Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
June 13, 2018
4:00pm

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for Board Meeting – June 13, 2018

DATE: May 31, 2018

NOTE: The DUR Board will meet at 4:00pm 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/ADHD Prescription Use in Reproductive-Aged Women – Appendix B

Action Item – Vote to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/Anhydrous Citric Acid) – Appendix C

Action Item – Vote to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension) – Appendix D

Action Item – Vote to Prior Authorize Admelog® (Insulin Lispro), Bydureon® BCise™ (Exenatide Extended-Release Autoinjector Pen), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin) – Appendix E

Action Item – Vote to Update the Prior Authorization Criteria for Tazorac® (Tazarotene Cream and Gel) – Appendix F

Action Item – Vote to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension) – Appendix G

Action Item – Vote to Prior Authorize Benznidazole – Appendix H

Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Imfinzi® (Durvalumab) and to Update the Current Prior Authorization Criteria – Appendix I

Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Erleada™ (Apalutamide) and Yonsa® (Abiraterone Acetate) – Appendix J

Action Item – Annual Review of Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor Medications and Vote to Prior Authorize Austedo® (Deutetrabenazine) for Tardive Dyskinesia – Appendix K

Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Cotempla XR-ODT™ [Methylphenidate Extended-Release (ER) Orally Disintegrating Tablet (ODT)], Mydayis® (Amphetamine/ Dextroamphetamine ER Capsule), and Adzenys ER™ (Amphetamine ER Suspension) – Appendix L

30-Day Notice to Prior Authorize Crysvita® (Burosumab-twza) – Appendix M

Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Baclofen 5mg Tablet, Esomep-EZS™ (Esomeprazole Kit), Lyrica® CR (Pregabalin Extended-Release), Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion), Sinuva™ (Mometasone Furoate Sinus Implant), Xepi™ (Ozenoxacin 1% Cream), Xhance™ (Fluticasone Propionate Nasal Spray), and ZTlido™ (Lidocaine 1.8% Topical System) – Appendix N

Annual Review of Atypical Antipsychotic Medications – Appendix O

Industry News and Updates – Appendix P

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

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – June 13, 2018 @ 4:00pm

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. April 11, 2018 DUR Minutes – Vote
B. April 11, 2018 DUR Recommendations Memorandum
C. May 9, 2018 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/ADHD Prescription Use in Reproductive-Aged Women – See Appendix B

A. Medication Coverage Activity for May 2018
B. Pharmacy Helpdesk Activity for May 2018
C. ADHD Prescription Use in Reproductive-Aged Women

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

5. Action Item – Vote to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/ Anhydrous Citric Acid) – See Appendix C

A. Introduction
B. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension) – See Appendix D

A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Admelog® (Insulin Lispro), Bydureon® BCise™ (Exenatide Extended-Release Autoinjector Pen), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin) – See Appendix E

A. Introduction
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Update the Prior Authorization Criteria for Tazorac® (Tazarotene Cream and Gel) – See Appendix F

A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension) – See Appendix G

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

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

10. Action Item – Vote to Prior Authorize Benznidazole – See Appendix H

A. Introduction
B. College of Pharmacy Recommendations

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

11. Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Imfinzi® (Durvalumab) and to Update the Current Prior Authorization Criteria – See Appendix I

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Lung Cancer Medications
D. Prior Authorization of Lung Cancer Medications
E. Market News and Updates
F. Imfinzi® (Durvalumab) Product Summary
G. Recommendations
H. Utilization Details of Lung Cancer Medications

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

12. Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Erleada™ (Apalutamide) and Yonsa® (Abiraterone Acetate) – See Appendix J

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

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

13. Action Item – Annual Review of Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor Medications and Vote to Prior Authorize Austedo® (Deutetrabenazine) for Tardive Dyskinesia – See Appendix K

A. Current Prior Authorization Criteria
B. Utilization of VMAT2 Inhibitor Medications
C. Prior Authorization of VMAT2 Inhibitor Medications
D. Market News and Updates
E. VMAT2 Inhibitor Cost Comparison
F. College of Pharmacy Recommendations
G. Utilization Details of VMAT2 Inhibitor Medications

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

14. Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Cotempla XR-ODT™ [Methylphenidate Extended-Release (ER) Orally Disintegrating Tablet (ODT)], Mydayis® (Amphetamine/Dextroamphetamine ER Capsule), and Adzenys ER™ (Amphetamine ER Suspension) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of ADHD and Narcolepsy Medications
C. Prior Authorization of ADHD and Narcolepsy Medications

D. Medicaid Drug Rebate Program
E. Market News and Updates
F. Cotempla XR-ODT™ (Methylphenidate ER ODT) Product Summary
G. Mydayis® (Amphetamine/Dextroamphetamine ER Capsule) Product Summary
H. Adzenys ER™ (Amphetamine ER Suspension) Product Summary
I. College of Pharmacy Recommendations
J. Utilization Details of ADHD and Narcolepsy Medications

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

15. 30-Day Notice to Prior Authorize Crysvita® (Burosumab-twza) – See Appendix M

A. Introduction
B. Market News and Updates
C. Crysvita® (Burosumab-twza) Product Summary
D. College of Pharmacy Recommendations

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

16. Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Baclofen 5mg Tablet, Esomep-EZS™ (Esomeprazole Kit), Lyrica® CR (Pregabalin Extended-Release), Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion), Sinuva™ (Mometasone Furoate Sinus Implant), Xepi™ (Ozenoxacin 1% Cream), Xhance™ (Fluticasone Propionate Nasal Spray), and ZTlido™ (Lidocaine 1.8% Topical System) – See Appendix N

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Special Formulations
D. Prior Authorization of Special Formulations
E. Baclofen 5mg Tablet Product Summary
F. ESOMEP-EZS™ (Esomeprazole Kit) Product Summary
G. Lyrica® CR (Pregabalin Extended-Release) Product Summary
H. Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion) Product Summary
I. Sinuva™ (Mometasone Furoate Sinus Implant) Product Summary
J. Xepi™ (Ozenoxacin 1% Cream) Product Summary
K. Xhance™ (Fluticasone Propionate Nasal Spray) Product Summary
L. ZTlido™ (Lidocaine 1.8% Topical System) Product Summary
M. College of Pharmacy Recommendations
N. Utilization Details of Special Formulations

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

17. Annual Review of Atypical Antipsychotic Medications – See Appendix O

A. Current Prior Authorization Criteria
B. Utilization of Atypical Antipsychotic Medications
C. Prior Authorization of Atypical Antipsychotic Medications
D. Medicaid Drug Rebate Program
E. Market News and Updates
F. College of Pharmacy Recommendations
G. Utilization Details of Atypical Antipsychotic Medications

Non-Presentation; Questions Only:

18. Industry News and Updates – See Appendix P

A. Introduction
B. News and Updates

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

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

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

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

A. Jynarque™ (Tolvaptan)
B. Opioid Analgesics and Medication Assisted Treatment (MAT) Medications
C. Atopic Dermatitis Medications
D. Brineura® (Cerliponase Alfa)
E. Radicava® (Edaravone)
F. Vimizim® (Elosulfase Alfa)
G. Botulinum Toxins

**Future business subject to change.*

21. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF APRIL 11, 2018

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Wendi Chandler, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist		x
Timothy Pham, Ph.D.; Postdoctoral Research Fellow	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Sarah Schmidt, Pharm.D., BCPS, BCOP; Clinical Assistant Professor	x	
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Christina Bulkley, Pharm.D.		x
Laura Tidmore, Pharm.D.	x	
Corby Thompson, Pharm.D.		x
Visiting Pharmacy Student(s): N/A		

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

OTHERS PRESENT:		
Jon Maguire, GSK	Jeff Knappen, Spark Therapeutics	Rei Nakamura, Spark Therapeutics
Trebla Grant, Kite	Nima Nabavi, Novo Nordisk	Matt Forney, Merck
Jim Chapman, AbbVie	Quynh Doan, AbbVie	Marc Parker, Sunovion
Jim Dunlap, PhRMA	Cris Valladares, Celgene	Scott Poole, Intersect ENT
Brent Hildebrand, Gilead	Aaron Shaw, BI	Brian Maves, Pfizer
Bob Atkins, Biogen	Amber Schrantz, Lilly	Terry McCurren, Otsuka America
Melvin Nwamadi, Abbott	Erica Brumleve, GSK	

PRESENT FOR PUBLIC COMMENT:	
Rei Nakamura	Spark Therapeutics

AGENDA ITEM NO. 1: CALL TO ORDER

1A: ROLL CALL

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: AGENDA ITEM NO. 6 SPEAKER: REI NAKAMURA

ACTION: NONE REQUIRED

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

3A: MARCH 14, 2018 DUR MINUTES – VOTE

3B: MARCH 14, 2018 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Cothran

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/METOCLOPRAMIDE (REGLAN®) INDUCED TARDIVE DYSKINESIA SAFETY MAILING UPDATE

4A: MEDICATION COVERAGE ACTIVITY FOR MARCH 2018

4B: PHARMACY HELP DESK ACTIVITY FOR MARCH 2018

4C: METOCLOPRAMIDE (REGLAN®) INDUCED TARDIVE DYSKINESIA SAFETY MAILING UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: VOTE TO PRIOR AUTHORIZE OCREVUS™ (OCRELIZUMAB)

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE LUXTURNA™ (VORETIGENE NEPARVOVEC-RZYL)

6A: INTRODUCTION

6B: OTHER AAV2 CLINICAL STUDIES

6C: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

The Drug Utilization Review (DUR) Board recommended the addition of the following to the criteria: A prior authorization request with patient-specific information may be submitted for consideration of Luxturna™ for members not meeting all of the current prior authorization criteria requirements.

Dr. Preslar moved to approve; seconded by Dr. Garton
ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE PROLASTIN®-C LIQUID [ALPHA$_1$-PROTEINASE INHIBITOR (HUMAN)]
7A: INTRODUCTION
7B: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Chandler
Dr. Garton moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE ARZERRA® (OFATUMUMAB), GAZYVA® (OBINUTUZUMAB), IMBRUVICA® (IBRUTINIB), VENCLEXTA™ (VENETOCLAX), AND ZYDELIG® (IDELALISIB)
8A: INTRODUCTION
8B: RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Schmidt
Dr. Huddleston moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF THE SOONERCARE PHARMACY BENEFIT
9A: SUMMARY
9B: MEDICAID DRUG REBATE PROGRAM
9C: ALTERNATIVE PAYMENT MODELS
9D: DRUG APPROVAL TRENDS
9E: TRADITIONAL VERSUS SPECIALTY PHARMACY PRODUCTS
9F: TOP 10 THERAPEUTIC CLASSES BY REIMBURSEMENT
9G: TOP 10 MEDICATIONS BY REIMBURSEMENT
9H: COST PER CLAIM
9I: CONCLUSION
9J: TOP 100 REIMBURSED DRUGS BY FISCAL YEAR
9K: TOP 50 MEDICATIONS BY TOTAL NUMBER OF CLAIMS
9L: TOP 10 TRADITIONAL AND SPECIALTY THERAPEUTIC CLASSES BY FISCAL YEAR
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 10: HEPATITIS C MEDICATION CRITERIA UPDATE
10A: INTRODUCTION
10B: UTILIZATION OF HEPATITIS C MEDICATIONS
10C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Holderread
Dr. Preslar moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF BENLYSTA® (BELIMUMAB)
11A: CURRENT PRIOR AUTHORIZATION CRITERIA
11B: UTILIZATION OF BENLYSTA® (BELIMUMAB)
11C: PRIOR AUTHORIZATION OF BENLYSTA® (BELIMUMAB)
11D: MARKET NEWS AND UPDATES
11E: COLLEGE OF PHARMACY RECOMMENDATIONS
11F: UTILIZATION DETAILS OF BENLYSTA® (BELIMUMAB)
Materials included in agenda packet; presented by Dr. Adams
Dr. Huddleston moved to approve; seconded by Ms. Varalli-Claypool
ACTION: MOTION CARRIED

AGENDA ITEM NO. 12: **ANNUAL REVIEW OF DIABETES MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ADMELOG® (INSULIN LISPRO), FIASP® (INSULIN ASPART), HUMULIN® R U-500 VIALS (INSULIN HUMAN 500 UNITS/ML), OZEMPIC® (SEMAGLUTIDE), STEGLATRO™ (ERTUGLIFLOZIN), SEGLUROMET™ (ERTUGLIFLOZIN/METFORMIN), AND STEGLUJAN™ (ERTUGLIFLOZIN/SITAGLIPTIN)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA
12B: UTILIZATION OF DIABETES MEDICATIONS
12C: PRIOR AUTHORIZATION OF DIABETES MEDICATIONS
12D: MARKET NEWS AND UPDATES
12E: ADMELOG® (INSULIN LISPRO) PRODUCT SUMMARY
12F: FIASP® (INSULIN ASPART) PRODUCT SUMMARY
12G: OZEMPIC® (SEMAGLUTIDE) PRODUCT SUMMARY
12H: STEGLATRO™ (ERTUGLIFLOZIN) PRODUCT SUMMARY
12I: SEGLUROMET™ (ERTUGLIFLOZIN/METFORMIN) PRODUCT SUMMARY
12J: STEGLUJAN™ (ERTUGLIFLOZIN/SITAGLIPTIN) PRODUCT SUMMARY
12K: COLLEGE OF PHARMACY RECOMMENDATIONS
12L: UTILIZATION DETAILS OF NON-INSULIN DIABETES MEDICATIONS
12M: UTILIZATION DETAILS OF INSULIN MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: **ANNUAL REVIEW OF ANTIHYPERTENSIVE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PREXXARTAN® (VALSARTAN ORAL SOLUTION), TEKTURNA® (ALISKIREN ORAL PELLETS), AND CAROSPIR® (SPIRONOLACTONE ORAL SUSPENSION)**

13A: CURRENT PRIOR AUTHORIZATION CRITERIA
13B: UTILIZATION OF ANTIHYPERTENSIVE MEDICATIONS
13C: PRIOR AUTHORIZATION OF ANTIHYPERTENSIVE MEDICATIONS
13D: MARKET NEWS AND UPDATES
13E: PREXXARTAN® (VALSARTAN ORAL SOLUTION) PRODUCT SUMMARY
13F: TEKTURNA® (ALISKIREN ORAL PELLETS) PRODUCT SUMMARY
13G: CAROSPIR® (SPIRONOLACTONE ORAL SUSPENSION) PRODUCT SUMMARY
13H: COLLEGE OF PHARMACY RECOMMENDATIONS
13I: UTILIZATION DETAILS OF ANTIHYPERTENSIVE MEDICATIONS

Materials included in agenda packet; presented by Dr. Abbott
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: **INDUSTRY NEWS AND UPDATES**

14A: INTRODUCTION
14B: NEWS AND UPDATES

Materials included in agenda packet; Non-presentation; Questions only
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: **U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**
NO LIVE MEETING SCHEDULED FOR MAY. MAY WILL BE PACKET ONLY MEETING.

