulfate, 3.5g magnesium oxide, and 12g anhydrous citric acid.
- Prepopik® powder should be reconstituted right before each administration by filling the supplied dosing cup with cold water up to the lower (5-ounce) line, pouring in the contents of one packet of Prepopik® powder, and stirring the mixture.
- Prepopik® can be dosed via two different dosing regimens:
    - The preferred method is the "Split-Dose" method:
        - The first dose should be taken the evening before the colonoscopy (e.g., 5:00 to 9:00PM) followed by five 8-ounce drinks of clear liquids before bed.
        - The second dose should be taken the next day approximately five hours before the colonoscopy followed by at least three 8-ounce drinks of clear liquids before the colonoscopy.
    - The alternative method is the "Day Before" method:
        - The first dose should be taken in the afternoon or early evening (e.g., 4:00 to 6:00PM) before the colonoscopy followed by five 8-ounce drinks of clear liquids before the next dose.
        - The second dose should be taken approximately six hours later in the late evening (e.g., 10:00PM to 12:00AM), the night before the colonoscopy followed by three 8-ounce drinks of clear liquids before bed.

Suclear® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/PEG-3350/Sodium Chloride/Sodium Bicarbonate/Potassium Chloride) Product Summary[8]

Indications: Suclear® (sodium sulfate/potassium sulfate/magnesium sulfate/PEG-3350/sodium chloride/sodium bicarbonate/potassium chloride) is a combination of osmotic laxatives indicated for cleansing of the colon in preparation for colonoscopy in adults.

Dosing:

- Suclear® is available as kit containing one 6-ounce bottle of oral solution (containing sodium sulfate, potassium sulfate, and magnesium sulfate), one 16-ounce mixing container, one 2-liter jug with powder for oral solution (containing polyethylene glycol 3350, sodium chloride, sodium bicarbonate, and potassium chloride), and four flavor packets.
- Suclear® should be prepared for administration in two separate doses. The first dose is prepared by diluting the 6-ounce bottle of oral solution with water in the 16-ounce mixing

container to a volume of 16-ounces; the second dose requires diluting the powder in the 2-liter jug with water to a volume of 2-liters.

- Suclear® can be dosed via two different dosing regimens:
  - The preferred method is the "Split-Dose" method:
    - First Dose: The evening before the colonoscopy (10 to 12 hours prior to second dose) patients should dilute the 6-ounce oral solution to a volume of 16-ounces and drink the contents. Patients should then refill the container with 16-ounces of water and drink it over the next two hours. Patients should again refill the container with 16-ounces of water and finish drinking it before going to bed.
    - Second Dose: The following morning on the day of the colonoscopy (patients should start at least 3 ½ hours prior to colonoscopy) patients should dissolve the powder of the second dose by adding water to the 2-liter jug. Using the 16-ounce container provided, patients should drink the entire 2-liter solution in the jug at a rate of one 16-ounce container every 20 minutes (this is four 16-ounce containers over a period of one and a half hours).
  - The alternative method is the "Day Before" method:
    - First Dose: On the evening before the colonoscopy (at least 3 ½ hours prior to bedtime) patients should dilute the 6-ounce oral solution to a volume of 16-ounces and drink the contents. Patients should then refill the container with 16-ounces of water and drink it over the next two hours.
    - Second Dose: Approximately 2 hours after starting the first dose, patients should dissolve the powder of the second dose by adding water to the 2-liter jug. Using the 16-ounce container provided, patients should drink the entire 2-liter solution in the jug at a rate of one 16-ounce container every 20 minutes (this is four 16-ounce containers over a period of one and a half hours). Patients should again refill the container with 16-ounces of water to the fill line and finish drinking it before going to bed.

SUPREP® (Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate) Product Summary[9]

Indications: SUPREP® (sodium sulfate/potassium sulfate/magnesium sulfate) is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.

Dosing:

- SUPREP® is available as a kit containing two 6-ounce bottles of oral solution (each containing sodium sulfate 17.5g, potassium sulfate 3.13g, and magnesium sulfate 1.6g) and one 19-ounce mixing container with a 16-ounce fill line.
- Each bottle of SUPREP® oral solution should be administered as 16-ounces of diluted SUPREP® solution with an additional 1 quart of water taken orally.
- SUPREP® should be taken as a split-dose oral regimen:
  - Day prior to colonoscopy: Early in the evening prior to colonoscopy patients should pour the contents of one bottle of SUPREP® into the mixing container provided, dilute with water to the 16-ounce fill line, and drink the entire amount. Patients

should then drink two additional containers filled to the 16-ounce line with water over the next hour.

- Day of colonoscopy: The morning of colonoscopy (10 to 12 hours after the evening dose) patients should prepare the bottle of SUPREP®, and drink the entire amount. Patients should then drink two additional containers filled to the 16-ounce line with water over the next hour.

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.

Utilization Details of Bowel Preparation Medications: Calendar Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Client	Cost/ Claim
Polyethylene Glycol Electrolyte Solution Products					
MOVIPREP SOL	663	635	$55,216.11	1.04	$83.28
GAVILYTE-G SOL	626	530	$10,640.93	1.18	$17.00
PEG 3350 SOL ELECTROL	296	250	$3,525.48	1.18	$11.91
GAVILYTE-N SOL FLAV PK	200	190	$3,502.11	1.05	$17.51
PEG-3350/KCL SOL /SODIUM	175	154	$3,488.59	1.14	$19.93
PEG-3350 SOL ELECTROL	158	143	$2,495.24	1.1	$15.79
GAVILYTE-C SOL	62	50	$1,196.46	1.24	$19.30
TRILYTE SOL	56	52	$1,148.21	1.08	$20.50
GOLYTELY SOL	48	45	$997.20	1.07	$20.78
COLYTE/FLAVR SOL PACKS	22	21	$1,054.72	1.05	$47.94
GOLYTELY SOL	14	14	$204.89	1	$14.64
Subtotal	**2,320**	**2,025**	**$83,469.94**	**1.15**	**$35.98**
Sodium Sulfate Products					
SUPREP BOWEL SOL PREP	985	941	$81,328.09	1.05	$82.57
Subtotal	**985**	**941**	**$81,328.09**	**1.05**	**$82.57**
Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid Products					
PREPOPIK PAK	134	130	$14,797.01	1.03	$110.43
Subtotal	**134**	**130**	**$14,797.01**	**1.03**	**$110.43**
Sodium Phosphate Oral Products					
OSMOPREP TAB 1.5GM	54	51	$8,854.88	1.06	$163.98
Subtotal	**54**	**51**	**$8,854.88**	**1.06**	**$163.98**
Total	**3,493**	**3,110***	**$188,449.92**	**1.12**	**$53.95**

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

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[6] OsmoPrep® Prescribing Information. Salix Pharmaceuticals, Inc. Available online at: https://shared.salix.com/shared/pi/osmoprep-pi.pdf?id=8251081. Last revised 10/2012. Last accessed 05/2016.
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Appendix O

Fiscal Year 2015 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)

Oklahoma Health Care Authority
June 2016

Introduction

Multiple formulations of medications are made for ease of administration, to increase bioavailability, or as new technologies created to provide a more efficient treatment response. Some of the new formulations incur greater costs for production resulting in greater costs for the payer and consumer. Clinical review of each product and its comparative cost to other formulations are provided in the following report for reference.

Current Prior Authorization Criteria

Sitavig® (Acyclovir Buccal Tablets) Approval Criteria:

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

Rasuvo® (Methotrexate Injection) and Otrexup™ (Methotrexate Injection) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
    a. Adults with severe, active rheumatoid arthritis (RA); or
    b. Children with active polyarticular juvenile idiopathic arthritis (pJIA); or
    c. Severe, recalcitrant, disabling psoriasis confirmed by biopsy or dermatologic consultation; and
2. Members with a diagnosis of RA or pJIA must have had an adequate trial of full dose NSAIDs; and
3. A patient-specific, clinically significant reason why the oral tablets or the generic injectable formulation cannot be used.

Purixan® (Mercaptopurine Oral Suspension) Approval Criteria:

1. An FDA approved diagnosis of acute lymphoblastic leukemia (ALL); and
2. An age restriction on members older than 10 years of age will apply. Members 10 years of age and younger would not require prior authorization for Purixan® therapy; and
3. Members older than 10 years of age would require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

Utilization of Special Formulations: Fiscal Year 2015

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	4	15	$11,144.94	$743.00	$24.33	1,030	458

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
There was no utilization of any of the prior authorized special formulations contained in this report during fiscal year 2014. The above table contains utilization of Purixan®. There was no utilization of Sitavig®, Rasuvo®, or Otrexup® during fiscal year 2015.

Demographics of Members Utilizing Special Formulations

- Due to the small number of members utilizing special formulations detailed demographic information cannot be provided.

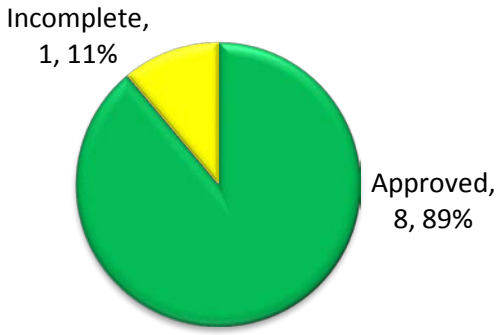
Top Prescriber Specialties of Special Formulations by Number of Claims

- The only prescriber specialty of special formulations during fiscal year 2015 was pediatric hematology/oncology.

Prior Authorization of Special Formulations

There were 9 prior authorization requests submitted for special formulations during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



Nuvessa™ (Metronidazole Vaginal Gel 1.3%) Product Summary [1,2,3]

Indication: Nuvessa™ (metronidazole vaginal gel 1.3%) is a nitroimidazole antimicrobial indicated for the treatment of bacterial vaginosis in non-pregnant women.

Dosing and Administration:

- Nuvessa™ is available as a vaginal gel containing 65mg of metronidazole in 5g of gel (1.3%) in a prefilled applicator.
- Nuvessa™ should be administered as a single-dose via prefilled, disposable applicator intravaginally once at bedtime.