16A: OTIC ANTI-INFECTIVE MEDICATIONS
16B: ELAPRASE® (IDURSULFASE)
16C: KUVAN® (SAPROPTERIN)
16D: GRANULOCYTE COLONY STIMULATING FACTORS (G-CSFs)
16E: OPHTHALMIC ANTI-INFLAMMATORIES
16F: ANTI-PARASITIC MEDICATIONS

16G: BOWEL PREPARATION MEDICATIONS

FUTURE BUSINESS SUBJECT TO CHANGE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ADJOURNMENT

The meeting was adjourned at 5:17pm.

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

Memorandum

Date: April 12, 2018

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

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Meeting of April 11, 2018

Recommendation 1: Metoclopramide (Reglan®) Induced Tardive Dyskinesia Safety Mailing Update

NO ACTION REQUIRED.

Recommendation 2: Vote to Prior Authorize Ocrevus™ (Ocrelizumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Ocrevus™ (ocrelizumab) with the following criteria:

Ocrevus™ (Ocrelizumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing or primary progressive forms of Multiple Sclerosis (MS); and
2. Approvals will not be granted for concurrent use with other disease modifying therapies; and
3. Ocrevus™ must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. The prescriber must agree that the member will be monitored for one hour after each infusion; and

4. Prescriber must verify hepatitis B virus (HBV) testing has been performed prior to initiating Ocrevus™ therapy and member does not have active HBV; and
5. Verification from the prescriber that member has no active infection(s); and
6. Verification from the prescriber that female members are not currently pregnant and will use contraception while receiving Ocrevus™ therapy and for six months after the last infusion of Ocrevus™; and
7. Compliance will be checked for continued approval.

Recommendation 3: Vote to Prior Authorize Luxturna™ (Voretigene Neparvovec-rzyl)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Luxturna™ (voretigene neparvovec-rzyl) with the following criteria with changes noted in red based on recommendations by the DUR Board:

Luxturna™ (Voretigene Neparvovec-rzyl) Approval Criteria:

1. An FDA approved diagnosis of biallelic *RPE65* mutation-associated retinal dystrophy; and
    a. Diagnosis must be confirmed by genetic testing; and
2. Member must have sufficient viable retinal cells in both eyes as determined by the treating physician(s); and
3. Member must have best corrected visual acuity of 20/60 or worse in both eyes and/or visual field less than 20 degrees in any meridian in both eyes; and
4. Member must be four years of age or older; and
5. Member must not have participated in a previous *RPE65* gene therapy study or have previously received treatment with Luxturna™; and
6. ~~Member must not have used high-dose retinoid compounds (>7,500 retinal equivalent units or >3,300 IU per day of vitamin A) in the past 18 months; and~~
7. Member must not have had intraocular surgery in the past 6 months; and
8. Female members of child bearing age must not be pregnant and must have a negative pregnancy test immediately prior to administration of Luxturna™; and
9. Male and female members of child bearing age must be willing to use effective contraception during treatment with Luxturna™ and for at least 4 months after administration of Luxturna™; and
10. Member must take the recommended systemic oral corticosteroid regimen, starting 3 days prior to administration of Luxturna™ to each eye, and continuing after administration of Luxturna™, as per package labeling of Luxturna™; and
11. Luxturna™ must be prescribed and administered by a retinal surgeon with expertise in the treatment of biallelic *RPE65* mutation-associated retinal dystrophy and in the administration of Luxturna™ at an Ocular Gene Therapy Treatment Center; and
    a. Luxturna™ must be shipped via cold chain supply shipping and delivery to the Ocular Gene Therapy Treatment Center where the member is scheduled to receive treatment; and
    b. Luxturna™ must be stored frozen prior to preparation for administration (Luxturna™ should be administered within 4 hours of preparation); and

c. The receiving facility must have in place a mechanism to track patient-specific Luxturna™ from receipt to storage to administration; and

12. Luxturna™ must be administered subretinally to each eye on separate days within a close interval, but no fewer than 6 days apart; and
    a. The scheduled procedure date for each eye must be provided; and
13. Only one single-dose vial per eye will be approved per member per lifetime; and
    a. Each single-dose vial of Luxturna™ is to be dispensed immediately prior to the scheduled procedure for the specific eye.
14. A prior authorization request with patient-specific information may be submitted for consideration of Luxturna™ for members not meeting all of the current prior authorization criteria requirements.

Recommendation 4: Vote to Prior Authorize Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)]

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Prolastin®-C Liquid [alpha$_1$-proteinase inhibitor (human)] with the following criteria:

Prolastin®-C Liquid [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
   a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
   b. Serum levels of AAT less than 11µmol/L; and
   c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C, Aralast NP™, Glassia®, and Zemaira®; and
8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

The College of Pharmacy also recommends adding Zemaira® to the current Aralast NP™ and Glassia® criteria based on net cost after rebates.

Aralast NP™, ~~and~~ Glassia®, and Zemaira® [Alpha$_1$-Proteinase Inhibitor (Human)] Approval Criteria:

1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha$_1$-antitrypsin (AAT) with clinical evidence of emphysema; and
2. Diagnosis confirmed by all of the following:
   a. Genetic confirmation of PiZZ, PiZ(null) or Pi(null, null) phenotype alpha$_1$-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; and
   b. Serum levels of AAT less than 11µmol/L; and
   c. Documented emphysema with airflow obstruction; and
3. Prescriber must document that member's forced expiratory volume in one second (FEV_1) is less than or equal to 65% predicted; and
4. Must be prescribed by a pulmonary disease specialist or advanced care practitioner specializing in pulmonary disease; and
5. The prescriber must verify the member is a non-smoker; and
6. The prescriber must verify the member does not have antibodies to IgA; and
7. A patient-specific, clinically significant reason why the member cannot use Prolastin®-C; and
8. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Recommendation 5: Vote to Prior Authorize Arzerra® (Ofatumumab), Gazyva® (Obinutuzumab), Imbruvica® (Ibrutinib), Venclexta™ (Venetoclax), and Zydelig® (Idelalisib)

MOTION CARRIED by unanimous approval.

Arzerra® (Ofatumumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first-line treatment of CLL in combination with chlorambucil or bendamustine; or
2. For relapsed or refractory disease as a single-agent or in combination with fludarabine and cyclophosphamide; or
3. As maintenance therapy as second-line extended dosing following complete or partial response to relapsed or refractory therapy (maximum 2 years).

Arzerra® (Ofatumumab) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. For previously treated disease that does not respond to primary therapy or for progressive or relapsed disease; and
2. As a single-agent or combination therapy; and
3. Member is rituximab-intolerant.

Gazyva® (Obinutuzumab) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. In combination with chlorambucil or bendamustine for first-line therapy; or
2. As a single-agent for relapsed or refractory disease.

Gazyva® (Obinutuzumab) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. Grade 1 or 2 patients with Stage I (≥7cm), contiguous Stage II (≥7cm), noncontiguous Stage II, Stage III, or Stage IV patients (first, second, or subsequent therapy); and
2. In combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine; and
3. When used for maintenance therapy a total of 12 doses will be approved.

Gazyva® (Obinutuzumab) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy in combination with bendamustine; or
2. Maintenance therapy as second-line consolidation or extended dosing in rituximab-refractory patients treated with obinutuzumab and bendamustine for a total of 12 doses.

Imbruvica® (Ibrutinib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 or 2 FL; and
2. As subsequent therapy (third-line or greater) for histologic transformation to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Graft-Versus-Host Disease (cGVHD) Diagnosis]:

1. A diagnosis of cGVHD after failure of one or more lines of therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Histologic Transformation of Marginal Zone Lymphoma (MZL) to Diffuse Large B-Cell Lymphoma Diagnosis]:

1. As third-line or greater therapy for patients who have transformed to non-germinal center diffuse large B-cell lymphoma.

Imbruvica® (Ibrutinib) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. Used as a single-agent or in combination with rituximab or lenalidomide/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Diffuse Large B-Cell Lymphoma Diagnosis or Acquired Immunodeficiency Syndrome (AIDS)-Related B-Cell Lymphoma Diagnosis]:

1. A diagnosis of non-germinal center diffuse large B-cell lymphoma; and
2. As second-line or subsequent therapy; and
3. Member is not a candidate for high-dose therapy.

Imbruvica® (Ibrutinib) Approval Criteria [Post-Transplant Lymphoproliferative Disorders Diagnosis]:

1. As second-line and subsequent therapy in patients with partial response, persistent, or progressive disease; and

2. Non-germinal center B-cell type.

Imbruvica® (Ibrutinib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. As first or subsequent therapy for CLL/SLL; and
2. As a single-agent or in combination with bendamustine/rituximab.

Imbruvica® (Ibrutinib) Approval Criteria [Hairy Cell Leukemia Diagnosis]:

1. As a single-agent in patients with indication for treatment for progression.

Imbruvica® (Ibrutinib) Approval Criteria [Waldenström's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma Diagnosis]:

1. As first or subsequent therapy; and
2. As a single-agent.

Venclexta™ (Venetoclax) Approval Criteria [Mantle Cell Lymphoma (MCL) Diagnosis]:

1. As second-line or subsequent therapy; and
2. As a single-agent only.

Venclexta™ (Venetoclax) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. For relapsed/refractory disease; and
2. In combination with rituximab or as a single-agent.

Zydelig® (Idelalisib) Approval Criteria [Follicular Lymphoma (FL) Diagnosis]:

1. A diagnosis of Grade 1 to 2 FL; and
2. As second-line or subsequent therapy for refractory or progressive disease; and
3. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Gastric or Nongastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma, Nodal or Splenic Marginal Zone Lymphoma (MZL) Diagnosis]:

1. As second-line or subsequent therapy for refractory or progressive disease; and
2. Refractory to both alkylator and rituximab therapy.

Zydelig® (Idelalisib) Approval Criteria [Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Diagnosis]:

1. For relapsed or refractory disease; and
2. In combination with rituximab or rituximab/bendamustine; or
3. As a single-agent.

Recommendation 6: Annual Review of the SoonerCare Pharmacy Benefit

NO ACTION REQUIRED.

Recommendation 7: Hepatitis C Medication Criteria Update

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends adding the following criteria to all prior authorized hepatitis C virus (HCV) medications regarding confirmation of chronic HCV infection:

1. Member has chronic HCV infection defined by:
    a. If the member has a liver fibrosis score ≥F1 (METAVIR equivalent) then only one detectable and quantifiable HCV RNA (>15 IU/mL) test within the last 12 months is required; or
    b. If the member has a liver fibrosis score <F1 (METAVIR equivalent) then the following must be met:
        i. Positive (i.e., reactive) HCV antibody test that is at least six months old and has a detectable and quantifiable HCV RNA (>15 IU/mL) test six months after date of positive HCV antibody test; or
        ii. Two detectable and quantifiable HCV RNA (>15 IU/mL) tests at least six months apart.

Recommendation 8: Annual Review of Benlysta® (Belimumab)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the changes shown in red based on the recent U.S. Food and Drug Administration (FDA) approval of the subcutaneous (subQ) formulation of Benlysta® (belimumab):

Benlysta® (Belimumab) Approval Criteria:

1. The intravenous (IV) formulation will be covered as a medical claim only benefit while the subcutaneous (subQ) formulation will be covered as a pharmacy only benefit; and
2. An FDA approved indication of the treatment of adults with active, autoantibody-positive, systemic lupus erythematosus (SLE) already receiving standard therapy; and
3. Documented inadequate response to at least two of the following medications:
    a. High-dose oral corticosteroids; or
    b. Methotrexate; or
    c. Azathioprine; or
    d. Mycophenolate; or
    e. Cyclophosphamide; and
4. Member must not have severe active lupus nephritis or severe active central nervous system lupus; and
5. Benlysta® will not be approved for combination use with biologic therapies or IV cyclophosphamide.

Recommendation 9: Annual Review of Diabetes Medications and 30-Day Notice to Prior Authorize Admelog® (Insulin Lispro), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Antihypertensive Medications and 30-Day Notice to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension)

NO ACTION REQUIRED.

Recommendation 11: Industry News and Updates

NO ACTION REQUIRED.

Recommendation 12: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

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

Memorandum

Date: May 10, 2018

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

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

Subject: Drug Utilization Review (DUR) Board Recommendations from Packet of May 09, 2018

Recommendation 1: 2018 Spring Pipeline Update

NO ACTION REQUIRED.

Recommendation 2: Annual Review of Anti-Parasitic Medications and 30-Day Notice to Prior Authorize Benznidazole

NO ACTION REQUIRED.

Recommendation 3: Annual Review of Bowel Preparation Medications and 30-Day Notice to Prior Authorize Clenpiq™ (Sodium Picosulfate/Magnesium Oxide/ Anhydrous Citric Acid)

NO ACTION REQUIRED.

Recommendation 4: Annual Review of Otic Anti-Infective Medications and 30-Day Notice to Prior Authorize Otiprio® (Ciprofloxacin Otic Suspension)

NO ACTION REQUIRED.

Recommendation 5: Annual Review of Granulocyte Colony-Stimulating Factors (G-CSFs)

NO ACTION REQUIRED.

Recommendation 6: Annual Review of Elaprase® (Idursulfase)

NO ACTION REQUIRED.

Recommendation 7: Annual Review of Kuvan® (Sapropterin)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Ophthalmic Anti-Inflammatories

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Topical Acne Products

NO ACTION REQUIRED.

Recommendation 10: Industry News and Updates

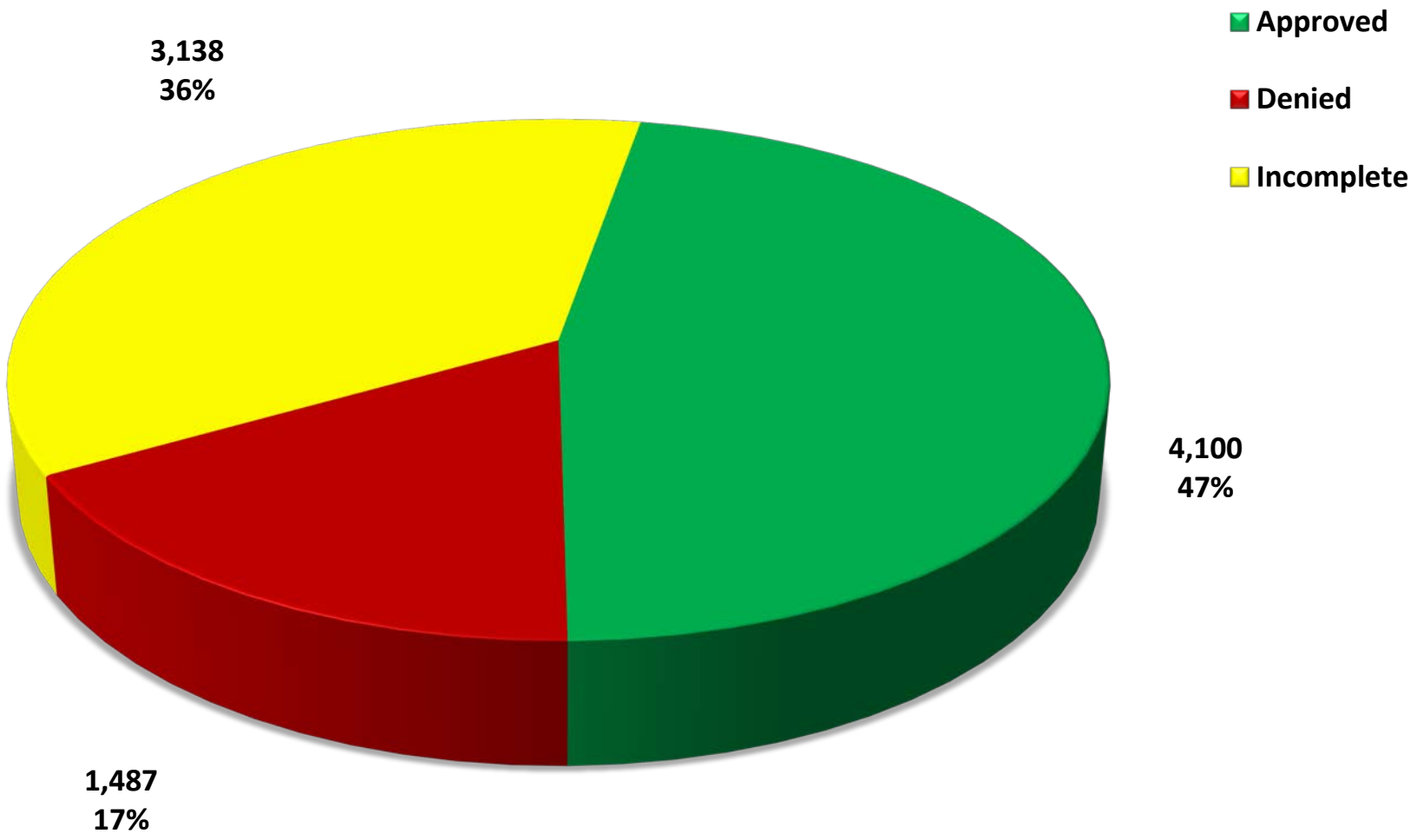
NO ACTION REQUIRED.

Recommendation 11: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates

NO ACTION REQUIRED.

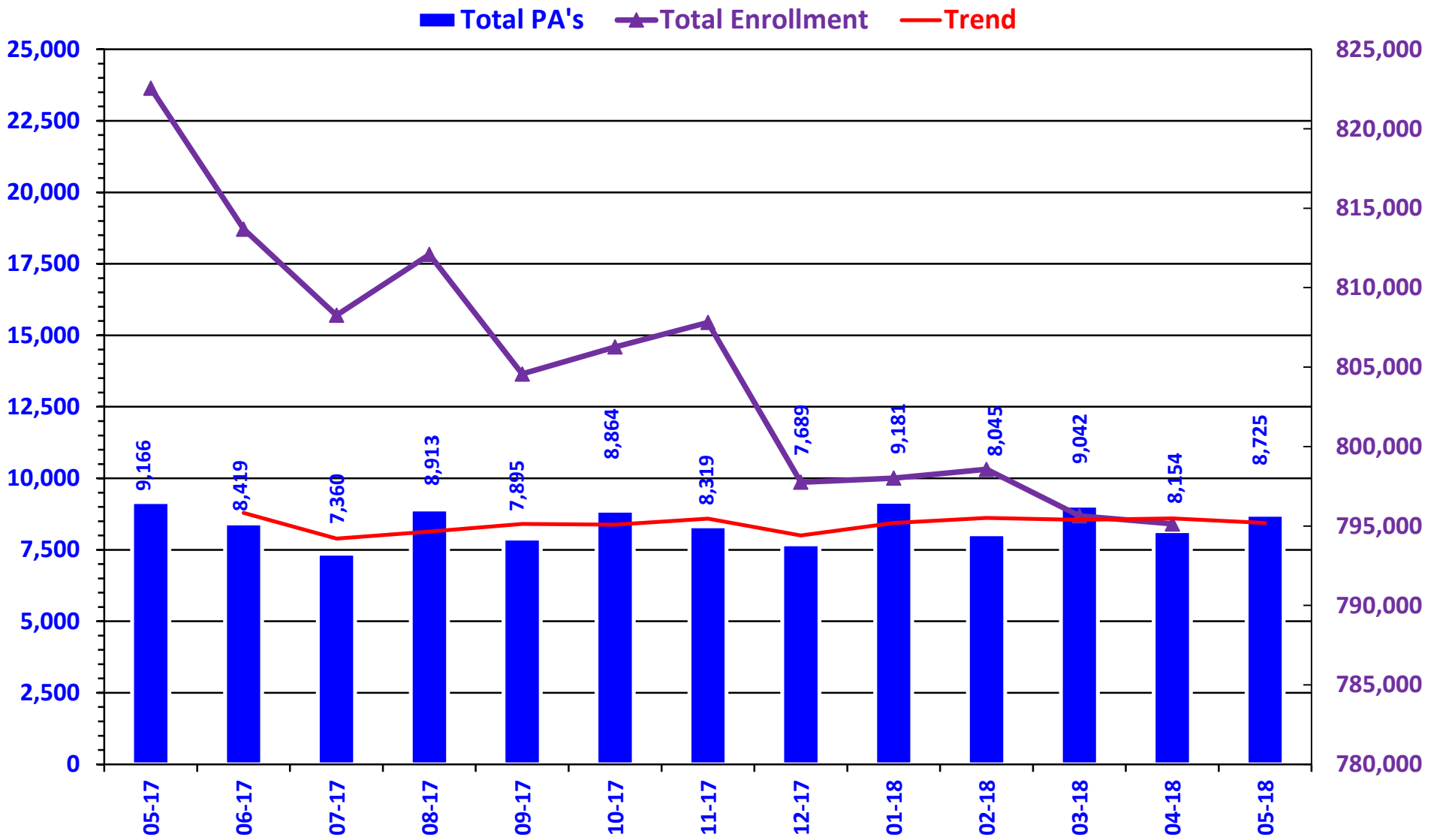
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: MAY 2018



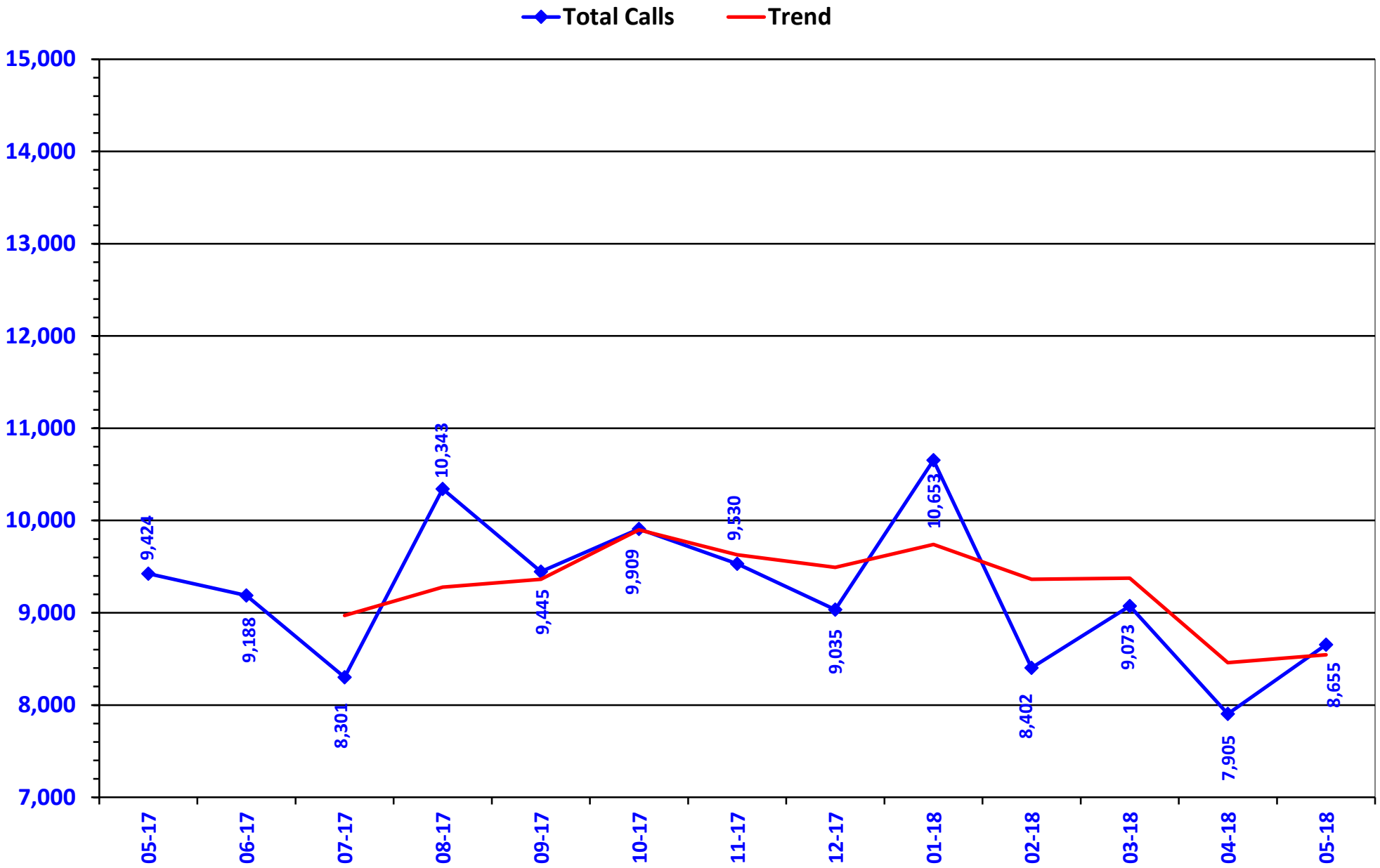
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: MAY 2017 – MAY 2018



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
MAY 2017 – MAY 2018



Prior Authorization Activity

5/1/2018 Through 5/31/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	225	20	61	144	318
Analgesic - NonNarcotic	17	0	4	13	0
Analgesic - Narcotic	447	209	55	183	153
Angiotensin Receptor Antagonist	17	6	5	6	313
Antiasthma	89	15	26	48	266
Antibiotic	36	19	3	14	325
Anticonvulsant	141	49	22	70	263
Antidepressant	170	57	29	84	307
Antidiabetic	224	90	48	86	350
Antigout	10	2	4	4	359
Antihistamine	40	8	15	17	257
Antimigraine	37	9	7	21	95
Antineoplastic	80	45	7	28	152
Antiulcers	199	44	68	87	139
Antiviral	10	7	1	2	78
Anxiolytic	45	31	5	9	242
Atypical Antipsychotics	204	124	15	65	336
Biologics	104	63	14	27	301
Bladder Control	77	16	29	32	359
Blood Thinners	266	159	20	87	338
Botox	38	29	9	0	335
Buprenorphine Medications	399	299	22	78	76
Cardiovascular	112	52	19	41	347
Cephalosporins	10	1	2	7	10
Chronic Obstructive Pulmonary Disease	150	24	52	74	335
Constipation/Diarrhea Medications	166	22	73	71	255
Contraceptive	28	23	0	5	212
Dermatological	228	65	68	95	251
Diabetic Supplies	541	316	17	208	181
Endocrine & Metabolic Drugs	110	74	7	29	145
Erythropoietin Stimulating Agents	20	13	2	5	101
Fibric Acid Derivatives	13	1	4	8	359
Fibromyalgia	228	45	117	66	301
Fish Oils	16	0	5	11	0
Gastrointestinal Agents	116	25	33	58	231
Glaucoma	11	3	3	5	160
Growth Hormones	82	60	6	16	156
Hematopoietic Agents	13	9	0	4	163
Hepatitis C	223	153	17	53	8
HFA Rescue Inhalers	50	1	13	36	360
Insomnia	55	5	24	26	184
Insulin	124	40	13	71	319
Miscellaneous Antibiotics	19	2	6	11	60
Multiple Sclerosis	59	30	7	22	211
Muscle Relaxant	54	7	17	30	72
Nasal Allergy	103	16	32	55	136
Neurological Agents	95	19	34	42	238
Neuromuscular Agents	11	5	3	3	294
NSAIDs	154	19	45	90	245
Ocular Allergy	57	11	12	34	105

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Ophthalmic Anti-infectives	19	2	5	12	6
Osteoporosis	28	5	10	13	359
Other*	325	65	92	168	285
Otic Antibiotic	22	4	6	12	12
Respiratory Agents	17	11	3	3	210
Statins	22	1	14	7	358
Stimulant	754	383	84	287	343
Testosterone	38	14	11	13	358
Topical Antifungal	29	4	10	15	53
Topical Corticosteroids	95	4	45	46	214
Vitamin	77	18	29	30	156
Pharmacotherapy	119	111	0	8	326
Emergency PAs	0	0	0	0	
Total	**7,268**	**2,964**	**1,409**	**2,895**	
Overrides					
Brand	33	27	1	5	313
Compound	20	16	1	3	75
Cumulative Early Refill	1	1	0	0	16
Diabetic Supplies	10	8	0	2	161
Dosage Change	335	317	1	17	11
High Dose	3	1	0	2	4
Ingredient Duplication	21	14	1	6	11
Lost/Broken Rx	125	120	0	5	12
NDC vs Age	270	178	26	66	249
Nursing Home Issue	30	30	0	0	10
Opioid Quantity	27	22	3	2	177
Other*	38	28	2	8	11
Quantity vs. Days Supply	532	370	44	118	258
STBS/STBSM	19	12	2	5	58
Stolen	11	10	0	1	13
Temporary Unlock	1	1	0	0	2
Third Brand Request	38	28	1	9	25
Wrong D.S. on Previous Rx	1	0	0	1	0
Overrides Total	**1,457**	**1,136**	**78**	**243**	
Total Regular PAs + Overrides	**8,725**	**4,100**	**1,487**	**3,138**	

Denial Reasons	
Unable to verify required trials.	2,514
Does not meet established criteria.	1,515
Lack required information to process request.	593
Other PA Activity	
Duplicate Requests	575
Letters	9,863
No Process	3
Changes to existing PAs	641
Helpdesk Initiated Prior Authorizations	618
PAs Missing Information	48

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

ADHD Prescription Use in Reproductive-Aged Women

Oklahoma Health Care Authority
June 2018

Introduction[1,2,3]

Attention-deficit/hyperactivity disorder (ADHD), as defined by the National Institute of Mental Health, is a brain disorder marked by an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. Medication use for the treatment of ADHD is on the rise and the safety of ADHD medication use during pregnancy remains unclear. It has been reported that half of the pregnancies in the United States are unintended, and ADHD medication use in these women could result in unnecessary risk to the fetus.