Other Formulations Available:

- Metronidazole Vaginal Gel 0.75%:
  - Metronidazole vaginal gel 0.75% is indicated for the treatment of bacterial vaginosis and is dosed once or twice daily for five days. Metronidazole vaginal gel 0.75% is available generically and is supplied in a 70g tube.
- Metronidazole 500mg Oral Tablet:
  - Twice daily oral administration of metronidazole 500mg for seven days is recommended by the Centers for Disease Control and Prevention (CDC) for the treatment of bacterial vaginosis. Metronidazole is available as a generic oral tablet.

Formulation Cost Comparison:

Product	Cost Per Gram	Dosing	Cost Per Treatment Course
Nuvessa™ (metronidazole vaginal gel 1.3%)	**$35.68[+]**	**5 grams one time**	**$178.40**
metronidazole vaginal gel 0.75%[Δ]	$1.31*	5 grams QD to BID for 5 days	$91.70
metronidazole 500mg oral tablet	$0.46*	500mg orally BID for 7 days	$6.44

Costs do not reflect rebated prices or net costs.
[+] Estimated acquisition cost (EAC)
*State maximum allowable cost (SMAC)
[Δ] Metronidazole vaginal gel has increased in price from $24.50 per 70 gram tube to $91.70 per 70 gram tube.
QD: Daily, BID: Twice daily

Fiscal Year 2015 Utilization: There was no utilization of Nuvessa™ during fiscal year 2015. A total of 1,227 members utilized metronidazole 0.75% gel during fiscal year 2015 accounting for 1,527 claims.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
VAGINAL METRONIDAZOLE PRODUCTS						
METRONIDAZOL GEL 0.75%VAG	1,431	1,150	$34,940.71	$2.30	1.24	$24.42
VANDAZOLE GEL 0.75%	94	81	$2,415.06	$2.91	1.16	$25.69
METROGEL-VAG GEL 0.75%	2	2	$57.00	$5.70	1	$28.50
SUBTOTAL	**1,527**	**1,227**	**$37,412.77**	**$2.34**	**1.24**	**$24.50**
ORAL METRONIDAZOLE PRODUCTS						
METRONIDAZOLE TAB 500MG	19,336	15,862	$202,356.17	$1.43	1.22	$10.47
SUBTOTAL	**19,336**	**15,862**	**$202,356.17**	**$1.43**	**1.22**	**$10.47**
TOTAL	**20,863**	**16,619***	**$239,768.94**	**$1.53**	**1.26**	**$11.49**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Metronidazole oral tablets have multiple indications; not all claims are for the diagnosis of bacterial vaginosis.

Zyclara® (Imiquimod 3.75% and 2.5% Cream) Product Summary [4,5]

Indication: Zyclara® (imiquimod 3.75% and 2.5% cream) is an immune cell activator indicated for the following:

- Topical treatment of clinically typical, visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.
- Topical treatment of external genital and perianal warts/condyloma acuminata (EGW) in patients 12 years and older.

Limitation of Use: Efficacy of imiquimod cream was not demonstrated for molluscum contagiosum in children 2 to 12 years of age.

Dosing and Administration:

- Zyclara® is available as 3.75% and 2.5% cream. Both strengths are available in a 30mL pump containing no less than 28 full actuations. The 3.75% strength is also available in single-use packets supplied in a box of 28.
- Zyclara® is for topical use only.
- The following recommended dosing regimens apply:
  - Actinic Keratosis:
    - Zyclara® should be 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. Up to 0.5 grams (two packets or two full actuations of the pump) of Zyclara® may be applied to the treatment area at each application. Zyclara® should be left on the skin for approximately eight hours, after which time the cream should be removed by washing the area with mild soap and water.
    - Local skin reactions in the treatment area are common. A rest period of several days may be taken if required by the patient's discomfort or severity of the local skin reaction. However, neither 2-week treatment cycle should be extended due to missed doses or rest periods.
    - Package labeling recommends prescribing no more than two boxes (56 packets) or two 7.5g pumps for the total 2-cycle treatment course.
  - External Genital Warts:
    - Zyclara® should be applied once daily to the external genital/perianal warts until total clearance or up to eight weeks. Patients should use up to 0.25 grams (one packet or one full actuation of the pump) at each application. Zyclara® should be applied prior to normal sleeping hours and left on the skin for approximately eight hours, then removed by washing the area with mild soap and water.
    - Local skin reactions at the treatment site are common, and may necessitate a rest period of several days. Non-occlusive dressings such as cotton gauze or cotton underwear may be used in the management of skin reactions.
    - Package labeling recommends prescribing up to two boxes (56 packets) or two 7.5 g pumps for the total treatment course. Use of excessive amounts of cream should be avoided.

Other Formulations Available:

- Imiquimod 5% Cream:
  - Imiquimod 5% cream is indicated for the treatment of Actinic Keratosis and external genital warts. Imiquimod 5% cream is available generically and is supplied in single use packets supplied in a box of 24.
  - For the diagnosis of Actinic Keratosis, imiquimod 5% cream is dosed as no more than one packet applied to the treatment area two times per week for a full 16 weeks. Package labeling states patients should be prescribed no more than 36 packets for the 16-week treatment period.
  - For the diagnosis of external genital warts, imiquimod 5% cream should be applied to the treatment area three times per week until there is clearance of the genital/perianal warts or for a maximum of 16 weeks. Imiquimod 5% cream is packaged in single-use packets which contain sufficient cream to cover a wart area of up to 20 cm^2; use of excessive amounts of cream should be avoided.

Formulation Cost Comparison:

Product	Cost Per Packet or Gram	Actinic Keratosis Dosing	Cost Per Treatment Course
Zyclara® (imiquimod 3.75% cream packets)	**$39.11[+]**	**2 packs daily for two 2-week periods**	**$2,190.16**
Zyclara® (imiquimod 3.75% and 2.75% cream supplied in a 7.5g pump)	**$146.02[+]**	**2 actuations daily for two 2-week periods**	**$2,190.30**
imiquimod 5% cream packet	$5.25*	1 pack twice weekly for 16 weeks	$252.00[Δ]

Costs do not reflect rebated prices or net costs.
[+]Estimated acquisition cost (EAC)
*State maximum allowable cost (SMAC)
[Δ] Cost for treatment reflects cost of 48 packets (even though only 32 packets are needed) to account for a pharmacy dispensing a package size of 24 packets at a time.

Fiscal Year 2015 Utilization: A total of 19 members utilized Zyclara® during fiscal year 2015. A total of 694 members utilized imiquimod 5% cream during fiscal year 2015 accounting for 873 claims.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
BRANDED IMIQUIMOD PRODUCTS						
ZYCLARA PUMP CRE 2.5%	12	7	$11,889.29	$30.33	1.71	$990.77
ZYCLARA PUMP CRE 3.75%	7	7	$7,259.54	$29.75	1	$1,037.08
ZYCLARA CRE 3.75%	7	5	$6,830.99	$34.15	1.4	$975.86
SUBTOTAL	**26**	**19**	**$25,979.82**	**$31.08**	**1.37**	**$999.22**
GENERIC IMIQUIMOD PRODUCTS						
IMIQUIMOD CRE 5%	873	694	$120,751.31	$3.36	1.26	$138.32
SUBTOTAL	**873**	**694**	**$120,751.31**	**$3.36**	**1.26**	**$138.32**
TOTAL	**899**	**711***	**$146,731.13**	**$3.99**	**1.26**	**$163.22**

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

Kristalose® (Lactulose Packets for Oral Solution) Product Summary [6,7,8]

Indication: Kristalose® (lactulose packets for oral solution) is a colonic acidifier indicated for the treatment of constipation. In patients with a history of constipation, lactulose therapy increases the number of bowel movements per day and the number of days on which bowel movements occur.

Dosing and Administration:

- 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 of Kristalose® is 10g to 20g of lactulose daily. The dose may be increased to 40g daily if necessary.
- Patients should be instructed to dissolve the contents of one packet in half a glass (four ounces) of water and drink the solution by mouth once daily.
- Twenty-four to 48 hours may be required to produce a normal bowel movement.

Other Formulations Available:

- Lactulose 10g/15mL Oral Solution:
  - Lactulose 10g/15mL oral solution is indicated for the treatment of constipation and for the prevention and treatment of portal-systemic encephalopathy, including the stages of hepatic pre-coma and coma.
  - Lactulose 10g/15mL oral solution is available as an oral solution in various bottle sizes ranging from 8 ounces to 64 ounces. It is also available in 1 ounce unit dose cups.
  - The usual dose of lactulose 10g/15mL oral solution is 15mL to 30mL, containing 10g to 20g, daily. The dose may be increased to 60mL (40g) if necessary.

Formulation Cost Comparison:

Product	Cost Per Packet or mL	Dosing	Cost for 30 Days
Kristalose® 10g (lactulose packets for oral solution)	**$6.51[+]**	**10g to 40g daily**	**$195.30-$781.20**
Kristalose® 20g (lactulose packets for oral solution)	**$6.90[+]**	**10g to 40g daily**	**$206.70-$413.40**
lactulose 10g/15mL oral solution supplied in a bottle or unit dose cup	$0.02*	10g to 40g daily	$9.00-$36.00

Costs do not reflect rebated prices or net costs.
[+]Estimated acquisition cost (EAC)
*State maximum allowable cost (SMAC)

Fiscal Year 2015 Utilization: A total of 4 members utilized Kristalose® during fiscal year 2015. A total of 3,475 members utilized lactulose 10g/15mL oral solution during fiscal year 2015 accounting for 8,585 claims.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
KRISTALOSE PRODUCTS						
KRISTALOSE PAK 20GM	10	3	$3,376.74	$11.26	3.33	$337.67
KRISTALOSE PAK 10GM	7	1	$2,557.62	$12.18	7	$365.37
SUBTOTAL	**17**	**4**	**$5,934.36**	**$11.64**	**4.25**	**$349.08**
OTHER LACTULOSE PRODUCTS						
LACTULOSE SOL 10GM/15	5,717	2,423	$90,903.52	$0.73	2.36	$15.90
GENERLAC SOL 10GM/15	1,747	953	$25,809.37	$0.68	1.83	$14.77
LACTULOSE SOL 10GM/15	550	183	$13,777.26	$1.12	3.01	$25.05
ENULOSE SOL 10GM/15	545	91	$9,956.27	$1.06	5.99	$18.27
CONSTULOSE SOL 10GM/15	26	15	$330.85	$0.56	1.73	$12.73
SUBTOTAL	**8,585**	**3,475**	**$140,777.27**	**$0.77**	**2.47**	**$16.40**
TOTAL	**8,602**	**3,478***	**$146,711.63**	**$0.80**	**2.47**	**$17.06**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Lactulose oral solution is also indicated for hepatic encephalopathy; not all claims are for the diagnosis of constipation.