In a study done by the Centers for Disease Control and Prevention (CDC), pharmacy claims data for privately insured women 15 to 44 years of age were analyzed to look at trends of ADHD prescriptions filled from 2003 to 2015. From 2003 to 2015, the number of women who filled at least one ADHD medication increased by 344%. A majority of the increase was due to stimulant medications. Use of non-stimulant medications, such as atomoxetine, was stable over the study time frame. The largest increase of ADHD medications occurred in the 25 to 29 year old age group, which rose 700% from 2003 to 2015. In 2015, the most common ADHD medications filled in this claims analysis were mixed amphetamine salts (60.8%), lisdexamfetamine (26.7%), and methylphenidate (18.1%). It is important to note that the data used did not include what indication the medication was used for, if the women were pregnant, or the incidence of pregnancy.

SoonerCare Claims Analysis

The following claims analysis for calendar year (CY) 2015 to CY 2017 was conducted by the University of Oklahoma College of Pharmacy. The results were compiled by loosely following the methodology of the study discussed in the introduction section of this report. Female members 15 to 44 years of age were included in the analysis.

ADHD Medication Usage in Women of Reproductive Age: CY 2015 to CY 2017[1]

The CDC analyzed pharmacy claims data from the Truven Health MarketScan Commercial Database from 2003 to 2015. The data was a collection of private, employer-sponsored insurance, including dependents, across the United States. Analysis was restricted to women 15 to 44 years of age, resulting in a sample size of 2.3 to 6.8 million each year (median = 4.6 million). SoonerCare pharmacy claims were analyzed from CY 2015 to CY 2017. Similar to the CDC study, the SoonerCare claims analysis was restricted to female members 15 to 44 years of age, resulting in a sample size of 165,865 to 224,144 (median = 223,998).

Results of the CDC analysis found a 344% increase from 2003 (0.9% of women) to 2015 (4.0% of women) in the percentage of reproductive-aged women (15 to 44 years of age) who filled at

least one ADHD prescription. While SoonerCare data did show an increase in the same population from 2015 to 2017, the total percentage of reproductive-aged women who filled at least one ADHD prescription peaked at 2.6% in CY 2016 and declined to 2.0% in CY 2017. The percentage change from 2015 to 2017 was less than 10% (9.9%), and did not consistently increase from year to year as the CDC trend results revealed.

The following is a table of the percentage of female SoonerCare members 15 to 44 years of age with a paid claim for an ADHD medication by age group and medication class. All age groups except the 20 to 24 year old age group saw an increase from 2015 to 2017 with the largest increase occurring in the 40 to 44 year old age group. All age groups in the SoonerCare analysis had a lower percentage of women with ADHD medication paid claims as compared to the CDC analysis during the overlapping year of 2015.

Percentage of Women 15 to 44 Years of Age With ADHD Medication Paid Claim(s)					
Age Group (Years)	**CDC 2015**	**SoonerCare 2015**	**SoonerCare 2016**	**SoonerCare 2017**	**SoonerCare % Change From 2015 to 2017**
15 to 19	5.4%	3.8%	5.1%	4.2%	9.5%
20 to 24	5.5%	0.8%	1.0%	0.7%	-13.3%
25 to 29	4.0%	0.9%	1.4%	1.0%	15.9%
30 to 34	3.3%	1.2%	1.9%	1.4%	9.7%
35 to 39	3.0%	1.3%	2.0%	1.4%	6.0%
40 to 44	2.9%	1.1%	1.7%	1.4%	22.8%
Medication Class	**CDC 2015**	**SoonerCare 2015**	**SoonerCare 2016**	**SoonerCare 2017**	**SoonerCare % Change From 2015 to 2017**
Any ADHD	4.0%	1.8%	2.6%	2.0%	9.9%
Stimulant	3.9%	1.5%	2.2%	1.6%	6.6%
Non-Stimulant	0.2%	0.4%	0.6%	0.5%	23.3%
Number of Women Included	**CDC 2015**	**SoonerCare 2015**	**SoonerCare 2016**	**SoonerCare 2017**	**SoonerCare % Change From 2015 to 2017**
Number of Women Included	4,580,924	223,998	165,865	224,144	0.07%

ADHD = attention-deficit/hyperactivity disorder; CDC = Centers for Disease Control and Prevention; % = percentage

Another important difference noted in the SoonerCare claims analysis and the CDC analysis is the non-stimulant vs. stimulant trends. The CDC found that the increase in percentage of women with paid claims for ADHD medications was attributable to the stimulant medications. During their analysis, stimulant claims rose 388% compared to non-stimulant medications (0%) which were stable throughout the study. The SoonerCare claims analysis revealed that while stimulant claims increased 6.58% from CY 2015 to CY 2017, non-stimulant claims increased at a greater pace (23.26%). This can likely be accounted for by the CDC analysis not including clonidine extended-release (ER; Kapvay®) and guanfacine ER (Intuniv®) in their analysis; these medications were included in the SoonerCare claims analysis. Additionally, the SoonerCare claims analysis included medications indicated for narcolepsy that do not have an ADHD indication [Provigil® (modafinil), Nuvigil® (armodafinil), and Xyrem® (sodium oxybate)]. The CDC

analysis only included medications indicated for ADHD, and excluded narcolepsy medications that do not have an ADHD indication. The reason for use of stimulant medications was not included as a part of either the SoonerCare claims analysis or the CDC analysis; stimulant medications are often used in the treatment of narcolepsy, and in order to ensure a comprehensive analysis, these medications were included in the SoonerCare analysis. Despite inclusion of these medications as a part of the stimulant claims, the SoonerCare ADHD percentage (1.8%) of female members with a claim for an ADHD medication was less than half of the CDC percentage (4.0%) during the overlapping year of 2015.

The following is a table of the percentages of women 15 to 44 years of age with an ADHD medication paid claim by medication type. During CY 2015, percentages were similar in both the SoonerCare and CDC analyses for lisdexamfetamine (Vyvanse®) and methylphenidate products (multiple products). Significant differences can be seen in the amphetamine/ amphetamine salts (multiple products), dextroamphetamine (Focalin®), and atomoxetine (Strattera®) percentages. Differences in this table are challenging to evaluate as they are likely a result of varying plan coverage and prior authorization criteria.

Percentage of Women 15 to 44 Years of Age with ADHD Medication Paid Claim(s) By Medication Type

ADHD Medication	CDC 2015	SoonerCare 2015	SoonerCare 2016	SoonerCare 2017
amphetamine salts or amphetamine	61.1%	34.0%	32.9%	30.9%
atomoxetine	3.8%	11.0%	10.5%	10.8%
clonidine ER	N/A	0.3%	0.3%	0.3%
dextroamphetamine	1.5%	0.1%	0.04%	0.1%
dexmethylphenidate	3.1%	4.5%	4.6%	4.6%
guanfacine ER	N/A	5.8%	6.7%	7.6%
lisdexamfetamine	26.7%	25.6%	27.5%	28.3%
methylphenidate	18.1%	17.8%	16.7%	16.7%
narcolepsy medications*	N/A	0.9%	0.89%	0.7%

ADHD = attention-deficit/hyperactivity disorder; CDC = Centers for Disease Control and Prevention; ER = extended-release; NA = not applicable

*Narcolepsy medications include: Provigil® (modafinil), Nuvigil® (armodafinil), and Xyrem® (sodium oxybate)

The following table contains the number of women of reproductive age with at least one paid claim for an ADHD medication per year and the average number of ADHD medication paid claims per member per year. The CDC analysis found an average of 7.2 paid claims per member per year while the SoonerCare analysis revealed 6.2 paid claims per member per year during the overlapping year of 2015. Despite an increase from CY 2015 to CY 2017, the CY 2017 SoonerCare average number of ADHD medication paid claims per member per year still remained less than the CDC average for 2015.

Number of Women with ≥1 ADHD Medication Paid Claim(s) Per Year and Average Number of ADHD Medication Paid Claim(s) Per Member Per Year				
Parameter	**CDC 2015**	**SoonerCare 2015**	**SoonerCare 2016**	**SoonerCare 2017**
# of Women* with ≥1 Paid Claim(s)	183,053	4,067	4,323	4,481
Average # of Paid Claims PMPY	7.2	6.2	6.4	6.5

ADHD = attention-deficit/hyperactivity disorder; CDC = Centers for Disease Control and Prevention; # = number; PMPY = per member per year
*Includes women of reproductive age (15 to 44 years of age)

Conclusions[1]

While stimulant use has increased in female SoonerCare members of reproductive age over the last three years, it does not appear to have increased at the rate of a large national study. Comparison is limited as the study timeframes are different; however, the overlapping year of 2015 allows for some assessment. During 2015, the SoonerCare percentage (1.8%) of female members of reproductive age with a claim for an ADHD medication was less than half of the CDC percentage (4.0%). A lower percentage of ADHD medication claims in female members of reproductive age was consistent across all age groups. Additionally, the average number of paid claims per member per year was lower in the SoonerCare population (CDC: 7.2 vs. SoonerCare: 6.2). Numbers were consistent despite the inclusion of additional medications in the SoonerCare analysis [non-stimulant medications (clonidine ER and guanfacine ER) and narcolepsy medications (modafinil, armodafinil, and sodium oxybate)]. These results may be indicative of appropriate management of ADHD medications in the SoonerCare population.

Recommendations[1]

Little information is known regarding the risks of ADHD medication use in pregnancy. Given that a large percentage of births are unplanned, ADHD medication use in females of reproductive age could result in early pregnancy exposure, a critical period for fetal development. The College of Pharmacy recommends education via letter or newsletter for members, prescribers, and pharmacies who are or have female members of reproductive age utilizing ADHD medications. Education should include linking providers and members to resources such as the CDC's *Treating for Two: Safer Medication Use in Pregnancy* initiative. The College of Pharmacy will continue to monitor appropriate stimulant use in this population and make recommendations to the Drug Utilization Review (DUR) Board where appropriate.

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[1] Anderson KN, Ailes EC, Danielson M, et al. Attention-Deficit/Hyperactivity Disorder Medication Prescription Claims Among Privately Insured Women Aged 15–44 Years — United States, 2003–2015. *MMWR* 2018; 67:66-70.
[2] National Institute of Mental Health. Attention Deficit Hyperactivity Disorder. Available online at: https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml. Issued 03/2016. Last accessed 04/30/2018.
[3] Brooks M. ADHD Prescriptions Skyrocket Among Young Women. *Medscape*. Available online at: https://www.medscape.com/viewarticle/891501?nlid=120168_745&src=WNL_mdplsfeat_180123_mscpedit_phar&uac=163910MN&spon=30&impID=1540890&faf=1. Issued 01/18/2018. Last accessed 05/15/2018.

Appendix C

Vote to Prior Authorize Clenpiq™ (Sodium Picosulfate/ Magnesium Oxide/Anhydrous Citric Acid)

Oklahoma Health Care Authority
June 2018

Introduction[1]

Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid oral solution) 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. Clenpiq™ is supplied in a carton containing two bottles, each bottle supplying 10mg of sodium picosulfate, 3.5 grams of magnesium oxide, and 12 grams of anhydrous citric acid in 160mL of cranberry-flavored, oral solution, along with an eight-ounce cup for measuring fluids for hydration. Clenpiq™ is ready-to-drink and does not require dilution prior to administration. Two doses of Clenpiq™ are required for a complete preparation for colonoscopy. The preferred method is the "split-dose" method (an alternative method is the "day-before" method) where the two doses are divided between the evening prior to the colonoscopy and the day of the procedure (at least 2 hours prior to the colonoscopy).

Cost Comparison:

Medication	Cost Per Course of Therapy
Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid)	**$128.00**
Prepopik® (sodium picosulfate/magnesium oxide/anhydrous citric acid)	$123.86
Moviprep® (PEG-3350/sodium sulfate/sodium chloride/potassium chloride/sodium ascorbate/ascorbic acid)	$95.79
Gavilyte®-G (PEG-3350/sodium sulfate/sodium bicarbonate/sodium chloride/potassium chloride)	$12.00

PEG-3350 = polyethylene glycol 3350
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Clenpiq™ with criteria similar to the other prior authorized bowel preparation medications:

Clenpiq™, ColPrep™ Kit, OsmoPrep®, Prepopik®, 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 why 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®.

[1] Clenpiq™ (sodium picosulfate/magnesium oxide/anhydrous citric acid) Prescribing Information. Ferring Pharmaceuticals, Inc. Available online at: http://www.ferringusa.com/wp-content/uploads/2018/04/ClenpiqPI-11-2017.pdf. Last revised 11/2017. Last accessed 04/16/2018.

Appendix D

Vote to Prior Authorize Otiprio®
(Ciprofloxacin Otic Suspension)

Oklahoma Health Care Authority
June 2018

Introduction[1,2,3,4]

Otiprio® (ciprofloxacin otic suspension) is a fluoroquinolone antibacterial indicated for the treatment of bilateral otitis media with effusion (OME) in patients 6 months of age and older undergoing tympanostomy tube placement or for the treatment of acute otitis externa (AOE) in patients 6 months of age and older due to *Pseudomonas aeruginosa (P. aeruginosa)* or *Staphylococcus aureus (S. aureus).* Otiprio® is available as an otic suspension containing ciprofloxacin 6% supplied in a single-dose, preservative-free glass vial containing 1mL of otic suspension. Otiprio® is for intratympanic or otic administration by a healthcare professional only. Otiprio® is the only single-dose otic drop approved by the U.S. Food and Drug Administration (FDA) for intratympanic administration. Other treatments commonly used during tympanostomy tube placement include ofloxacin or ciprofloxacin administered into the ear intraoperatively and then twice daily for five days following the procedure.

Cost Comparison:

Medication	Cost Per Vial or mL	Cost Per Treatment
Otiprio® (ciprofloxacin 6%)	**$283.20**	**$283.20**
Ciprodex® (ciprofloxacin/dexamethasone 0.3%/0.1%)	$27.93	$209.48
Cipro® HC (ciprofloxacin/HC 0.2%/1%)	$28.50	$285.00
Coly-Mycin® S (colistin/neomycin/TZ/HC 3mg/3.3mg/10mg/0.5mg)	$20.34	$203.40

TZ = thonzonium; HC = hydrocortisone
Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the placement of Otiprio® (ciprofloxacin 6% otic suspension) into the Special Prior Authorization (PA) Tier of the Otic Anti-Infective Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Otiprio® (Ciprofloxacin 6% Otic Suspension) Approval Criteria:

1. An FDA approved indication of one of the following:
    a. For the treatment of bilateral otitis media with effusion in members undergoing tympanostomy tube placement; or
    b. For the treatment of acute otitis externa due to *Pseudomonas aeruginosa (P. aeruginosa) or Staphylococcus aureus (S. aureus);* and
2. Member must be 6 months of age or older; and

3. Otiprio® must be administered by a health care professional; and
4. A patient-specific, clinically significant reason why appropriate lower tiered otic anti-infective medications cannot be used; and
5. A quantity limit of 1 vial per treatment course will apply.