Recommendations

The College of Pharmacy recommends the prior authorization of Nuvessa™ (metronidazole vaginal gel 1.3%), Zyclara® (imiquimod) 2.5% and 3.75% cream, 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%).

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 acuminate (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 member cannot use the liquid lactulose formulation.

[1] Nuvessa™ Product Information. Allergan. Available online at: http://www.allergan.com/assets/pdf/nuvessa_pi. Last revised 01/2015. Last accessed 05/2016.
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Appendix P

Fiscal Year 2015 Annual Review of Topical Antifungal Products and 30-Day Notice to Prior Authorize Econazole Nitrate 1% Cream and Clotrimazole 1% Solution

Oklahoma Health Care Authority
June 2016

Current Prior Authorization Criteria

Topical Antifungal Medications		
Tier-1	**Tier-2**	**Special PA**
ciclopirox cream	butenafine (Mentax®)	efinaconazole (Jublia®)
clotrimazole (Rx) cream, solution	ciclopirox solution, shampoo, gel, suspension (Penlac® and Loprox®)	tavaborole (Kerydin™)
clotrimazole (OTC)* cream	clotrimazole/betamethasone cream, lotion	
econazole cream	ketoconazole foam (Extina®)	
ketoconazole cream, shampoo	ketoconazole gel (Xolegel™)	
nystatin cream, ointment, powder	luliconazole cream (Luzu™)	
terbinafine (OTC)* cream	miconazole/zinc oxide/white petrolatum (Vusion®)	
tolnaftate (OTC)*cream	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 to 20 years of age without prior authorization.

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 or clotrimazole/ betamethasone requires a patient-specific, clinically significant reason why the member cannot use the individual components separately.
4. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).

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

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

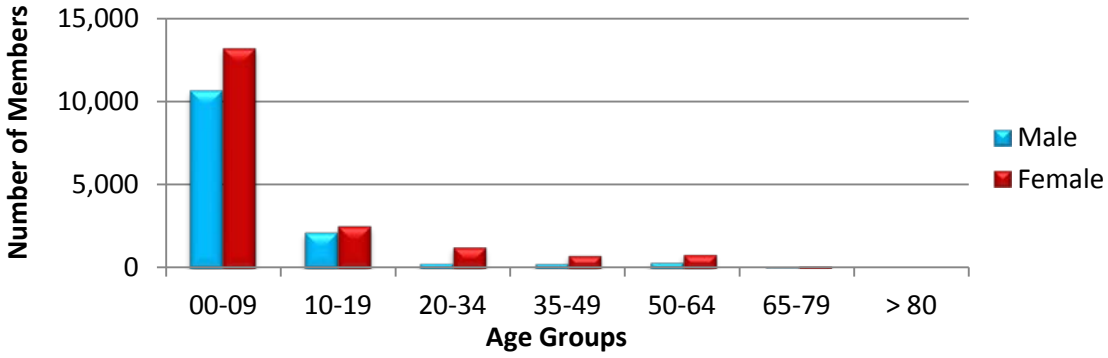
Utilization of Topical Antifungal Products: Fiscal Year 2015

Comparison of Fiscal Years

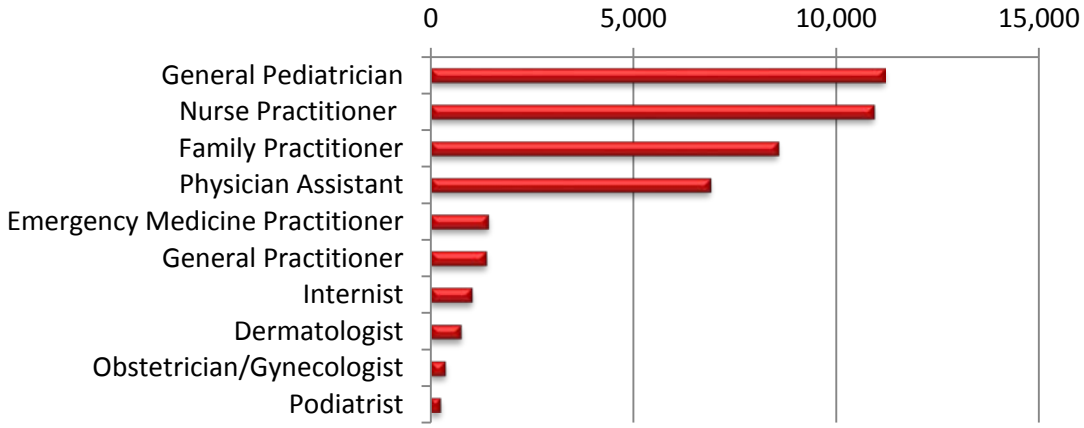
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	33,523	47,940	$1,039,580.75	$21.69	$1.55	1,719,810	669,035
2015	32,687	47,841	$1,110,682.79	$23.22	$1.63	1,724,914	681,205
% Change	**-2.50%**	**-0.20%**	**6.80%**	**7.10%**	**5.20%**	**0.30%**	**1.80%**
Change	**-836**	**-99**	**$71,102.04**	**$1.53**	**$0.08**	**5,104**	**12,170**

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

Demographics of Members Utilizing Topical Antifungal Products

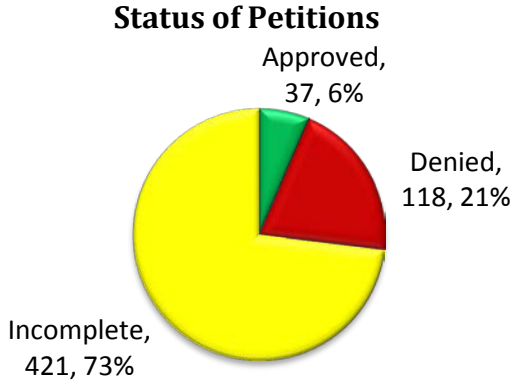


Top Prescriber Specialties of Topical Antifungal Products by Number of Claims



Prior Authorization of Topical Antifungal Products

There were 576 prior authorization requests submitted for the Topical Antifungal Product Based Prior Authorization (PBPA) category during fiscal year 2015. The following chart shows the status of the submitted petitions.



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

Anticipated Patent Expirations:

- Ecoza™ (econazole nitrate topical foam 1%): January 2018
- Loprox® Gel (ciclopirox): September 2018
- Extina® (ketoconazole foam 2%): October 2018
- Xolegel™ (ketoconazole gel): November 2020
- Kerydin™ (tavaborole 5% solution): May 2027
- Vusion® (miconazole/zinc oxide/white petrolatum): March 2028
- Jublia® (efinaconazole 10% topical solution): October 2030
- Naftin® (naftifine gel 2%): January 2033
- Luzu™ (luliconazole): April 2034

Pricing Trends:

- 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. This makes the cost of a 30g tube $101.40. In August 2014, the cost was $0.39 per gram with a 30g tube costing $11.70.
    - Clotrimazole 1% solution has undergone a similar change in pricing, with the cost rising from $0.29 per milliliter (mL) in August 2014 to $2.04 per mL after the SMAC price update in February 2016. This results in an increase from $8.70 for a 30mL bottle to the current cost of $61.20 for a 30mL bottle.
- There are other alternatives available in Tier-1 of the Topical Antifungals PBPA category for econazole nitrate 1% cream. Clotrimazole 1% cream (OTC) has coverage similar to econazole with the exception of *Trichophyton tonsurans*, *Microsporum audouini* and *Microsporum gypseum*. Tier-1 tolnaftate cream covers *Trichophyton tonsurans* and

Microsporum audouini. There is no lowered tiered topical for *Microsporum gypseum*, however, the current recommendation is to treat this with an oral antifungal, such as terbinafine, which is available without prior authorization.

- Clotrimazole 1% solution is indicated for the topical treatment of candidiasis due to *Candida albicans* and tinea versicolor due to *Malassezia furfur*. Clotrimazole 1% cream (prescription version) is a Tier-1 alternative for these indications.
- Tier-1 ketoconazole cream also provides coverage of *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Epidermophyton floccosum* as well as treatment of cutaneous candidiasis caused by *Candida*.

Recommendations

The College of Pharmacy recommends the following changes to the Topical Antifungal 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. The existing criteria for this category will apply.
3. Initiate a mailing 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 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.

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 product nystatin/triamcinolone ~~or clotrimazole/betamethasone~~ requires a patient-specific, clinically significant reason why the member cannot use the individual components separately.
4. For treatment of onychomycosis, a trial of oral antifungals (6 weeks for fingernails and 12 weeks for toenails) will be required for consideration of approval of Penlac® (ciclopirox solution).

Utilization Details of Topical Antifungal Products: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 UTILIZATION						
NYSTATIN PRODUCTS						
NYSTATIN CRE 100000	17,380	13,295	$298,496.06	$1.42	$17.17	26.88%
NYSTATIN OIN 100000	6,659	5,216	$168,011.77	$2.08	$25.23	15.13%
NYSTOP POW 100000	2,420	1,613	$72,711.80	$1.90	$30.05	6.55%
NYSTATIN POW 100000	921	596	$24,839.86	$1.92	$26.97	2.24%
NYAMYC POW 100000	733	342	$24,440.12	$3.10	$33.34	2.20%
SUBTOTAL	**28,113**	**21,062**	**$588,499.61**	**$1.68**	**$20.93**	**53.00%**
CLOTRIMAZOLE PRODUCTS						
CLOTRIMAZOLE CRE 1%	9,836	7,771	$207,552.49	$1.52	$21.10	18.69%
CLOTRIMAZOLE SOL 1%	180	155	$2,960.84	$0.99	$16.45	0.27%
CLOTRIMAZOLE POW	21	16	$174.10	$0.38	$8.29	0.02%
ATHLETE FOOT CRE 1%	21	20	$156.32	$0.51	$7.44	0.01%
SUBTOTAL	**10,058**	**7,962**	**$210,843.75**	**$1.51**	**$20.96**	**18.99%**
KETOCONAZOLE PRODUCTS						
KETOCONAZOLE CRE 2%	4,565	3,706	$129,327.08	$1.74	$28.33	11.64%
KETOCONAZOLE SHA 2%	2,684	1,695	$38,853.39	$0.47	$14.48	3.50%
SUBTOTAL	**7,249**	**5,401**	**$168,180.47**	**$1.08**	**$23.20**	**15.14%**
ECONAZOLE PRODUCTS						
ECONAZOLE CRE 1%	1,180	892	$120,960.76	$6.58	$102.51	10.89%
SUBTOTAL	**1,180**	**892**	**$120,960.76**	**$6.58**	**$102.51**	**10.89%**
CICLOPIROX PRODUCTS						
CICLOPIROX CRE 0.77%	771	618	$14,275.57	$1.36	$18.52	1.29%
SUBTOTAL	**771**	**618**	**$14,275.57**	**$1.36**	**$18.52**	**1.29%**
TERBINAFINE PRODUCTS						
ATHLETE FOOT CRE 1%	28	25	$430.72	$1.08	$15.38	0.04%
TERBINAFINE CRE 1%	369	323	$4,842.71	$0.94	$13.12	0.44%
LAMISIL AT CRE 1%	36	33	$569.65	$1.19	$15.82	0.05%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ATHLETE FOOT CRE AF	2	2	$31.15	$1.25	$15.58	0.00%
SUBTOTAL	**435**	**383**	**$5874.23**	**$0.97**	**$13.50**	**0.53%**
TOLNAFTATE PRODUCTS						
TOLNAFTATE CRE 1%	9	9	$79.72	$0.59	$8.86	0.01%
SM ANTIFUNGL CRE 1%	3	3	$32.49	$1.02	$10.83	0.00%
SUBTOTAL	**12**	**12**	**$112.21**	**$0.67**	**$9.35**	**0.01%**
MICONAZOLE PRODUCTS						
ANTIFUNGAL CRE 2%	4	1	$29.80	$1.06	$7.45	0.00%
SUBTOTAL	**4**	**1**	**$29.80**	**$1.06**	**$7.45**	**0.00%**
TIER-1 SUBTOTAL	**47,822**	**36,331**	**$1,108,776.40**	**$1.63**	**$23.19**	**99.85%**
TIER-2 UTILIZATION						
CLOTRIMAZOLE/BETAMETHASONE PRODUCTS						
CLOTRIM/BETA CRE DIPROP	6	6	$313.50	$3.37	$52.25	0.03%
SUBTOTAL	**6**	**6**	**$313.50**	**$3.37**	**$52.25**	**0.03%**
CICLOPIROX PRODUCTS						
CICLOPIROX SOL 8%	5	5	$169.98	$0.94	$34.00	0.02%
CICLOPIROX SUS 0.77%	3	2	$105.37	$1.40	$35.12	0.01%
SUBTOTAL	**8**	**7**	**$275.35**	**$1.08**	**$34.42**	**0.03%**
NYSTATIN/TRIAMCINOLONE PRODUCTS						
NYSTAT/TRIAM CRE	2	2	$238.46	$5.30	$119.23	0.02%
SUBTOTAL	**2**	**2**	**$238.46**	**$5.30**	**$119.23**	**0.02%**
NAFTIFINE PRODUCTS						
NAFTIN CRE 2%	1	1	$310.28	$6.90	$310.28	0.03%
SUBTOTAL	**1**	**1**	**$310.28**	**$6.90**	**$310.28**	**0.03%**
OXICONAZOLE PRODUCTS						
OXISTAT CRE 1%	2	1	$768.80	$19.22	$384.40	0.07%
SUBTOTAL	**2**	**1**	**$768.80**	**$19.22**	**$384.40**	**0.07%**
TIER-2 SUBTOTAL	**19**	**17**	**$1,906.39**	**$3.99**	**$100.34**	**0.18%**
TOTAL	**47,841**	**32,687***	**$1,110,682.79**	**$1.63**	**$23.22**	**100%**

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

[1] U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised April 2016. Last accessed April 28, 2016.
[2] Econazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; February 2014. Last accessed May 3, 2016.
[3] Clotrimazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; April 2015. Last accessed May 3, 2016.
[4] Ketoconazole. Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; January 2015. Last accessed May 3, 2016.
[5] Treat JR. Tinea capitis. In: UpToDate, Rosen T, Levy ML, Ofori AO (Eds). UpToDate [database online]. Waltham, MA. Last revised July 28, 2015. Last accessed May 3, 2016.

Appendix Q

Calendar Year 2015 Annual Review of Natpara®
(Parathyroid Hormone Injection)

Oklahoma Health Care Authority
June 2016

Introduction[1,2,3,4]

Hypoparathyroidism is a rare, orphan disease involving mineral metabolism characterized by low serum calcium, elevated serum phosphors, and absent or low parathyroid hormone (PTH) levels in the systemic circulation. Hypoparathyroidism prevalence in the United States is estimated between 60,000 to 115,000 persons. Hypoparathyroidism symptoms often include paresthesia, cramps, or tetany, but the disorder can also manifest acutely with seizures, bronchospasm, laryngospasm, or cardiac rhythm disturbances.

Dietary calcium and oral calcium supplementation is the primary treatment along with vitamin D supplementation. Two main goals of chronic management therapy include prevention of signs and symptoms of hypocalcemia and maintaining the serum calcium concentration slightly below normal or in the low normal range. Thiazide diuretics promote renal tubular calcium retention and are commonly used when hypercalciuria is present. Recombinant human parathyroid hormone (rhTPH) may be considered if the physician and patient feel that good control is not achieved by conventional therapy, oral calcium and vitamin D medications required to control serum calcium or symptoms are too high, or in certain circumstances that are beyond facile correction with calcium and active vitamin D (e.g., gastrointestinal tract (GI) disorders that are associated with malabsorption). The most recent guidelines published in *The Journal of Clinical Endocrinology and Metabolism,* recommend to take in account the fact that rhPTH is currently an expensive drug when deciding treatment.

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

Current Prior Authorization Criteria

Natpara® (Parathyroid Hormone) Approval Criteria:

1. An FDA approved diagnosis as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism; and
    a. Natpara® is not FDA approved for hypoparathyroidism caused by calcium-sensing receptor mutations.
    b. Natpara® is not FDA approved for hypoparathyroidism due to acute post-surgery.

2. Magnesium deficiency must be ruled out; and
3. Member must have pretreatment serum calcium above 7.5mg/dL before starting Natpara®; and
4. Prescriber must verify the member has sufficient 25-hydroxyvitamin D level per standard of care; and
5. Member must be unable to be adequately well-controlled on calcium supplements and active forms of vitamin D alone; and
6. Health care provider and dispensing pharmacy must be certified through the Natpara® REMS Program; and
7. A quantity limit of two cartridges (each package contains two 14-day cartridges) per 28 days will apply. The maximum covered dose will be 100mcg per day.

Utilization of Natpara® (Parathyroid Hormone): Calendar Year 2015

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2015	1	9	$75,246.67	$8,360.74	$298.60	18	252

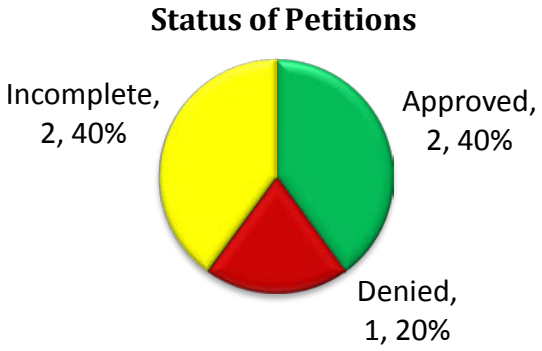
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

Top Prescriber Specialties of Natpara® (Parathyroid Hormone) by Number of Claims

- The only prescriber specialty listed on paid claims for Natpara® during calendar year 2015 was an endocrinologist.

Prior Authorization of Natpara® (Parathyroid Hormone)

There were 5 prior authorization requests submitted for Natpara® during calendar year 2015. The following chart shows the status of the submitted petitions.



Market News and Updates[5,6]

Anticipated Exclusivity Expiration:

- Natpara® (parathyroid hormone): June 2018

Recent Practice Guidelines:

- **August 2015:** The European Society of Endocrinology Clinical Guideline: Treatment of Chronic Hypoparathyroidism in Adults was published in the *European Journal of Endocrinology*. The guidelines recommend against the routine use of replacement therapy with parathyroid (PTH) or PTH analogues.
- **November 2015:** Management of Hypoparathyroidism: Summary Statement and Guidelines was published in *The Journal of Clinical Endocrinology and Metabolism* (JCEM). The workshop addressed key aspects of the diagnosis, etiology, epidemiology, evaluation, and treatment of hypoparathyroidism. RhPTH is considered last line or in circumstances where conventional management of chronic hypoparathyroidism is not effective.