Otic Anti-Infective Medications		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	ciprofloxacin 0.2% (Cetraxal®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	ciprofloxacin/fluocinolone (Otovel®)	**ciprofloxacin 6% (Otiprio®)**
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Coly-Mycin® S)	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	
	ofloxacin (Floxin® Otic)	

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

[1] Otonomy, Inc. Otonomy Announces FDA Approval of OTIPRIO(R) for Acute Otitis Externa. *Globe Newswire*. Available online at: https://globenewswire.com/news-release/2018/03/02/1414291/0/en/Otonomy-Announces-FDA-Approval-of-OTIPRIO-R-for-Acute-Otitis-Externa.html. Issued 03/02/2018. Last accessed 05/16/2018.
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[3] Otonomy, Inc. Otonomy Announces FDA Approval of OTIPRIO(TM) for the Treatment of Pediatric Patients Undergoing Tympanostomy Tube Placement Surgery. *Globe Newswire*. Available online at: http://investors.otonomy.com/news-releases/news-release-details/otonomy-announces-fda-approval-otipriotm-treatment-pediatric. Issued 12/11/2015. Last accessed 05/01/2018.
[4] Otiprio® Prescribing Information. Otonomy, Inc. Available online at: https://otiprio.com/prescribing-information.pdf. Last revised 03/2018. Last accessed 05/15/2018.

Appendix E

Vote to Prior Authorize Admelog® (Insulin Lispro), Bydureon® BCise™ (Exenatide Extended-Release Autoinjector Pen), Fiasp® (Insulin Aspart), Humulin® R U-500 Vials (Insulin Human 500 Units/mL), Ozempic® (Semaglutide), Steglatro™ (Ertugliflozin), Segluromet™ (Ertugliflozin/Metformin), and Steglujan™ (Ertugliflozin/Sitagliptin)

Oklahoma Health Care Authority
June 2018

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

Admelog® (insulin lispro) is a rapid-acting human insulin analog indicated to improve glycemic control in adults and pediatric patients 3 years of age and older with type 1 and type 2 diabetes mellitus (DM). It is supplied as a 100 units/mL (U-100) solution for subcutaneous (SQ) or intravenous (IV) use in a 10mL multiple-dose vial (MDV) or as a 3mL single-patient-use SoloStar® prefilled pen. The dose of Admelog® should be individualized based on route of administration, the patient's metabolic needs, blood glucose monitoring results, and glycemic control. The wholesale acquisition cost (WAC) of five Admelog® SoloStar® pens (one package or 15mL) is $450.90.

Bydureon® BCise™ [exenatide extended-release (ER) autoinjector pen] is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM. Bydureon® BCise™ is an autoinjector pen with a hidden needle that removes the need for attaching the needle and depressing a plunger as is the case with Bydureon® pen. Additionally, the BCise™ formulation only requires 15 seconds of shaking for preparation compared to the pen which requires tapping at least 80 times prior to administration. The national average drug acquisition cost (NADAC) of four Bydureon® BCise™ pens (one month supply) is $632.60.

Fiasp® (insulin aspart) is a rapid-acting human insulin analog indicated to improve glycemic control in adults with DM. It contains niacinamide (vitamin B_3) to increase the speed of initial absorption and a formulation-stabilizing amino acid (L-arginine). It is supplied as a U-100 solution in a 10mL MDV or as a 3mL single-patient-use FlexTouch® prefilled pen for SQ or IV use. The dose of Fiasp® should be individualized based on route of administration, the patient's metabolic needs, blood glucose monitoring results, and glycemic control. The WAC of five Fiasp® FlexTouch® pens (one package or 15mL) is $532.20.

Ozempic® (semaglutide) is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM. It is supplied as an injection containing 2mg of semaglutide in a 1.5mL pre-filled, single-patient-use pen injector packaged in a carton containing either one or two pens. The recommended starting dose is 0.25mg via SQ injection

once weekly, with or without meals, for four weeks. The maximum dose is 1mg once weekly. The WAC of four Ozempic® 1mg pens (one month supply) is $675.99.

Steglatro™ (ertugliflozin) is a sodium/glucose cotransporter-2 (SGLT-2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM. It is supplied as an oral tablet in two strengths: 5mg and 15mg. The recommended starting dose is 5mg once daily, taken in the morning, with or without food. The maximum recommended dose is 15mg once daily. The WAC of one Steglatro™ 15mg tablet is $8.94, resulting in a monthly cost of $268.20.

Segluromet™ (ertugliflozin/metformin) is a combination product containing an SGLT-2 inhibitor (ertugliflozin) and a biguanide (metformin) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin. It is supplied as an oral tablet in four strengths (ertugliflozin/ metformin): 2.5mg/500mg, 2.5mg/1,000mg, 7.5mg/500mg, and 7.5mg/1,000mg. The maximum recommended dose is 7.5mg ertugliflozin/1,000mg metformin twice daily with meals. The WAC of one Segluromet™ 7.5mg/1,000mg tablet is $4.47, resulting in a monthly cost of $268.20.

Steglujan™ (ertugliflozin/sitagliptin) is a combination product containing an SGLT-2 inhibitor (ertugliflozin) and a dipeptidyl peptidase-4 (DPP-4) inhibitor (sitagliptin) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM when treatment with both ertugliflozin and sitagliptin is appropriate. It is supplied as an oral tablet in two strengths (ertugliflozin/sitagliptin): 5mg/100mg and 15mg/100mg. The recommended starting dose is 5mg ertugliflozin/100mg sitagliptin once daily, taken in the morning, with or without food. The maximum recommended dose is 15mg ertugliflozin/100mg sitagliptin once daily. The WAC of one Steglujan™ 15mg/100mg tablet is $17.45, resulting in a monthly cost of $523.50.

Recommendations

The College of Pharmacy recommends the prior authorization of Admelog® (insulin lispro), Fiasp® (insulin aspart), and Humulin® R U-500 vials (insulin human 500 units/mL) with the following criteria:

Admelog® (Insulin Lispro) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Humalog® (insulin lispro) must be provided.

Fiasp® (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 NovoLog® (insulin aspart) must be provided.

Humulin® R U-500 Vials (Insulin Human 500 Units/mL) Approval Criteria:

1. An FDA approved diagnosis of diabetes mellitus; and

2. A patient-specific, clinically significant reason why the member cannot use the Humulin® R U-500 KwikPen® (insulin human 500units/mL), which is available without prior authorization, must be provided.

The College of Pharmacy also recommends the following changes to the Diabetes Medications Product Based Prior Authorization (PBPA) criteria and tier chart based on net costs after rebates:

1. Add Bydureon® BCise™ [exenatide extended-release (ER) autoinjector pen] into the Special Prior Authorization (PA) Tier.
    a. Authorization of Bydureon® BCise™ will require tier trials be met, and a patient-specific, clinically significant reason why the member cannot use other available formulations of exenatide must be provided. Current Special PA criteria will apply.
2. Place Ozempic® (semaglutide), Steglatro™ (ertugliflozin), Segluromet™ (ertugliflozin/metformin), and Steglujan™ (ertugliflozin/sitagliptin) into Tier-3. Current Tier-3 criteria will apply.
3. Add a patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with an alternative glucagon-like peptide-1 (GLP-1) receptor agonist to the Soliqua® (insulin glargine/lixisenatide) criteria.
4. Add a patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with Victoza® (liraglutide) to the Xultophy® (insulin degludec/ liraglutide) criteria.
5. Add a patient-specific, clinically significant reason why the member cannot take the immediate-release formulation to the Invokamet® XR (canagliflozin/metformin ER) and Jentadueto® XR (linagliptin/metformin ER) criteria.

The recommended changes are shown in red in the following criteria and tier chart:

Diabetes Medications Special Prior Authorization (PA) Approval Criteria:

1. Member must be currently stabilized on the requested product or have attempted at least three other categories of Tier-2 or Tier-3 medications, or have a documented clinical reason why the requested product is necessary for the member; and
2. Use of Invokamet® XR [canagliflozin/metformin extended-release (ER)] or Jentadueto® XR (linagliptin/metformin ER) will require a patient-specific, clinically significant reason why the member cannot take the immediate-release formulation(s); or
3. Use of Bydureon® BCise™ (exenatide ER autoinjector pen) will require tier trials be met, and a patient-specific, clinically significant reason why the member cannot use other available formulations of exenatide must be provided.

Soliqua® 100/33 (Insulin Glargine/Lixisenatide) Approval Criteria:

1. An FDA approved diagnosis of type 2 diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with an alternative glucagon-like peptide-1 (GLP-1) receptor agonist must be provided.
3. Current Tier-3 criteria will apply.

Xultophy® 100/3.6 (Insulin Degludec/Liraglutide) Approval Criteria:

1. An FDA approved diagnosis of type 2 diabetes mellitus; and
2. A patient-specific, clinically significant reason why the member cannot use Lantus® (insulin glargine) with Victoza® (liraglutide) must be provided.
3. Current Tier-3 criteria will apply.

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
Alpha-Glucosidase Inhibitors acarbose (Precose®) **Biguanides** metformin (Glucophage®) metformin SR (Glucophage XR®) metformin/glipizide (Metaglip®) metformin/glyburide (Glucovance®) **Glinides** repaglinide (Prandin®) **Sulfonylureas** chlorpropamide glimepiride (Amaryl®) glipizide (Glucotrol®) glipizide SR (Glucotrol XL®) glyburide (Diabeta®) glyburide micronized (Micronase®) Tolbutamide (Orinase®) **Thiazolidinediones** pioglitazone (Actos®)	**DPP-4 Inhibitors** 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 ER (Bydureon® pen and vial) liraglutide (Victoza®) **SGLT-2 Inhibitors** dapagliflozin (Farxiga®) dapagliflozin/metformin ER (Xigduo® XR) empagliflozin (Jardiance®) empagliflozin/metformin (Synjardy®) empagliflozin/metformin ER (Synjardy® XR)	**Alpha-Glucosidase Inhibitors** miglitol (Glyset®) **Dopamine Agonists** bromocriptine (Cycloset®) **DPP-4 Inhibitors** alogliptin (Nesina®) alogliptin/metformin (Kazano®) alogliptin/pioglitazone (Oseni®) linagliptin (Tradjenta®) linagliptin/metformin (Jentadueto®) **GLP-1 Agonists** albiglutide (Tanzeum®) dulaglutide (Trulicity®) lixisenatide (Adlyxin™) **semaglutide (Ozempic®)** **GLP-1 Agonists/Insulin** insulin degludec/liraglutide (Xultophy® 100/3.6)+ insulin glargine/lixisenatide (Soliqua® 100/33)+ **SGLT-2 Inhibitors** canagliflozin (Invokana®) canagliflozin/metformin (Invokamet®) **ertugliflozin (Steglatro™)** **ertugliflozin/metformin (Segluromet™)** **SGLT-2/DPP-4 Inhibitors** dapagliflozin/saxagliptin (Qtern®) empagliflozin/linagliptin (Glyxambi®) **ertugliflozin/sitagliptin (Steglujan™)**	**Amylinomimetics** pramlintide (Symlin®) **Biguanides** metformin ER (Fortamet®, Glumetza®) metformin solution (Riomet®) **DPP-4 Inhibitors** linagliptin/metformin ER (Jentadueto® XR) **GLP-1 Agonists** **exenatide ER autoinjector pen (Bydureon® BCise™)** **SGLT-2 Inhibitors** canagliflozin/metformin ER (Invokamet® XR)

Diabetes Medications*			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
		Thiazolidinediones pioglitazone/glimepiride (Duetact®) pioglitazone/metformin (Actoplus Met®, Actoplus Met XR®) rosiglitazone (Avandia®) rosiglitazone/glimepiride (Avandaryl®) rosiglitazone/metformin (Avandamet®)	

*Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
PA = prior authorization; SR = sustained-release; ER = extended-release; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium-glucose cotransporter-2
+Unique criteria applies.

[1] Admelog® (insulin lispro injection) Prescribing Information. Sanofi-Aventis U.S., LLC. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209196s000lbl.pdf. Last revised 12/2017. Last accessed 05/14/2018.
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[6] Steglatro™ (ertugliflozin tablet) Prescribing Information. Merck & Co., Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf. Last revised 12/2017. Last accessed 05/14/2018.
[7] Segluromet™ (ertugliflozin/metformin tablet) Prescribing Information. Merck & Co., Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209806s000lbl.pdf. Last revised 12/2017. Last accessed 05/14/2018.
[8] Steglujan™ (ertugliflozin/sitagliptin tablet) Prescribing Information. Merck & Co., Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209805s000lbl.pdf. Last revised 12/2017. Last accessed 05/14/2018.

Appendix F

Vote to Update the Prior Authorization Criteria for Tazorac® (Tazarotene Cream and Gel)

Oklahoma Health Care Authority
June 2018

Introduction

The current prior authorization criteria for Tazorac® (tazarotene cream and gel) was voted on by the Drug Utilization Review (DUR) Board in July 2017 and went into effect in December 2017. At that time, the net costs after rebates of brand name Tazorac® (all strengths and formulations) were significantly less than generic tazarotene (generic is currently only available as 0.1% cream); thus, the brand formulation was preferred. However, since that time, the net cost of brand name Tazorac® 0.1% cream has increased significantly and is no longer less costly than generic tazarotene 0.1% cream. The current net costs after rebates for brand name Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel remain significantly less than the brand or generic formulation of the 0.1% cream.

Recommendations

The College of Pharmacy recommends the following changes noted in red to the current Tazorac® (tazarotene cream and gel) prior authorization criteria, based on current net costs:

Tazorac® (Tazarotene Cream and Gel) Approval Criteria:

1. An FDA approved indication of acne vulgaris or plaque psoriasis; and
2. Female members must not be pregnant and must be willing to use an effective method of contraception during treatment; and
3. Authorization of ~~generic~~ tazarotene 0.1% cream will require a patient-specific, clinically significant reason why the member cannot use the other formulations of tazarotene (brand Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel are preferred) ~~will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred)~~; and
4. For a diagnosis of acne vulgaris, the following must be met:
    a. Member must be 20 years of age or younger; and
    b. Based on current net costs, Tazorac® 0.05% cream, 0.05% gel, and 0.1% gel will not require prior authorization for members 20 years of age or younger; and
5. A quantity limit of 60 grams per 30 days will apply.

Appendix G

Vote to Prior Authorize Prexxartan® (Valsartan Oral Solution), Tekturna® (Aliskiren Oral Pellets), and CaroSpir® (Spironolactone Oral Suspension)

Oklahoma Health Care Authority
June 2018

Introduction[1,2,3,4]

Prexxartan® (valsartan oral solution) is an angiotensin II receptor blocker (ARB) indicated for the treatment of hypertension (HTN) in adults and pediatric patients 6 years of age and older to lower blood pressure (BP); heart failure (HF; NYHA Class II to IV); and stable left ventricular failure or left ventricular dysfunction following myocardial infarction (MI). Prexxartan®, 4mg/mL solution, is supplied in bottles containing 473mL, bottles containing 120mL, and unit dose cups containing 20mL. Prexxartan® is not therapeutically equivalent to the tablet formulation of Diovan®. The peak concentration of valsartan with Prexxartan® is higher than with Diovan®.

Tekturna® (aliskiren oral pellets) is a renin inhibitor indicated for the treatment of HTN in adults and children 6 years of age and older to lower BP. Tekturna® 37.5mg oral pellets are supplied as dispensing capsules, each containing 12 pellets; each pellet contains 3.125mg of aliskiren, equivalent to 3.453mg of aliskiren hemifumarate. The capsules containing the oral pellets should not be swallowed. The oral pellets may be taken by opening the dispensing capsule, emptying the contents into a spoon, and then administering by mouth, followed immediately by milk or water without chewing or crushing. Tekturna® is also supplied as tablets containing 150mg or 300mg of aliskiren.

CaroSpir® (spironolactone oral suspension) is an antagonist of aldosterone indicated for the treatment of NYHA Class III to IV HF and reduced ejection fraction to increase survival, manage edema, and to reduce the need for hospitalization for HF; as an add-on therapy for the treatment of HTN to lower BP; and management of edema in adult cirrhotic patients when edema is not responsive to fluid and sodium restrictions. CaroSpir® 25mg/5mL oral suspension is supplied in 118mL bottles and 473mL bottles. CaroSpir® is not therapeutically equivalent to Aldactone®. For an equivalent dose, CaroSpir® results in 15 to 37% higher serum concentration compared to Aldactone® tablets. Information about the dose proportionality of spironolactone tablets is limited and, based on the results of studies comparing the suspension formulation to the tablet formulation, doses of the suspension greater than 100mg might result in spironolactone concentrations that could be higher than expected. In patients requiring a dose greater than 100mg, another formulation should be used. The National Institute for Occupational Safety and Health (NIOSH) recommends appropriate procedures for handling of spironolactone tablets in healthcare settings. When cutting, crushing, manipulating, or handling uncoated tablets, NIOSH recommends the use of double gloves and a protective gown.

Market News and Updates[5]

Prexxartan®: In March 2018, Medicure, Inc. provided an update on the status of Prexxartan® and stated that its launch is currently on hold pending resolution of a dispute that Medicure had become aware of between Carmel Biosciences, Inc., as the owner of the New Drug Application, and the third party manufacturer of the product. The company provided a further update in a later press release stating that it had been named in a civil claim from the third party manufacturer of Prexxartan® against Carmel Biosciences, Inc. The claim disputes the rights granted by Carmel to Medicure with respect to Prexxartan®.

Recommendations

The College of Pharmacy recommends the prior authorization of Prexxartan® (valsartan oral solution), Tekturna® (aliskiren oral pellets), and CaroSpir® (spironolactone oral suspension) with the following criteria:

Prexxartan® (Valsartan Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use valsartan oral tablets in place of the oral solution formulation even when the tablets are crushed must be provided.

Tekturna® (Aliskiren Oral Pellets) Approval Criteria:

1. An FDA approved indication; and
2. A recent trial, within the previous six months and at least four weeks in duration, of an angiotensin I converting enzyme inhibitor (ACEI) [or an angiotensin II receptor blocker (ARB) if previous trial of an ACEI] and a diuretic, used concomitantly at recommended doses, that did not yield adequate blood pressure control; and
3. Member must be 6 years of age or older; and
4. A patient-specific, clinically significant reason why the member cannot use Tekturna® tablets must be provided.

CaroSpir® (Spironolactone Oral Suspension) Approval Criteria:

1. An FDA approved indication; and
2. A patient-specific, clinically significant reason why the member cannot use spironolactone oral tablets must be provided.

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

1. Moving Cardizem® SR [diltiazem sustained-release (SR)], Verelan® [verapamil extended-release (ER) capsule], Capoten® (captopril), and Capozide® [captopril/ hydrochlorothiazide (HCTZ)] from Tier-1 to Tier-2. Current Tier-2 criteria will apply.
2. Moving Exforge® (amlodipine/valsartan) and Micardis® (telmisartan) from Tier-2 to Tier-1.

The recommended changes are shown in red in the following tier charts:

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

PA = prior authorization; IV = intravenous

Angiotensin Converting Enzyme Inhibitors (ACEIs) / Hydrochlorothiazide (HCTZ) Combinations		
Tier-1	**Tier-2**	**Special PA**
benazepril/HCTZ (Lotensin® HCT)	**captopril/HCTZ (Capozide®)**	fosinopril/HCTZ (Monopril-HCT®)
enalapril/HCTZ (Vasoretic®)		
lisinopril/HCTZ (Prinzide®, Zestoretic®)		
moexipril/HCTZ (Uniretic®)		
quinapril/HCTZ (Accuretic®)		

PA = prior authorization

Angiotensin Receptor Blockers (ARBs) and ARB Combination Products		
Tier-1	**Tier-2**	**Tier-3**
irbesartan (Avapro®)	amlodipine/olmesartan (Azor®)	azilsartan (Edarbi®)
irbesartan/HCTZ (Avalide®)	amlodipine/valsartan/HCTZ (Exforge® HCT)	azilsartan/chlorthalidone (Edarbyclor®)
losartan (Cozaar®)	olmesartan (Benicar®)	candesartan (Atacand®)
losartan/HCTZ (Hyzaar®)	olmesartan/HCTZ (Benicar HCT®)	candesartan/HCTZ (Atacand® HCT)
telmisartan (Micardis®)	olmesartan/amlodipine/HCTZ (Tribenzor®)	eprosartan (Teveten®)
valsartan (Diovan®)		eprosartan/HCTZ (Teveten® HCT)
valsartan/amlodipine (Exforge®)		telmisartan/amlodipine (Twynsta®)
valsartan/HCTZ (Diovan HCT®)		telmisartan/HCTZ (Micardis® HCT)

HCTZ = hydrochlorothiazide

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
amlodipine (Norvasc®)	amlodipine/atorvastatin (Caduet®)	diltiazem CD 360mg (Cardizem® CD)
diltiazem (Cardizem®)	diltiazem LA (Cardizem® LA, Matzim® LA)	
diltiazem (Tiazac®, Taztia XT®)	**diltiazem SR (Cardizem® SR)**	

Calcium Channel Blockers (CCBs)		
Tier-1	**Tier-2**	**Special PA**
diltiazem CD (Cardizem® CD)*	isradipine (Dynacirc®, Dynacirc CR®)	
diltiazem ER (Cartia XT®, Diltia XT®)	nicardipine (Cardene® SR)	
diltiazem XR (Dilacor® XR)	nisoldipine (Sular®)	
felodipine (Plendil®)	verapamil (Covera-HS®)	
nicardipine (Cardene®)	verapamil ER (**Verelan®**, Verelan® PM)	
nifedipine (Adalat®, Procardia®)		
nifedipine ER (Adalat® CC)		
nifedipine ER		
nifedipine XL (Nifedical XL®, Procardia XL®)		
nimodipine (Nimotop®)		
verapamil (Calan®, Isoptin®)		
verapamil SR (Calan® SR, Isoptin® SR)		

PA = prior authorization; XR, XL, ER = extended-release; SR = sustained-release; LA = long-acting; CD = controlled-delivery
*All strengths other than 360mg.

[1] Prexxartan® Prescribing Information. Carmel Bioscience, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209139s000lbl.pdf. Last revised 12/2017. Last accessed 04/23/2018.
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[3] CaroSpir® Prescribing Information. CMP Pharma, Inc. Available online at: https://www.carospir.com/prescribing-information/. Last revised 08/2017. Last accessed 04/23/2018.
[4] Spironolactone. Micromedex Solutions (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available online at: http://www.micromedexsolutions.com/. Last accessed 06/04/2018.
[5] Medicure Inc. Medicure Announces Further Up-Date on Prexxartan®. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/medicure-announces-further-up-date-on-prexxartan-678221793.html. Issued 03/28/2018. Last accessed 05/16/2018.

Appendix H

Vote to Prior Authorize Benznidazole

Oklahoma Health Care Authority
June 2018

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

Chagas disease, also known as American trypanosomiasis, is caused by infection with *Trypanosoma cruzi* (*T. cruzi*), a protozoan parasite. According to the Centers for Disease Control and Prevention (CDC), an estimated 8 million people in Mexico, Central America, and South America have Chagas disease, and most do not know they are infected. The epidemiology of Chagas disease is changing due to migration of individuals within and outside of endemic areas as well as successful programs to reduce transmission in endemic areas. As a result, there are a large number of infected individuals living in Latin America and in the United States, Spain, and other European countries. It is estimated that 300,000 infected immigrants may be living in the United States. The major route of Chagas transmission is vector-borne transmission via infected triatomine bugs. Transmission can also occur from mother to fetus, via transfusion of infected blood components, via transplantation of an organ from an infected donor, via ingestion of contaminated food or drink, or via laboratory exposure.

According to the CDC, anti-parasitic treatment is indicated for all cases of acute or reactivated Chagas disease and for chronic *T. cruzi* infection in children up to 18 years of age. Congenital infections are considered acute disease. Treatment is also strongly recommended for adults up to 50 years of age with chronic infection who do not have advanced Chagas cardiomyopathy. The decision to treat adults older than 50 years of age with chronic *T. cruzi* infection with anti-parasitic medications should be considered on an individual basis, weighing the potential benefits and risks for the patient. The two medications used to treat *T. cruzi* infection are nifurtimox and benznidazole. Benznidazole is approved by the U.S. Food and Drug Administration (FDA) for children 2 to 12 years of age and is commercially available. Nifurtimox is not currently FDA approved, but is available under investigational protocols from the CDC. Side effects are fairly common with both medications and tend to occur more frequently and are more severe in older patients. In general, benznidazole is better tolerated and is therefore favored as the first-line treatment for Chagas disease by most experts.

Benznidazole is a nitroimidazole antimicrobial indicated in pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by *T. cruzi*. Benznidazole is supplied as 12.5mg and 100mg tablets. Benznidazole is dosed by body weight. The total daily dose for pediatric patients 2 to 12 years of age is 5mg/kg to 8mg/kg orally administered in two divided doses separated by approximately 12 hours for a duration of 60 days. Please refer to the prescribing information for detailed information on the recommended dosages of benznidazole tablets. The wholesale acquisition cost (WAC) of benznidazole 100mg tablets is $3.00 per tablet, resulting in an approximate cost of $720.00 for treatment of a 60kg patient for 60 days. The College of Pharmacy received input from an infectious disease specialist regarding benznidazole. The specialist recommended prior authorization of benznidazole to ensure appropriate usage on the advice of experts.

Recommendations

The College of Pharmacy recommends the prior authorization of benznidazole tablets with the following criteria:

Benznidazole Tablets Approval Criteria:

1. An FDA approved diagnosis of Chagas disease (American trypanosomiasis) caused by *Trypanosoma cruzi*; and
2. Benznidazole must be prescribed by or in consultation with an infectious disease specialist; and
3. Female members of reproductive potential must have a pregnancy test prior to treatment with benznidazole; and
4. Female members of reproductive potential must be willing to use effective contraception during treatment with benznidazole tablets and for 5 days after the last dose; and
5. Member must not have taken disulfiram within the last two weeks; and
6. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug. The approval duration will be for 60 days of therapy.

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[1] Centers for Disease Control and Prevention (CDC). Parasites – American Trypanosomiasis (also known as Chagas Disease). Available online at: https://www.cdc.gov/parasites/chagas/. Last revised 05/24/2016. Last accessed 04/18/2018.

[2] CDC. Parasites – American Trypanosomiasis (also known as Chagas Disease). Antiparasitic Treatment. Available online at: https://www.cdc.gov/parasites/chagas/health_professionals/tx.html. Last revised 05/15/2018. Last accessed 05/16/2018.

[3] Bern C. Chagas disease: Acute and congenital Trypanosoma cruzi infection. *UpToDate*. Available online at: http://www.uptodate.com/contents/chagas-disease-acute-and-congenital-trypanosoma-cruzi-infection?search=chagas+disease&source=search_result&selectedTitle=1%7E70#H1591888841. Last revised 09/06/2017. Last accessed 04/18/2018.

[4] Bern C. Chagas disease: Epidemiology and prevention. *UpToDate*. Available online at: http://www.uptodate.com/contents/chagas-disease-epidemiology-and-prevention?topicRef=114181&source=see_link. Last revised 09/05/2017. Last accessed 04/18/2018.

[5] Bern C, Montgomery SP, Herwaldt BL. Evaluation and Treatment of Chagas Disease in the United States: A Systematic Review. *JAMA*. 2007; 298 (18):2171–2181.

[6] Bern C. Chagas disease: Antitrypanosomal drug therapy. *UpToDate*. Available online at: http://www.uptodate.com/contents/chagas-disease-antitrypanosomal-drug-therapy?topicRef=114192&source=see_link. Last revised 09/06/2017. Last accessed 04/18/2018.

[7] U.S. Food and Drug Administration (FDA). FDA News Release. FDA approves first U.S. treatment for Chagas disease. Available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573942.htm. Issued 08/29/2017. Last accessed 04/09/2018.

[8] Benznidazole Tablets Prescribing Information. Exeltis USA, Inc. Available online at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209570lbl.pdf. Last revised 08/2017. Last accessed 04/09/2018.

[9] OptumRx. Benznidazole - New orphan drug approval. Available online at: https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapprovals_benznidazole_2017-0830.pdf. Issued 08/2017. Last accessed 04/09/2018.

Appendix I

Calendar Year 2017 Annual Review of Lung Cancer Medications and 30-Day Notice to Prior Authorize Imfinzi® (Durvalumab) and to Update the Current Prior Authorization Criteria

Oklahoma Health Care Authority
June 2018

Introduction[1,2]

The American Cancer Society estimates that approximately 234,030 new lung cancer cases will be diagnosed in 2018, 84% of which are estimated to be non-small cell lung cancer (NSCLC).[1] Lung cancer is the leading cause of cancer death accounting for 25% of all cancer-related deaths among both males and females. Lung cancer is most commonly diagnosed in older people with the average age at diagnosis being 70 years. Over 95% of all lung cancer cases are classified as either small cell lung cancer (SCLC) or NSCLC. Defining the cell type is essential as the prognosis and treatment of the two types differs substantially. NSCLC is more common than SCLC, with NSCLC accounting for approximately 84% of all lung cancer diagnoses. There are many subtypes of NSCLC including adenocarcinomas, squamous cell carcinomas, and large cell carcinomas. Each subtype falls under the broad term of NSCLC, as the approach to initial treatment of localized disease is similar among the subtypes.

However, in advanced stages, treatment decisions are guided by the stage of the disease, histology, and molecular features of the tumor.[2] Patient-specific factors such as performance status and comorbid conditions are also considered when determining treatment plans. Surgical resection provides the best chance for cure in patients with stage I to II NSCLC and can be used in combination with cisplatin-based systemic chemotherapy and radiation. Chemotherapy or immunotherapy are the treatments of choice for stage III to IV NSCLC. The role of molecularly targeted-therapy and immunotherapy has become part of standard-of-care treatment plans in select patients with NSCLC. SCLC differs in that there is no role for surgery in the treatment of this histology. Chemotherapy and radiation are the treatments of choice for SCLC.[2]

Current Prior Authorization Criteria

Criteria for Keytruda® (pembrolizumab), Opdivo® (nivolumab), and Yervoy® (ipilimumab) for indications other than lung cancer diagnoses can be found in the October 2017 Drug Utilization Review (DUR) Board packet. These medications and criteria are reviewed annually with the skin cancer medications.