Recommendations

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

Utilization Details of Natpara® (Parathyroid Hormone): Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
NATPARA INJ 100MCG	8	1	$66,886.96	$298.60	$8,360.87	88.89%
NATPARA INJ 75MCG	1	1	$8,359.71	$298.56	$8,359.71	11.11%
TOTAL	**9**	**1***	**$75,246.67**	**$298.60**	**$8,360.29**	**100.00%**

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

[1] Bilezikian, JP, et al. Hypoparathyroidism in the Adult: Epidemiology, Diagnosis, Pathophysiology, Target Organ Involvement, Treatment, and Challenges for Future Research. *Journal of Bone and Mineral Research*. 2011 Oct; 26 (10):2317-37.
[2] Brandi ML, Bilexikian JP, Shoback D, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines. *J Clin Endocrinol Metab.* 2016 Mar 4:jc20153907. [Epub ahead of print].
[3] FDA News Release. FDA Approved Natpara to control low blood calcium levels in patients with hyperparathyroidism. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm431358.htm. Issued 01/2015. Last accessed 05/2016.
[4] Natpara® Prescribing Information. NPS Pharma. Available online at: https://natpara.com/prescribing-information/PDF#page=1. Last revised 01/2015. Last accessed 05/2016.
[5] Niazi, SK. Biosimilars and Interchangeable Biologics Strategic Elements. Available at: https://books.google.com/books?id=5PYYCwAAQBAJ&pg=PA499&lpg=PA499&dq=natpara+patent+expiration&source=bl&ots=oYiqAyyJP2&sig=fQZqi3cymc-ObmvJnOb-y3gtJXE&hl=en&sa=X&ved=0ahUKEwjtoKi76NfMAhXp64MKHehPBjcQ6AEITjAI#v=onepage&q=natpara%20patent%20expiration&f=false. Last revised 2016. Last accessed 05/2016.
[6] Bollerslev J, Rejnmark L, Marcocci C, et al. European Society of Endocrinology Clinical Guideline: Treatment of chronic hypoparathyroidism in adults. *Eur J Endocrinol*. 2015 Aug; 173 (2): G1-G20.

Appendix R

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

FDA NEWS RELEASE

For Immediate Release: April 11th, 2016

FDA approves new drug for chronic lymphocytic leukemia in patients with a specific chromosomal abnormality

The U.S. Food and Drug Administration approved Venclexta (venetoclax) for the treatment of patients with chronic lymphocytic leukemia (CLL) who have a chromosomal abnormality called 17p deletion and who have been treated with at least one prior therapy. Venclexta is the first FDA-approved treatment that targets the B-cell lymphoma 2 (BCL-2) protein, which supports cancer cell growth and is overexpressed in many patients with CLL.

According to the National Cancer Institute, CLL is one of the most common types of leukemia in adults, with approximately 15,000 new cases diagnosed each year. CLL is characterized by the progressive accumulation of abnormal lymphocytes, a type of white blood cell. Patients with CLL who have a 17p deletion lack a portion of the chromosome that acts to suppress cancer growth. This chromosomal abnormality occurs in approximately 10 percent of patients with untreated CLL and in approximately 20 percent of patients with relapsed CLL.

The efficacy of Venclexta was tested in a single-arm clinical trial of 106 patients with CLL who have a 17p deletion and who had received at least one prior therapy. Trial participants took Venclexta orally every day, beginning with 20 mg and increasing over a five-week period to 400 mg. Results showed that 80 percent of trial participants experienced a complete or partial remission of their cancer.

Venclexta is indicated for daily use after detection of 17p deletion is confirmed through the use of the FDA-approved companion diagnostic Vysis CLL FISH probe kit.

The most common side effects of Venclexta include low white blood cell count (neutropenia), diarrhea, nausea, anemia, upper respiratory tract infection, low platelet count (thrombocytopenia) and fatigue. Serious complications can include pneumonia, neutropenia with fever, fever, autoimmune hemolytic anemia, anemia and metabolic abnormalities known as tumor lysis syndrome. Live attenuated vaccines should not be given to patients taking Venclexta.

The FDA granted the Venclexta application breakthrough therapy designation, priority review status, and accelerated approval for this indication. These are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions. Venclexta also received orphan drug designation, which provides incentives such as tax credits, user fee waivers and eligibility for exclusivity to assist and encourage the development of drugs for rare diseases.

Venclexta is manufactured by AbbVie Inc. of North Chicago, Illinois, and marketed by AbbVie and Genentech USA Inc. of South San Francisco, California. The Vysis CLL FISH probe kit is manufactured by Abbott Molecular of Des Plaines, Illinois.

FDA NEWS RELEASE

For Immediate Release: April 29th, 2016

FDA approves first generic Crestor

The U.S. Food and Drug Administration approved the first generic version of Crestor (rosuvastatin calcium) tablets for the following uses:

- in combination with diet for the treatment of high triglycerides (hypertriglyceridemia) in adults;
- in combination with diet for treatment of patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia), a disorder associated with improper breakdown of cholesterol and triglycerides;
- either alone or in combination with other cholesterol treatment(s) for adult patients with homozygous familial hypercholesterolemia, a disorder associated with high low-density lipoprotein (LDL) cholesterol.

Generic drugs approved by the FDA have the same quality and strength as brand-name drugs. Generic drug manufacturing and packaging sites must pass the same quality standards as those of brand-name drugs. Watson Pharmaceuticals Inc. of Parsippany, New Jersey has received approval to market generic rosuvastatin calcium in multiple strengths.

Rosuvastatin calcium is in a class of drugs called statins, which work by stopping an enzyme called HMG-CoA reductase from making cholesterol. Statins should be used in addition to a diet restricted in saturated fat and cholesterol.
In the clinical trials for Crestor, the most common side effects reported by participants taking Crestor included headache, pain in muscles (myalgia), abdominal pain, abnormal weakness (asthenia), and nausea. Rosuvastatin calcium should not be used in women who are pregnant or may become pregnant as it may cause fetal harm. Women who require treatment with rosuvastatin should be advised not to nurse their infants.

FDA NEWS RELEASE

For Immediate Release: April 29th, 2016

FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease

The U.S. Food and Drug Administration approved Nuplazid (pimavanserin) tablets, the first drug approved to treat hallucinations and delusions associated with psychosis experienced by some people with Parkinson's disease.
Hallucinations or delusions can occur in as many as 50 percent of patients with Parkinson's disease at some time during the course of their illness. People who experience them see or hear things that are not there (hallucinations) and/or have false beliefs (delusions). The hallucinations and delusions experienced with Parkinson's disease are serious symptoms, and can lead to thinking and emotions that are so impaired that the people experiencing them may not relate to loved ones well or take appropriate care of themselves.
An estimated 50,000 Americans are diagnosed with Parkinson's disease each year, according to the National Institutes of Health, and about one million Americans have the condition. The neurological disorder typically occurs in people over age 60, when cells in the brain that produce a chemical called dopamine become impaired or die. Dopamine helps transmit signals between the areas of the brain that produce smooth, purposeful movement -- like eating, writing and shaving. Early symptoms of the disease are subtle and occur gradually. In some people Parkinson's disease progresses more quickly than in others. As the disease progresses, the shaking, or tremor, which affects the majority of people with Parkinson's disease, may begin to interfere with daily activities. Other symptoms may include depression and other emotional changes; hallucinations and delusions; difficulty in swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions.
The effectiveness of Nuplazid was shown in a six-week clinical trial of 199 participants. Nuplazid was shown to be superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions without worsening the primary motor symptoms of Parkinson's disease.
As with other atypical antipsychotic drugs, Nuplazid has a Boxed Warning alerting health care professionals about an increased risk of death associated with the use of these drugs to treat older people with dementia-related psychosis. No drug in this class is approved to treat patients with dementia-related psychosis.
In clinical trials, the most common side effects reported by participants taking Nuplazid were: swelling, usually of the ankles, legs, and feet due to the accumulation of excessive fluid in the tissue (peripheral edema); nausea; and abnormal state of mind (confused state).
Nuplazid was granted breakthrough therapy designation for the treatment of hallucinations and delusions associated with Parkinson's disease. Breakthrough therapy designation is a program designed to expedite the development and review of drugs that are intended to treat a serious condition and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint. The drug was also granted a priority review. The FDA's priority review program provides for an expedited review of drugs that offer a significant improvement in the safety or effectiveness for the treatment, prevention, or diagnosis of a serious condition.
Nuplazid is marketed by Acadia Pharmaceuticals Inc. of San Diego, California.

FDA NEWS RELEASE

For Immediate Release: May 18th, 2016

FDA approves new, targeted treatment for bladder cancer

The U.S. Food and Drug Administration approved Tecentriq (atezolizumab) to treat the most common type of bladder cancer, called urothelial carcinoma. This is the first product in its class (PD-1/PD-L1 inhibitors) approved to treat this type of cancer.

Tecentriq targets the PD-1/PD-L1 pathway (proteins found on the body's immune cells and some cancer cells). By blocking these interactions, Tecentriq may help the body's immune system fight cancer cells. Tecentriq is the first FDA-approved PD-L1 inhibitor and the latest in the broader class of PD-1/PD-L1 targeted biologics approved by the FDA in the last two years.

Tecentriq is approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has worsened during or following platinum-containing chemotherapy, or within 12 months of receiving platinum-containing chemotherapy, either before (neoadjuvant) or after (adjuvant) surgical treatment. Urothelial carcinoma is the most common type of bladder cancer and occurs in the urinary tract system, involving the bladder and related organs. The National Cancer Institute (NCI) estimates 76,960 new cases of bladder cancer and 16,390 deaths from the disease in 2016.

The safety and efficacy of Tecentriq were studied in a single-arm clinical trial involving 310 patients with locally advanced or metastatic urothelial carcinoma. This trial measured the percentage of patients who experienced complete or partial shrinkage of their tumors (objective response rate). The study also looked at the difference in effect based on "positive" versus "negative" expression of the PD-L1 protein on patients' tumor-infiltrating immune cells. In all patients, 14.8 percent of participants experienced at least a partial shrinkage of their tumors, an effect that lasted from more than 2.1 to more than 13.8 months at the time of the response analysis. In patients who were classified as "positive" for PD-L1 expression, 26 percent of participants experienced a tumor response (compared to 9.5 percent of participants who were classified as "negative" for PD-L1 expression).

While patients who received Tecentriq experienced a tumor response across the study, the greater effect in those who were classified as "positive" for PD-L1 expression suggests that the level of PD-L1 expression in tumor-infiltrating immune cells may help identify patients who are more likely to respond to treatment with Tecentriq. Therefore, the FDA also approved the Ventana PD-L1 (SP142) assay to detect PD-L1 protein expression levels on patients' tumor-infiltrating immune cells and help physicians determine which patients may benefit most from treatment with Tecentriq.

The most common side effects of treatment with Tecentriq were fatigue, decreased appetite, nausea, urinary tract infection, fever and constipation. Tecentriq also has the potential to cause infection and serious side effects that result from the immune system effect of Tecentriq (known as "immune-mediated side effects"). These severe immune-mediated side effects involve healthy organs, including the lung, colon and endocrine system.

The FDA granted the Tecentriq application breakthrough therapy designation, priority review status and accelerated approval for this indication. These are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions.

Tecentriq is marketed by Genentech based in San Francisco, California. The Ventana PD-L1 (SP142) assay complementary diagnostic for Tecentriq is marketed by Ventana Medical Systems, based in Tucson, Arizona.

FDA NEWS RELEASE

For Immediate Release: May 26th, 2016

FDA approves first buprenorphine implant for treatment of opioid dependence

The U.S. Food and Drug Administration 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, as part of a complete treatment program.

Until this day, buprenorphine for the treatment of opioid dependence was only approved as a pill or a film placed under the tongue or on the inside of a person's cheek until it dissolved. While effective, a pill or film may be lost, forgotten or stolen. However, as an implant, Probuphine provides a new treatment option for people in recovery who may value the unique benefits of a six-month implant compared to other forms of buprenorphine, such as the possibility of improved patient convenience from not needing to take medication on a daily basis. An independent FDA advisory committee supported the approval of Probuphine in a meeting held earlier this year.

Expanding the use and availability of medication-assisted treatment (MAT) options like buprenorphine is an important component of the FDA's opioid action plan and one of three top priorities for the U.S. Department of Health and Human Services' Opioid Initiative aimed at reducing prescription opioid and heroin related overdose, death and dependence.

Opioid dependence is the diagnostic term used for the more common concept, “addiction,” in the Probuphine clinical trials. Addiction is defined as a cluster of behavioral, cognitive and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use, persisting in drug use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, as well as the possibility of the development of tolerance or development of physical dependence. Physical dependence is not the same as addiction. Newer diagnostic terminology uses the term “opioid use disorder,” which includes both milder forms of problematic opioid use as well as addiction.

MAT is a comprehensive approach that combines approved medications (currently, methadone, buprenorphine or naltrexone) with counseling and other behavioral therapies to treat patients with opioid use disorder. Regular adherence to MAT with buprenorphine reduces opioid withdrawal symptoms and the desire to use, without causing the cycle of highs and lows associated with opioid misuse or abuse. At sufficient doses, it also decreases the pleasurable effects of other opioids, making continued opioid abuse less attractive. According to the Substance Abuse and Mental Health Services Administration, patients receiving MAT for their opioid use disorder cut their risk of death from all causes in half.

Probuphine should be used as part of a complete treatment program that includes counseling and psychosocial support. Probuphine consists of four, one-inch-long rods that are implanted under the skin on the inside of the upper arm and provide treatment for six months. Administering Probuphine requires specific training because it must be surgically inserted and removed. Only a health care provider who has completed the training and become certified through a restricted program called the Probuphine Risk Evaluation and Mitigation Strategy (REMS) program should insert and remove the implants. If further treatment is needed, new implants may be inserted in the opposite arm for one additional course of treatment. The FDA is requiring postmarketing studies to establish the safety and feasibility of placing the Probuphine implants for additional courses of treatment.

The safety and efficacy of Probuphine were demonstrated in a randomized clinical trial of adults who met the clinical criteria for opioid dependence and were considered stable after prior buprenorphine treatment. A response to MAT was measured by urine screening and self-reporting of illicit opioid use during the six month treatment period. Sixty-three percent of Probuphine-treated patients had no evidence of illicit opioid use throughout the six months of treatment – similar to the 64 percent of those who responded to sublingual buprenorphine alone.

The most common side effects from treatment with Probuphine include implant-site pain, itching, and redness, as well as headache, depression, constipation, nausea, vomiting, back pain, toothache and oropharyngeal pain. The safety and efficacy of Probuphine have not been established in children or adolescents less than 16 years of age. Clinical studies of Probuphine did not include participants over the age of 65.

Probuphine has a boxed warning that provides important safety information for health care professionals, including a warning that insertion and removal of Probuphine are associated with the risk of implant migration, protrusion, expulsion and nerve damage resulting from the procedure. Probuphine must be prescribed and dispensed according to the Probuphine REMS program because of the risks of surgical complications and because of the risks of accidental overdose, misuse and abuse if an implant comes out or protrudes from the skin. As part of this program, Probuphine can only be prescribed and dispensed by health care providers who are certified with the REMS program and have completed live training, among other requirements.

Probuphine implants contain a significant amount of drug that can potentially be expelled or removed, resulting in the potential for accidental exposure or intentional misuse and abuse if the implant comes out of the skin. Patients should be seen during the first week after insertion and a visit schedule of no less than once-monthly is recommended for continued counseling and psychosocial support.

Probuphine is marketed by San Francisco-based Titan Pharmaceuticals Inc. and Braeburn Pharmaceuticals based in Princeton, New Jersey.

FDA NEWS RELEASE

For Immediate Release: May 27th, 2016

FDA approves new diagnostic imaging agent to detect recurrent prostate cancer

The U.S. Food and Drug Administration approved Axumin, a radioactive diagnostic agent for injection. Axumin is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated prostate specific antigen (PSA) levels following prior treatment.

Prostate cancer is the second leading cause of death from cancer in U.S. men. In patients with suspected cancer recurrence after primary treatment, accurate staging is an important objective in improving management and outcomes.
Two studies evaluated the safety and efficacy of Axumin for imaging prostate cancer in patients with recurrent disease. The first compared 105 Axumin scans in men with suspected recurrence of prostate cancer to the histopathology (the study of tissue changes caused by disease) obtained by prostate biopsy and by biopsies of suspicious imaged lesions. Radiologists onsite read the scans initially; subsequently, three independent radiologists read the same scans in a blinded study.
The second study evaluated the agreement between 96 Axumin and C11 choline (an approved PET scan imaging test) scans in patients with median PSA values of 1.44 ng/mL. Radiologists on-site read the scans, and the same three independent radiologists who read the scans in the first study read the Axumin scans in this second blinded study. The results of the independent scan readings were generally consistent with one another, and confirmed the results of the onsite scan readings. Both studies supported the safety and efficacy of Axumin for imaging prostate cancer in men with elevated PSA levels following prior treatment.
Axumin is a radioactive drug and should be handled with appropriate safety measures to minimize radiation exposure to patients and healthcare providers during administration. Image interpretation errors can occur with Axumin PET imaging. A negative image does not rule out the presence of recurrent prostate cancer and a positive image does not confirm the presence of recurrent prostate cancer. Clinical correlation, which may include histopathological evaluation of the suspected recurrence site, is recommended.
The most commonly reported adverse reactions in patients are injection site pain, redness, and a metallic taste in the mouth.
Axumin is marketed by Blue Earth Diagnostics, Ltd., Oxford, United Kingdom.

FDA NEWS RELEASE

For Immediate Release: May 27th, 2016

FDA approves Zinbryta to treat multiple sclerosis

The U.S. Food and Drug Administration approved Zinbryta (daclizumab) for the treatment of adults with relapsing forms of multiple sclerosis (MS). Zinbryta is a long-acting injection that is self- administered by the patient monthly.
MS is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communication between the brain and other parts of the body. It is among the most common causes of neurological disability in young adults and occurs more frequently in women than men. For most people with MS, episodes relapses are initially followed by remissions. Over time, recovery may be incomplete, leading to progressive decline in function and increased disability. Most people experience their first symptoms of MS between the ages of 20 and 40.
The effectiveness of Zinbryta was shown in two clinical trials. One trial compared Zinbryta and Avonex in 1,841 participants who were studied for 144 weeks. Patients on Zinbryta had fewer clinical relapses than patients taking Avonex. The second trial compared Zinbryta with placebo and included 412 participants who were treated for 52 weeks. In that study, those receiving Zinbryta had fewer relapses compared to those receiving placebo.
Zinbryta should generally be used only in patients who have had an inadequate response to two or more MS drugs because Zinbryta has serious safety risks, including liver injury and immune conditions. Because of the risks, Zinbryta has a boxed warning and is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy.
The boxed warning tells prescribers that the drug can cause severe liver injury, including life-threatening and fatal events. Health care professionals should perform blood tests to monitor the patient’s liver function prior to starting Zinbryta, monthly before each dose, and for up to six months after the last dose.
The boxed warning also highlights other important risks of Zinbryta treatment including immune conditions, such as inflammation of the colon (non-infectious colitis), skin reactions, and enlargement of lymph nodes (lymphadenopathy).
Additional highlighted warnings include hypersensitivity reactions (anaphylaxis or angioedema), increased risk of infections, and symptoms of depression and/or suicidal ideation.
The most common adverse reactions reported by patients receiving Zinbryta in the clinical trial that compared it to Avonex include cold symptoms (nasopharyngitis), upper respiratory tract infection, rash, influenza, dermatitis, throat (oropharyngeal) pain, eczema, and enlargement of lymph nodes. The most common

adverse reactions reported by patients receiving Zinbryta when compared to placebo are depression, rash, and increased alanine aminotransferase.
Zinbryta is manufactured by Biogen, Inc. of Cambridge, Massachusetts.