Alecensa® (Alectinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of recurrent or metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
    a. Progressed on or intolerant to crizotinib; or

b. Member has asymptomatic disease with rapid radiologic progression on crizotinib; and
3. Alectinib must be used as a single-agent only.

Alunbrig® (Brigatinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. Progressed on or intolerant to crizotinib; and
4. Brigatinib must be used as a single-agent only.

Cyramza® (Ramucirumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease after progression; and
3. Member must have an ECOG performance status of 0 to 2; and
4. Ramucirumab must be used in combination with docetaxel.

Cyramza® (Ramucirumab) Approval Criteria [Colorectal Cancer Diagnosis]:
1. A diagnosis of colorectal cancer; and
2. Subsequent therapy for metastatic disease after progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine; and
3. Ramucirumab must be used in combination with an irinotecan-based regimen.

Cyramza® (Ramucirumab) Approval Criteria [Esophageal Cancer Diagnosis]:
1. A diagnosis of unresectable, locally advanced, recurrent, or metastatic esophageal or esophagogastric junction adenocarcinoma; and
2. Member must have a Karnofsky performance score ≥60% or an ECOG performance status of 0 to 2; and
3. Ramucirumab must be used as a single-agent or in combination with paclitaxel.

Cyramza® (Ramucirumab) Approval Criteria [Gastric Cancer Diagnosis]:
1. A diagnosis of gastric cancer; and
2. Member is not a surgical candidate or has unresectable, locally advanced, recurrent or metastatic disease; and
3. Member must have a Karnofsky performance score ≥60% or an ECOG performance status of 0 to 2; and
4. Ramucirumab must be used as a single-agent or in combination with paclitaxel.

Gilotrif® (Afatinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:
The following criteria must be met when used in the <u>first-line setting:</u>
1. A diagnosis of metastatic NSCLC; and
2. Epidermal growth factor receptor (EGFR) mutation detected; and
3. Afatinib when used in the first-line setting must be used as a single-agent only.

The following criteria must be met when used in the <u>second-line setting:</u>
1. A diagnosis of metastatic NSCLC; and
2. Progressed following platinum-based chemotherapy; and

3. Afatinib when used in the second-line setting may be used as a single-agent or in combination with cetuximab in patients with a known sensitizing EGFR mutation who are T790M negative.

Gilotrif® (Afatinib) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. A diagnosis of head and neck cancer; and
2. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
3. Non-nasopharyngeal cancer must be one of the following:
    a. Newly diagnosed T4b, any N, M0 disease, unresectable nodal disease with no metastases, or for patients who are unfit for surgery and have an ECOG performance status of 3; or
    b. Metastatic (M1) disease at initial presentation, recurrent/persistent disease with distant metastases, or unresectable locoregional recurrence or second primary with prior radiation therapy (RT) and an ECOG performance status of 0 to 2; or
    c. Unresectable locoregional recurrence without prior RT and an ECOG performance status of 3; and
4. Afatinib must be used as a single-agent only.

Keytruda® (Pembrolizumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC; and
2. The member has not previously failed other PD-1 inhibitors [e.g., Opdivo® (nivolumab)]; and
3. Tumor proportion scores for PD-L1 expression as follows:
    a. Single-agent, first-line: ≥50%; or
    b. First-line in combination with carboplatin and pemetrexed: no expression required; or
    c. Single-agent, second-line: ≥1%; and
4. Member meets <u>one</u> of the following:
    a. Previously untreated metastatic non-squamous NSCLC in combination with pemetrexed and carboplatin; or
    b. New diagnosis as first-line therapy (patient has not received chemotherapy to treat disease) if:
        i. Tumor does not express sensitizing Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations; and
        ii. Member must have an ECOG performance status of 0 to 1; or
    c. Single-agent for disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin):
        i. Patients with EGFR-mutation-positive disease should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and

1. *Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib*

ii. Patients with ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations*; and
   1. *Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib*

iii. Member must have an ECOG performance status of 0 to 2.

Opdivo® (Nivolumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Diagnosis of metastatic NSCLC; and
2. Tumor histology is one of the following:
   a. Adenocarcinoma; or
   b. Squamous cell; or
   c. Large cell; and
3. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
4. Member must have an ECOG performance status of 0 to 2; and
5. The patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
6. Nivolumab must be used as a single-agent; and
7. Dose as follows: Single-agent: 240mg every two weeks.

Opdivo® (Nivolumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of SCLC; and
2. One of the following criteria is met:
   a. Disease relapsed within six months of initial chemotherapy; or
   b. Disease progression on initial chemotherapy; and
3. Nivolumab must be used as a single-agent or in combination with ipilimumab; and
4. Member must have an ECOG performance status of 0 to 2; and
5. The patient has not previously failed other PD-1 inhibitors [(e.g., Keytruda® (pembrolizumab)].

Tagrisso® (Osimertinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC; and
2. Epidermal growth factor receptor (EGFR) T790M mutation-positive disease; and
3. Following progression on erlotinib, afatinib, or gefitinib for asymptomatic disease, symptomatic brain lesions, or multiple symptomatic systemic lesions; and
4. Osimertinib must be used for subsequent therapy only.

Tarceva® (Erlotinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of NSCLC; and
2. Recurrence or metastatic disease; and
3. Epidermal growth factor receptor (EGFR) mutation detected; and

4. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Cancer Diagnosis]:

1. A diagnosis of pancreatic cancer; and
2. Locally advanced unresectable or metastatic disease; and
3. Member must have an ECOG performance status of 0 to 2; and
4. Erlotinib must be used as a first-line agent only; and
5. Erlotinib must be used in combination with gemcitabine.

Tarceva® (Erlotinib) Approval Criteria [Kidney Cancer Diagnosis]:

1. A diagnosis of kidney cancer; and
2. Non-clear cell type; and
3. Relapsed disease or for surgically unresectable stage IV disease; and
4. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Bone Cancer – Chordoma Diagnosis]:

1. A diagnosis of bone cancer – chordoma; and
2. Recurrent disease; and
3. Erlotinib must be used as a single-agent only.

Tarceva® (Erlotinib) Approval Criteria [Pancreatic Adenocarcinoma Diagnosis]:

1. A diagnosis of pancreatic adenocarcinoma; and
2. Locally advanced, unresectable disease or metastatic disease; and
3. Member must have an ECOG performance status of 0 to 2; and
4. Erlotinib must be used in combination with gemcitabine.

Tecentriq® (Atezolizumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of NSCLC; and
2. Subsequent therapy for metastatic disease; and
3. Member must have an ECOG performance status of 0 to 2; and
4. Atezolizumab must be used as a single-agent only.

Tecentriq® (Atezolizumab) Approval Criteria [Urothelial Carcinoma]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Progressed on or following platinum-containing chemotherapy or cisplatin ineligible patients.

Xalkori® (Crizotinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC (first-line or subsequent therapy); and
    a. Anaplastic lymphoma kinase (ALK) or ROS1 positivity; or
    b. MET amplification; and
2. Crizotinib must be used as a single-agent only.

Xalkori® (Crizotinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:

1. A diagnosis of soft tissue sarcoma – IMT; and

2. ALK positivity; and
3. Crizotinib must be used as a single-agent only.

Yervoy® (Ipilimumab) Approval Criteria [Small Cell Lung Cancer (SCLC) Diagnosis]:

1. Diagnosis of SCLC; and
2. One of the following criteria is met:
   a. Disease relapsed within six months of initial chemotherapy; or
   b. Disease is progressive on initial chemotherapy; and
3. Used in combination with nivolumab; and
4. Member must have an ECOG performance status 0 to 2.

Zykadia® (Ceritinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC; and
2. ALK positivity; and
3. Ceritinib must be used as a single-agent only.

Zykadia® (Ceritinib) Approval Criteria [Soft Tissue Sarcoma – Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation Diagnosis]:

1. A diagnosis of soft tissue sarcoma – IMT; and
2. ALK positivity; and
3. Ceritinib must be used as a single-agent only.

Utilization of Lung Cancer Medications: Calendar Year 2017

Lung Cancer Medications Calendar Year Comparison: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	15	85	$463,449.75	$5,452.35	$382.07	2,532	1,213
2017	7	36	$258,295.31	$7,174.87	$352.86	968	732
% Change	**-53.30%**	**-57.60%**	**-44.30%**	**31.60%**	**-7.60%**	**-61.80%**	**-39.70%**
Change	**-8**	**-49**	**-$205,154.44**	**$1,722.52**	**-$29.21**	**-1,564**	**-481**

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

Calendar Year 2017 Utilization of Lung Cancer Medications: Medical Claims

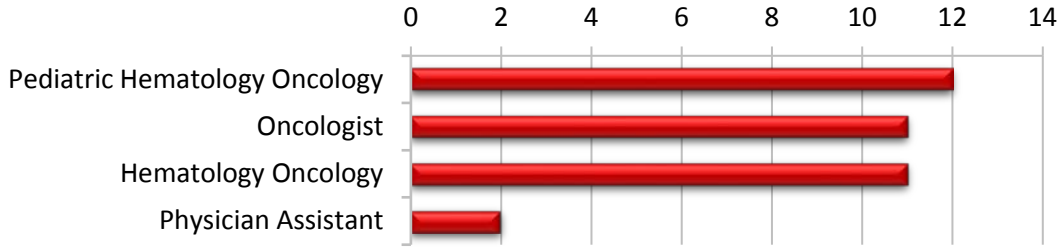
*Total Members	Total Claims	Total Cost	Cost/Claim
456	1,722	$7,377,241.04	$4,284.11

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

Demographics of Members Utilizing Lung Cancer Medications: Pharmacy Claims

- Due to the small number of members utilizing lung cancer medications during calendar year 2017, detailed demographic information could not be provided.

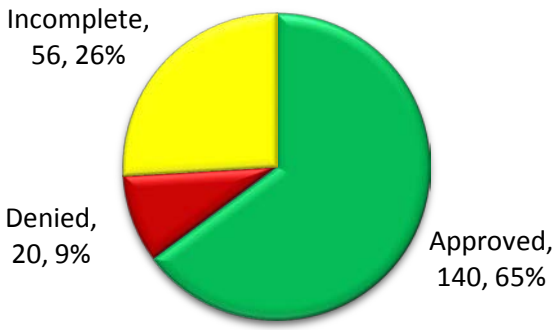
Top Prescriber Specialties of Lung Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Lung Cancer Medications

The prior authorization for lung cancer medications (other than Keytruda®, Opdivo®, and Yervoy®) was not implemented until October 2017. Current utilizers were grandfathered which may account for a larger number of prior authorization approvals than would occur in a typical year. While the following chart does reflect prior authorizations submitted during calendar year 2017 for lung cancer medications, it is not reflective of a true annual submission rate for all lung cancer medications. There were a total of 216 prior authorization requests submitted during calendar year 2017. The following chart shows the status of submitted petitions for calendar year 2017.

Status of Petitions



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

National Comprehensive Cancer Network (NCCN) guidelines for the treatment of NSCLC and SCLC are continually updated, but the major indications for new products are reflected in the product summaries section of this report.

Anticipated Patent Expiration(s):

- Tarceva® (erlotinib): May 2021
- Alimta® (pemetrexed): May 2022
- Xalkori® (crizotinib): November 2029
- Gilotrif® (afatinib): December 2029
- Zykadia® (ceritinib): February 2032
- Alecensa® (alectinib): March 2032
- Tagrisso® (osimertinib): August 2032

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

- **May 2017:** The FDA granted accelerated approval to Keytruda® (pembrolizumab) in combination with Alimta® (pemetrexed) and carboplatin for the treatment of patients with previously untreated metastatic, non-squamous NSCLC.
- **May 2017:** The FDA granted regular approval to Zykadia® (ceritinib) for patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive.
- **September 2017:** The FDA approved Mvasi® (bevacizumab-awwb) as a biosimilar to Avastin® (bevacizumab). Mvasi® is the first biosimilar approved in the United States for the treatment of cancer. Mvasi® is not yet available on the market and will be reviewed with the Drug Utilization Review (DUR) Board once cost and launch information become available.
- **October 2017:** The FDA approved a supplemental New Drug Application (sNDA) for Alunbrig® (brigatinib) 180mg tablets. Initially brigatinib was only available in 30mg tablets.
- **November 2017:** The FDA granted regular approval to Alecensa® (alectinib) for treatment of patients with ALK-positive, metastatic NSCLC.
- **December 2017:** The FDA granted regular approval to Opdivo® (nivolumab) for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or in patients with metastatic disease who have undergone complete resection. Nivolumab was previously approved for the treatment of patients with unresectable or metastatic melanoma.
- **January 2018:** The FDA granted approval to Gilotrif® (afatinib) for a broadened indication in first-line treatment of patients with metastatic NSCLC whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations.
- **February 2018:** The FDA approved Imfinzi® (durvalumab) for patients with unresectable stage 3 NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.
- **March 2018:** The FDA approved a supplemental Biologics License Application (sBLA) for updating the Opdivo® (nivolumab) dosing schedule to include 480mg infused every four weeks for a majority of approved indications. The 480mg dose is in addition to the previously available option of 240mg every two weeks. Nivolumab also was approved for a shorter 30-minute infusion across all approved indications.
- **April 2018:** The FDA approved Opdivo® (nivolumab) and Yervoy® (ipilimumab) in combination for the treatment of intermediate or poor risk, previously untreated, advanced renal cell carcinoma (RCC).
- **April 2018:** The FDA approved Tagrisso® (osimertinib) for the first-line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.

FDA Safety Alert:

- **May 2018:** The FDA issued a drug safety alert regarding decreased survival associated with the use of Keytruda® (pembrolizumab) or Tecentriq® (atezolizumab) as monotherapy in clinical trials to treat patients with metastatic urothelial cancer who

have not received prior therapy and who have low expression of the protein programmed death ligand 1 (PD-L1).

Imfinzi® (Durvalumab) Product Summary[8]

Imfinzi® (Durvalumab):

- **Therapeutic Class:** PD-L1 blocking antibody
- **Indication(s):**
  - Patients with locally advanced or metastatic urothelial carcinoma who:
    - Have disease progression during or following platinum-containing chemotherapy
    - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
  - Patients with unresectable, stage 3 NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy
- **How Supplied:** 500mg/10mL and 120mg/2.4mL single-dose vials for intravenous (IV) infusion
- **Dose:** 10mg/kg IV over 60 minutes every 2 weeks until disease progression or unacceptable toxicity; a maximum of 12 months is recommended for a diagnosis of NSCLC
- **Cost:** The wholesale acquisition cost (WAC) of one 500mg/10mL vial of durvalumab is $3,478.80

Recommendations

Alecensa® (Alectinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of recurrent or metastatic NSCLC; and
2. Anaplastic lymphoma kinase (ALK) positivity; and
3. ~~Progressed on or intolerant to crizotinib; or~~
4. ~~Member has asymptomatic disease with rapid radiologic progression on crizotinib; and~~
5. Alectinib may be used in first-line or recurrent setting; and
6. Alectinib must be used as a single-agent only.