FDA NEWS RELEASE

For Immediate Release: May 31st, 2016

FDA approves Ocaliva for rare, chronic liver disease

On Friday, May 27, the U.S. Food and Drug Administration granted accelerated approval for Ocaliva (obeticholic acid) for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as a single therapy in adults unable to tolerate UDCA.
PBC is a chronic, or long lasting, disease that causes the small bile ducts in the liver to become inflamed, damaged and ultimately destroyed. This causes bile to remain in the liver, which damages the liver cells over time, and results in cirrhosis, or scarring of the liver. As cirrhosis progresses, and the amount of scar tissue in the liver increases, the liver loses its ability to function.
Ocaliva, given orally, binds to the farnesoid X receptor (FXR), a receptor found in the nucleus of cells in the liver and intestine. FXR is a key regulator of bile acid metabolic pathways. Ocaliva increases bile flow from the liver and suppresses bile acid production in the liver, thus reducing the exposure of the liver to toxic levels of bile acids.
The FDA's approval is based on a reduction in the level of the biomarker alkaline phosphatase (ALP), as a surrogate endpoint which, based on multiple levels of evidence (mechanistic, clinical trial, epidemiologic), could be relied upon to be reasonably likely to predict clinical benefit, including an improvement in transplant free-survival. The safety and efficacy of Ocaliva were demonstrated in a controlled clinical trial with 216 participants. After twelve months, the proportion of participants achieving reductions in ALP levels was higher among Ocaliva-treated participants compared to placebo-treated participants.
The most common side effects of Ocaliva are severe pruritus, fatigue, abdominal pain and discomfort, joint pain (arthralgia), pain in the middle part of the throat (oropharyngeal), dizziness and constipation. Ocaliva should not be used in patients with complete biliary obstruction.
There is one other approved treatment for PBC, UDCA, which was approved by the FDA in 1997. UDCA is effective in more than 50 percent of patients, but up to 40 percent of patients do not achieve an adequate reduction in blood chemistries (e.g., ALP and/or total bilirubin) with UDCA, while 5-10 percent are unable to tolerate UDCA.
The FDA granted Ocaliva fast track designation, a process designed to facilitate the development, and expedite the review of drugs that are intended to treat serious conditions and that demonstrate the potential to address an unmet medical need. The FDA also granted Ocaliva an orphan drug designation.Orphan drug designation provides incentives such as tax credits, user fee waivers and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.
Ocaliva was approved under the agency's accelerated approval program, which allows the approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials.
An improvement in survival, progression to cirrhosis, or other disease-related symptoms in patients being treated with Ocaliva has not yet been established, although a confirmatory trial is currently ongoing.
Ocaliva is manufactured by New York, New York-based Intercept Pharmaceuticals, Inc.

Safety Announcements

FDA Drug Safety Communication: FDA warns that prescribing of Nizoral (ketoconazole) oral tablets for unapproved uses including skin and nail infections continues; linked to patient death

[5-19-2016] The U.S. Food and Drug Administration (FDA) is warning health care professionals to avoid prescribing the antifungal medicine ketoconazole oral tablets to treat skin and nail fungal infections. Use of this medication carries the risk of serious liver damage, adrenal gland problems, and harmful interactions with other medicines that outweigh its benefit in treating these conditions, which are not approved uses of the drug.

We approved label changes for oral ketoconazole tablets in 2013 to reflect these serious risks and to remove the indications for treatment of skin and nail fungal infections. However, an FDA safety review found that oral ketoconazole continues to be prescribed for these types of conditions. In the 18 months ending in June 2015, skin and nail fungal infections were the only diagnoses cited for the use of oral ketoconazole in an office-based physician surveys database. Since the 2013 labeling change, one patient death has been reported to the FDA due to liver failure associated with oral ketoconazole prescribed to treat a fungal infection of the nails.

Health care professionals should use ketoconazole tablets only to treat serious fungal infections when no other antifungal therapies are available. Skin and nail fungal infections in otherwise healthy persons are not life-threatening, and so the risks associated with oral ketoconazole outweigh the benefits. Other treatment options are available over-the-counter and by prescription, but are also associated with risks that should be weighed against their benefits.

Patients should discuss with their health care professionals the risks and benefits of available therapies before using any medicine to treat skin and nail fungal infections. Patients taking ketoconazole tablets should seek medical attention right away if they experience any of these signs and symptoms of liver problems, which include loss of appetite, nausea, vomiting, or abdominal discomfort; yellowing of the skin or the whites of the eyes (jaundice); unusual darkening of the urine or lightening of the stools; or pain and discomfort in the right upper abdomen where the liver is located.

Ketoconazole in tablet form is indicated to treat serious infections caused by fungi and should be used only when other effective therapy is not available or tolerated. It works by killing the fungus or preventing it from growing. During the 12-month period ending in June 2015, approximately 217,000 patients received dispensed prescriptions for oral ketoconazole from U.S. outpatient retail pharmacies. Ketoconazole is only available as a generic. The topical forms of ketoconazole that are applied to the skin or nails have not been associated with liver damage, adrenal problems, or drug interactions.

In a July 2013 Drug Safety Communication, we warned that ketoconazole tablets should not be used as a first-line treatment for any fungal infection because it can cause severe liver injury and adrenal gland problems, and advised it can lead to harmful interactions with other medicines. We determined that the risks outweigh the benefits for treating skin and nail fungal infections and approved label changes removing this indication from the drug label and limited its labeled indication to treating only serious fungal infections.

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

Safety Announcements

FDA Drug Safety Communication: Interim clinical trial results find increased risk of leg and foot amputations, mostly affecting the toes, with the diabetes medicine canagliflozin (Invokana, Invokamet); FDA to investigate

[5-18-2016] The U.S. Food and Drug Administration (FDA) is alerting the public about interim safety results from an ongoing clinical trial that found an increase in leg and foot amputations, mostly affecting the toes, in patients treated with the diabetes medicine canagliflozin (Invokana, Invokamet). It has not been determined whether canagliflozin increases the risk of leg and foot amputations. They are currently investigating this new safety issue and will update the public when they have more information.

Patients should not stop or change their diabetes medicines without first talking to their health care professional. Doing so can lead to uncontrolled blood sugar levels that can be harmful. Over time, this can cause serious problems, including blindness, nerve and kidney damage, and heart disease. Patients taking canaglifozin should notify their health care professionals right away if they notice any new pain or tenderness, sores or ulcers, or infections in their legs or feet.

Health care professionals should follow the recommendations in the canagliflozin drug labels. Monitor patients for the signs and symptoms described above and advise patients to seek medical advice if they experience them.

Canagliflozin is a prescription medicine used with diet and exercise to lower blood sugar in adults with type 2 diabetes. It belongs to a class of drugs called sodium-glucose cotransporter-2 (SGLT2) inhibitors. Canagliflozin lowers blood sugar by causing the kidneys to remove sugar from the body through the urine. It is available as a single-ingredient product under the brand name Invokana and also in combination with the diabetes medicine metformin under the brand name Invokamet.

In the ongoing Canagliflozin Cardiovascular Assessment Study (CANVAS) clinical trial, the trial's independent data monitoring committee (IDMC) identified an increased risk of leg and foot amputations. The amputations

occurred about twice as often in patients treated with canagliflozin compared to patients treated with placebo. An interim analysis showed that over a year's time, the risks of amputation for patients in the trial were equivalent to:

- 7 out of every 1,000 patients treated with 100 mg daily of canagliflozin
- 5 out of every 1,000 patients treated with 300 mg daily of canagliflozin
- 3 out of every 1,000 patients treated with placebo

Patients in the CANVAS trial have been followed for an average of 4.5 years to date. The IDMC has recommended, based on an overall assessment, that the CANVAS trial continue.

The IDMC has also reported that a second, similar trial evaluating canagliflozin, the CANVAS-R trial, has not shown the same risks of increased leg and foot amputations to date. Patients in the CANVAS-R trial have been followed for an average of 9 months.

They are continuing to evaluate this safety issue and will update the public when they have more information. They urge health care professionals and patients to report side effects involving canagliflozin or other medicines to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together

[5-12-2016] The U.S. Food and Drug Administration is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

An FDA safety review has shown that fluoroquinolones when used systemically (i.e. tablets, capsules, and injectable) are associated with disabling and potentially permanent serious side effects that can occur together. These side effects can involve the tendons, muscles, joints, nerves, and central nervous system. As a result, we are requiring the drug labels and Medication Guides for all fluoroquinolone antibacterial drugs to be updated to reflect this new safety information. We are continuing to investigate safety issues with fluoroquinolones and will update the public with additional information if it becomes available.

Patients should contact your health care professional immediately if you experience any serious side effects while taking your fluoroquinolone medicine. Some signs and symptoms of serious side effects include tendon, joint and muscle pain, a "pins and needles" tingling or pricking sensation, confusion, and hallucinations. Patients should talk with your health care professional if you have any questions or concerns.

Health care professionals should stop systemic fluoroquinolone treatment immediately if a patient reports serious side effects, and switch to a non-fluoroquinolone antibacterial drug to complete the patient's treatment course.

We previously communicated safety information associated with systemic fluoroquinolone antibacterial drugs in August 2013 and July 2008.

We urge patients and health care professionals to report side effects involving fluoroquinolone antibacterial drugs and other drugs to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns about rare but serious skin reactions with mental health drug olanzapine (Zyprexa, Zyprexa Zydis, Zyprexa Relprevv, and Symbyax)

[5-10-2016] The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. We are adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

Patients taking olanzapine-containing products who develop a fever with a rash and swollen lymph glands, or swelling in the face, should seek medical care right away. The combined symptoms together are commonly seen in DRESS. Talk with your health care professional about any questions or concerns. Do not stop taking olanzapine or change your dose without first talking with your health care professional. Sudden stopping of the medicine can be harmful without your health care professional's direct supervision.

Health care professionals should immediately stop treatment with olanzapine if DRESS is suspected. When prescribing the medicine, explain the signs and symptoms of severe skin reactions to your patients and tell them when to seek immediate medical care.

Olanzapine is an antipsychotic medicine used to treat mental health disorders schizophrenia and bipolar disorder. It can decrease hallucinations, in which people hear or see things that do not exist, and other psychotic symptoms such as disorganized thinking. Olanzapine is available under the brand names Zyprexa, Zyprexa Zydis, Zyprexa Relprevv, and Symbyax, and also as generics.
DRESS may start as a rash that can spread to all parts of the body. It can include fever and swollen lymph nodes and a swollen face. It causes a higher-than-normal number of infection-fighting white blood cells called eosinophils that can cause inflammation, or swelling. DRESS can result in injury to organs including the liver, kidneys, lungs, heart, or pancreas, and can lead to death.
A search of the FDA Adverse Event Reporting System (FAERS) database identified 23 cases of DRESS reported with olanzapine worldwide since 1996, when the first olanzapine-containing product was approved. FAERS includes only reports submitted to FDA, so there are likely to be additional cases about which we are unaware. One patient taking olanzapine experienced DRESS and died; however, this patient was taking multiple medicines that could also have contributed to death.
We urge health care professionals, patients, and caregivers to report side effects involving olanzapine (Zyprexa, Zyprexa Zydis, Zyprexa Relprevv, and Symbyax, and generics), or other medicines to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA warns about new impulse-control problems associated with mental health drug aripiprazole (Abilify, Abilify Maintena, Aristada)

[5-3-2016] The U.S. Food and Drug Administration (FDA) is warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have stopped when the medicine was discontinued or the dose was reduced. These impulse-control problems are rare, but they may result in harm to the patient and others if not recognized.
Although pathological gambling is listed as a reported side effect in the current aripiprazole drug labels, this description does not entirely reflect the nature of the impulse-control risk that we identified. In addition, we have become aware of other compulsive behaviors associated with aripiprazole, such as compulsive eating, shopping, and sexual actions. These compulsive behaviors can affect anyone who is taking the medicine. As a result, we are adding new warnings about all of these compulsive behaviors to the drug labels and the patient Medication Guides for all aripiprazole products.
Patients and caregivers should be alert for uncontrollable and excessive urges and behaviors while taking aripiprazole. It is important to talk with a health care professional as soon as possible if you or a family member experiences any of these uncontrollable urges, in order to prevent or limit possible harm. Patients should not suddenly stop taking their aripiprazole medicine without first talking to their health care professional.
Health care professionals should make patients and caregivers aware of the risk of these uncontrollable urges when prescribing aripiprazole, and specifically ask patients about any new or increasing urges while they are being treated with aripiprazole. Closely monitor for new or worsening uncontrollable urges in patients at higher risk for impulse-control problems. These include those with a personal or family history of obsessive-compulsive disorder, impulse-control disorder, bipolar disorder, impulsive personality, alcoholism, drug abuse, or other addictive behaviors. Consider reducing the dose or stopping the medicine if such urges develop.
Aripiprazole is used to treat certain mental disorders, including schizophrenia, bipolar disorder, Tourette's disorder, and irritability associated with autistic disorder. It may also be used in combination with antidepressants to treat depression. Aripiprazole can decrease hallucinations and other psychotic symptoms such as disorganized thinking. It can stabilize mood, improve depression, and decrease the tics of Tourette's disorder.
Aripiprazole is available under the brand names Abilify, Abilify Maintena, Aristada, and also as generics.
A search of the FDA Adverse Event Reporting System (FAERS) database and the medical literature in the 13 years since the approval of the first aripiprazole product (Abilify) in November 2002 identified a total of 184 case reports in which there was an association between aripiprazole use and impulse-control problems. There were 167 U.S. cases, which included adults and children. Pathological gambling was the most common (164 cases), but other compulsive behaviors including compulsive eating, spending or shopping, and sexual behaviors were also reported. FAERS includes only reports submitted to FDA, so there may be additional cases about which we are unaware. In order to provide context for these drug-associated events,

approximately 1.6 million patients received an aripiprazole prescription from U.S. outpatient retail pharmacies during 2015.
In the majority of cases, patients with no prior history of the compulsive behaviors experienced uncontrollable urges only after starting aripiprazole treatment. Within days to weeks of reducing the dose or discontinuing aripiprazole, these uncontrollable urges stopped.
We strongly advise health care professionals, patients, and caregivers to report side effects involving aripiprazole (Abilify, Abilify Maintena, Aristada) and other drugs to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function

[4-8-2016] The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. The FDA was asked to review numerous medical studies regarding the safety of metformin use in patients with mild to moderate impairment in kidney function, and to change the measure of kidney function in the metformin drug labeling that is used to determine whether a patient can receive metformin. We have concluded our review, and are requiring changes to the labeling of all metformin-containing medicines to reflect this new information.
Health care professionals should follow the latest recommendations when prescribing metformin-containing medicines to patients with impaired kidney function. Patients should talk to their health care professionals if they have any questions or concerns about taking metformin.
Metformin-containing medicines are available by prescription only and are used along with diet and exercise to lower blood sugar levels in patients with type 2 diabetes. Metformin-containing medicines are available as single-ingredient products and also in combination with other drugs used to treat diabetes. The current drug labeling strongly recommends against metformin use in some patients whose kidneys do not work normally because use of metformin in these patients can increase the risk of developing a serious and potentially deadly condition called lactic acidosis, in which too much lactic acid builds up in the blood.
We have concluded from the review of studies published in the medical literature that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function. The FDA is requiring changes to the metformin labeling to reflect this new information and provide specific recommendations on the drug's use in patients with mild to moderate kidney impairment.
We are also recommending that the measure of kidney function used to determine whether a patient can receive metformin be changed from one based on a single laboratory parameter (blood creatinine concentration) to one that provides a better estimate of kidney function in patients with kidney disease (i.e., glomerular filtration rate estimating equation (eGFR)).
Health care professionals and patients should report side effects involving metformin or other medicines to the FDA MedWatch program.

Safety Announcements

FDA Drug Safety Communication: FDA to review study examining use of oral fluconazole (Diflucan) in pregnancy

[4-26-2016] The U.S. Food and Drug Administration (FDA) is evaluating the results of a Danish study that conclude there is a possible increased risk of miscarriage with the use of oral fluconazole (Diflucan) for yeast infections. We are also reviewing additional data and will communicate our final conclusions and recommendations when our review is complete.
Health care professionals should be aware that the Centers for Disease Control and Prevention guidelines recommend only using topical antifungal products to treat pregnant women with vulvovaginal yeast infections, including for longer periods than usual if these infections persist or recur.
Patients who are pregnant or actively trying to get pregnant should talk to their health care professionals about alternative treatment options for yeast infections.
Oral fluconazole is used to treat yeast infections of the vaginal area, mouth, and esophagus. It is also used to treat a fungal infection of the brain and spinal cord called cryptococcal meningitis that most often affects people with weakened immune systems, and used to prevent yeast infections that can spread to the rest of the body in cancer patients who have a weakened immune system.

The current FDA drug label states that data available from studies in people do not suggest an increased risk of problems during pregnancy or abnormalities in developing babies when women are exposed to a single 150 mg dose of oral fluconazole to treat vaginal yeast infections. However, high doses of oral fluconazole (400-800 mg/day) taken by pregnant women for much longer than a single dose have resulted in reports of abnormalities at birth. In the Danish study, most of the oral fluconazole use appeared to be one or two doses of 150 mg.
Until FDA's review is complete and more is understood about this study and other available data, we advise cautious prescribing of oral fluconazole in pregnancy.
We urge both healthcare professionals and patients to report adverse events involving fluconazole to the FDA MedWatch program.

Safety Announcements

FDA announced that a safety review has found type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure

[4-27-2016] On April 5, 2016, FDA announced that a safety review has found type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure, particularly in patients who already have heart or kidney disease. Heart failure can result in the heart not being able to pump enough blood to meet the body's needs. As a result, we are adding new warnings to the drug labels about this safety issue. Saxagliptin and alogliptin are dipeptidyl peptidase-4 (DPP-4) inhibitor drugs, which are used with diet and exercise in adults with type 2 diabetes.
Health care professionals should consider discontinuing the medicine in patients who develop heart failure and monitor their diabetes control. If a patient's glucose level is not well-controlled with their current treatment, other diabetes medicines may be required.
The FDA evaluated two large clinical trials conducted in patients with heart disease. These clinical trials were also discussed at the FDA Endocrinologic and Metabolic Drugs Advisory Committee meeting in April 2015. Each trial showed that more patients who received saxagliptin or alogliptin containing medicines were hospitalized for heart failure compared to patients who received placebo. In the saxagliptin trial, 3.5% of patients who received the drug were hospitalized for heart failure versus 2.8% of patients who received a placebo. This is the same as 35 out of every 1,000 patients compared to 28 out of every 1,000 patients. Risk factors included a history of heart failure or kidney impairment. In the alogliptin trial, 3.9% of alogliptin-treated patients were hospitalized for heart failure versus 3.3% in the placebo group. This is the same as 39 out of every 1,000 patients compared to 33 out of every 1,000 patients.
As a result, we have added new Warnings and Precautions to the labels of medicines that contain saxagliptin or alogliptin to inform of the potential increased risk of heart failure.
Side effects involving saxagliptin, alogliptin, or other medicines should be reported to FDA's MedWatch program at www.fda.gov/medwatch.

Safety Announcements

FDA Drug Safety Communication: FDA approves brand name change for antidepressant drug Brintellix (vortioxetine) to avoid confusion with antiplatelet drug Brilinta (ticagrelor)

[5-2-2016] The U.S. Food and Administration (FDA) has approved a brand name change for the antidepressant Brintellix (vortioxetine) to decrease the risk of prescribing and dispensing errors resulting from name confusion with the blood-thinning medicine Brilinta (ticagrelor). The new brand name of the drug will be Trintellix, and it is expected to be available starting in June 2016. No other changes will be made to the label or packaging, and the medicine is exactly the same.
Because of the lag time associated with manufacturing bottles with the new brand name, health care professionals and patients may continue to see bottles labeled with the brand name Brintellix during the transition period.
Health care professionals should check carefully to make sure they have prescribed or dispensed the correct medicine. During the transition to the new name change from Brintellix to Trintellix, prescribers can reduce the risk of name confusion by including the generic name of the medication they are ordering, in addition to the brand name and indication for use. Patients should make sure they have received the correct medicine. Trintellix tablets will look the same as the Brintellix tablets. Those having any questions or concerns should talk to their prescriber or pharmacist.

Brintellix/Trintellix (vortioxetine) is used to treat a certain type of depression called major depressive disorder in adults. It is in a class of antidepressants called serotonin reuptake inhibitors (SSRIs) that work by affecting chemicals in the brain that may become unbalanced.
In a July 2015 Drug Safety Communication, we warned that name confusion between Brintellix and Brilinta had resulted in prescribing and dispensing errors since Brintellix was approved in September 2013. Due to continued reports of name confusion between the two medicines used for very different purposes, FDA worked with Brintellix manufacturer Takeda Pharmaceuticals to change the drug's brand name.
Individuals responsible for ordering and stocking the medicine should be aware that Trintellix will have a new National Drug Code (NDC) number. It is important for drug information content publishers and medication-related electronic system administrators to use the new brand name Trintellix and NDC number once Takeda makes vortioxetine available under the new name Trintellix.

Current Drug Shortages Index (as of May 1st, 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 (Adriamycin) 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***