Imfinzi® (Durvalumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of stage III NSCLC; and
2. Disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Imfinzi® (Durvalumab) Approval Criteria [Urothelial Carcinoma Diagnosis]:

1. A diagnosis of locally advanced or metastatic urothelial carcinoma; and
2. Progressed on or following platinum-containing chemotherapy.

Opdivo® (Nivolumab) Approval Criteria [Adjuvant Treatment of Melanoma Diagnosis]:

1. Patient has complete resection of melanoma; and
2. Diagnosis of stage IIIB/C melanoma following complete resection; and

3. The patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Nivolumab must be used as a single-agent; and
5. Dose as follows:
    a. Single-agent: 240mg every two weeks or 480mg every 4 weeks; and
    b. Maximum duration of 1 year.

Opdivo® (Nivolumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. For nivolumab monotherapy:
    a. A diagnosis of relapsed or surgically unresectable stage IV disease; and
    b. Failed prior therapy with one of the following medications:
        i. Sunitinib; or
        ii. Sorafenib; or
        iii. Pazopanib; or
        iv. Axitinib; or
2. For nivolumab use in combination with ipilimumab:
    a. A diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of patients with intermediate or poor risk, previously untreated advanced RCC; and
3. Member must have an ECOG performance status of 0 to 2; and
4. The patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
5. Dose as follows:
    a. Single-agent: 240mg every two weeks or 480mg every four weeks; or
    b. In combination with ipilimumab: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every three weeks for a maximum of four doses, then nivolumab 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

1. Diagnosis of unresectable or metastatic melanoma; and
2. Nivolumab must be used as a single-agent, or in combination with ipilimumab:
    a. As first-line therapy for untreated melanoma; or
    b. As second-line or subsequent therapy for documented disease progression while receiving or since completing most recent therapy:
        i. If the patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
        ii. Member must have an ECOG performance status of 0 to 2; and
3. Dose as follows:
    a. Single-agent: 240mg every two weeks; or
    b. In combination with ipilimumab: 1mg/kg, followed by ipilimumab on the same day, every three weeks for four doses, then 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. Diagnosis of metastatic NSCLC; and
2. Tumor histology is one of the following:
    a. Adenocarcinoma; or
    b. Squamous cell; or
    c. Large cell; and
3. Disease progression on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin); and
4. Member must have an ECOG performance status of 0 to 2; and
5. The patient has not previously failed other PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
6. Nivolumab must be used as a single-agent; and
7. Dose as follows: Single-agent: 240mg every two weeks or 480mg every four weeks.

Opdivo® (Nivolumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. A diagnosis of recurrent or metastatic head and neck cancer; and
2. Squamous cell histology; and
3. Patient has received prior platinum-containing regimen (e.g., cisplatin, carboplatin); and
4. Member must have an ECOG performance status of 0 to 1; and
5. Dose as follows: ~~3mg/kg every two weeks~~ 240mg every two weeks or 480mg every four weeks.

Tagrisso™ (Osimertinib) Approval Criteria [Non-Small Cell Lung Cancer (NSCLC) Diagnosis]:

1. A diagnosis of metastatic NSCLC; and
    a. Epidermal growth factor receptor (EGFR) T790M mutation-positive disease and following progression on erlotinib, afatinib, or gefitinib for asymptomatic disease, symptomatic brain lesions, or multiple symptomatic systemic lesions; or
    b. First-line treatment of patients with EGFR exon 19 deletions or exon 21 L858R mutations.
2. ~~Osimertinib must be used for subsequent therapy only.~~

Yervoy® (Ipilimumab) Approval Criteria [Renal Cell Carcinoma (RCC) Diagnosis]:

1. A diagnosis of relapsed or surgically unresectable stage IV disease in the initial treatment of patients with intermediate or poor risk, previously untreated, advanced RCC; and
2. Ipilimumab must be used in combination with nivolumab; and
3. The member has not failed previous PD-L1 or PD-1 inhibitors [e.g., Keytruda® (pembrolizumab)]; and
4. Dose as follows: nivolumab 3mg/kg followed by ipilimumab 1mg/kg on the same day, every three weeks for a maximum of four doses, then nivolumab 240mg every two weeks or 480mg every four weeks.

Utilization Details of Lung Cancer Medications: Calendar Year 2017

Pharmacy Claims: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
AFATINIB PRODUCTS					
GILOTRIF TAB 30MG	9	1	$69,827.52	9	$7,758.61
GILOTRIF TAB 40MG	5	3	$38,386.36	1.67	$7,677.27
SUBTOTAL	**14**	**3**	**$108,213.88**	**4.67**	**$7,729.56**
BEVACIZUMAB PRODUCTS					
AVASTIN INJ 400/16ML	9	3	$41,224.08	3	$4,580.45
AVASTIN INJ 100/4ML	3	2	$4,434.10	1.5	$1,478.03
SUBTOTAL	**12**	**3**	**$45,658.18**	**4**	**$3,804.85**
ERLOTINIB PRODUCTS					
TARCEVA TAB 150MG	6	1	$47,634.05	6	$7,939.01
SUBTOTAL	**6**	**1**	**$47,634.05**	**6**	**$7,939.01**
OSIMERTINIB PRODUCTS					
TAGRISSO TAB 40MG	3	1	$42,591.90	3	$14,197.30
TAGRISSO TAB 80MG	1	1	$14,197.30	1	$14,197.30
SUBTOTAL	**4**	**1**	**$56,789.20**	**4**	**$14,197.30**
TOTAL	**36**	**7***	**$258,295.31**	**5.14**	**$7,174.87**

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

Medical Claims: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
J9035 BEVACIZUMAB INJECTION	1,100	341	$2,634,788.62	$2,395.26
J9271 PEMBROLIZUMAB INJECTION	131	32	$1,294,137.08	$9,807.86
J9299 NIVOLUMAB INJECTION	353	61	$2,244,654.53	$6,358.79
J9305 PEMETREXED INJECTION	147	33	$845,986.95	$5,755.01
J9308 RAMUCIRUMAB INJECTION	22	6	$160,365.86	$7,289.35
J9228 IPILIMUMAB INJECTION	7	5	$197,308.00	$28,186.86
TOTAL	**1,722+**	**456***	**$7,377,241.04**	**$4,284.11**

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

[1] American Cancer Society. Cancer Facts & Figures 2018. Available online at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Last accessed 05/24/2018.

[2] National Comprehensive Cancer Network. Non-small cell lung cancer (Version 4.2018). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Last revised 04/26/2018. Small cell lung cancer (Version 2.2018). Available online at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Last revised 01/17/2018. Last accessed 05/24/2018.

[3] U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/. Last revised 02/2018. Last accessed 03/19/2018.

[4] FDA. Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm. Last revised 05/03/2018. Last accessed 05/04/2018.

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[6] Bristol-Myers Squibb Company. Bristol-Myers Squibb's Opdivo® (nivolumab) Now the First and Only FDA-Approved PD-1 Inhibitor to Offer Every Four-Week Dosing. *Business Wire*. Available online at: https://news.bms.com/press-release/corporatefinancial-news/bristol-myers-squibbs-opdivo-nivolumab-now-first-and-only-fda-. Issued 03/06/2018. Last accessed 06/05/2018.

[7] FDA. FDA Alerts Health Care Professionals and Oncology Clinical Investigators about an Efficacy Issue Identified in Clinical Trials for Some Patients Taking Keytruda (pembrolizumab) or Tecentriq (atezolizumab) as Monotherapy to Treat Urothelial Cancer with Low Expression of PD-L1. Available online at: https://www.fda.gov/Drugs/DrugSafety/ucm608075.htm. Issued 05/18/2018. Last accessed 05/22/2018.

[8] Imfinzi® Prescribing Information. AstraZeneca. Available online at: https://www.azpicentral.com/imfinzi/imfinzi.pdf#page=1. Last revised 02/2018. Last accessed 05/24/2018.

Appendix J

Calendar Year 2017 Annual Review of Prostate Cancer Medications and 30-Day Notice to Prior Authorize Erleada™ (Apalutamide) and Yonsa® (Abiraterone Acetate)

Oklahoma Health Care Authority
June 2018

Introduction[1,2,3]

According to the National Cancer Institute, in 2018, an estimated 164,690 men will be diagnosed with prostate cancer, making prostate cancer approximately 10% 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 PSA levels may indicate prostate cancer. PSA has been used as a screening marker for prostate cancer over the last three decades with its peak utilization occurring in the early 1990s and gradually declining 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 five years. Early detection of prostate cancer can lead to over-treatment of cancers that do not impact life expectancy. This 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 over-treated.[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 (ADT) making up the main components of therapy.[3] Androgens, the most common of which is testosterone, promote the growth of prostate cancers. 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 ADT and surgery. ADT is usually recommended for initial treatment of men with metastatic (stage IV) prostate cancer and 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.

Current Prior Authorization Criteria

Jevtana® (Cabazitaxel) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Member must have been previously treated with a docetaxel-containing regimen; and
3. Cabazitaxel should be used in combination with prednisone.

Provenge® (Sipuleucel-T) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer (CRCP); 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. Member must have an ECOG performance status of 0 to 1.

Xofigo® (Radium-223 Dichloride) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Member must have symptomatic bone metastases; and
3. Member must not have known visceral metastatic disease; and
4. Prescriber must verify radium-223 dichloride will not 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 gram/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 and platelet count ≥100 x 10^9/L (radium-223 dichloride should be delayed 6 to 8 weeks otherwise).

Xtandi® (Enzalutamide) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer (CRPC).

Zytiga® (Abiraterone) Approval Criteria [Castration-Resistant Prostate Cancer (CRPC) Diagnosis]:

1. A diagnosis of metastatic, CRPC; and
2. Abiraterone must be used in combination with a corticosteroid.

Utilization of Prostate Cancer Medications: Calendar Year 2017

Prostate Cancer Medications Calendar Year Comparison: Pharmacy Claims

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	6	26	$248,383.59	$9,553.22	$318.44	3,120	780
2017	10	39	$367,196.00	$9,415.28	$313.84	4,680	1,170
% Change	**66.70%**	**50.00%**	**47.80%**	**-1.40%**	**-1.40%**	**50.00%**	**50.00%**
Change	**4**	**13**	**$118,812.41**	**-$137.94**	**-$4.60**	**1,560**	**390**

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

Prostate Cancer Medications Calendar Years Comparison: Medical Claims

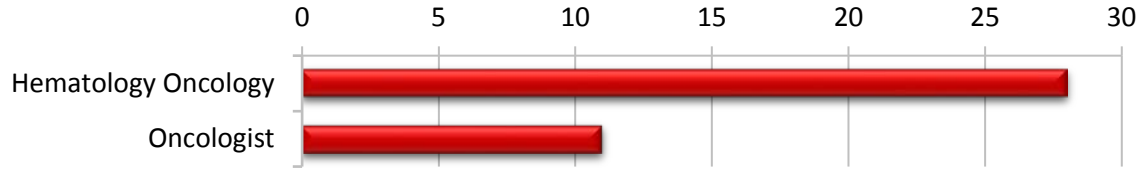
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Total Units
2016	2	4	$36,319.20	$9,079.80	240
2017	1	2	$37,305.60	$18,652.80	240
% Change	**-50.00%**	**-50.00%**	**2.72%**	**105.43%**	**0.00%**
Change	**-1**	**-2**	**$986.40**	**$9,573.00**	**0**

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

Demographics of Members Utilizing Prostate Cancer Medications: Pharmacy Claims

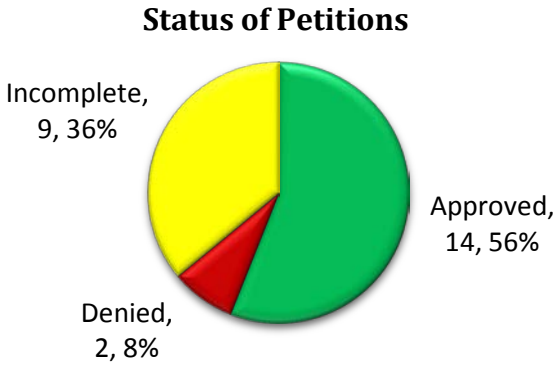
- Due to the small number of members utilizing prostate cancer medications during calendar year 2017, detailed demographic information could not be provided. All members were male and 45 years of age or older.

Top Prescriber Specialties of Prostate Cancer Medications By Number of Claims: Pharmacy Claims



Prior Authorization of Prostate Cancer Medications

There were 25 prior authorization requests submitted for prostate cancer medications during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.



Market News and Updates[4,5,6,7,8]

Anticipated Patent Expiration(s):

- Xofigo® (radium-223 dichloride): January 2020
- Xtandi® (enzalutamide): August 2027
- Zytiga® (abiraterone): August 2027
- Jevtana® (cabazitaxel): April 2031

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

- **September 2017:** The FDA approved a lower dose (20mg/m^2 every three weeks) of Jevtana® (cabazitaxel) in combination with prednisone for the treatment of patients with metastatic, castration-resistant prostate cancer (CRPC) previously treated with a docetaxel-containing treatment regimen. Cabazitaxel (25mg/m^2 every three weeks) was approved for this indication in 2010.
- **February 2018:** The FDA approved Zytiga® (abiraterone) tablets in combination with prednisone for the treatment of metastatic, high-risk, castration-sensitive prostate cancer (CSPC).
- **February 2018:** The FDA approved Erleada™ (apalutamide), an androgen receptor inhibitor, for the treatment of patients with non-metastatic, CRPC.
- **May 2018:** The FDA approved Yonsa® (abiraterone acetate), an ultramicrosize formulation of the oral CYP17 inhibitor abiraterone acetate (approved as Zytiga®), to be used in combination with methylprednisolone for the treatment of metastatic, CRPC.

Product Summaries[7,8]

Erleada™ (Apalutamide):

- **Therapeutic Class:** Androgen receptor inhibitor
- **Indication(s):** Treatment of patients with non-metastatic, CRPC
- **How Supplied:** 60mg oral tablets
- **Dose:** 240mg (four 60mg tablets) by mouth once daily
  - Tablets should be swallowed whole and can be taken with or without food
  - Patients should also receive a concomitant gonadotropin-releasing hormone (GnRH) analog or should have had bilateral orchiectomy
- **Cost:** The wholesale acquisition cost (WAC) per apalutamide 60mg tablet is $91.00, resulting in a daily cost of $364.00.

Yonsa® (Abiraterone Acetate):

- **Therapeutic Class:** CYP17 inhibitor of androgen synthesis
- **Indication(s):** Treatment of patients with metastatic, CRPC
- **How Supplied:** 125mg oral tablets
- **Dose:** 500mg (four 125mg tablets) by mouth once daily
  - Tablets should be swallowed whole and can be taken with or without food
  - Patients should also receive a concomitant GnRH analog or should have had bilateral orchiectomy
  - Should be administered with methylprednisolone 4mg by mouth twice daily
- **Cost:** The WAC per abiraterone acetate 125mg tablet is $76.74, resulting in a daily cost of $306.96.

Recommendations

Erleada™ (Apalutamide) Approval Criteria:

1. A diagnosis of non-metastatic prostate cancer; and
2. Castration-resistant or disease progression while on androgen deprivation therapy; and
3. Prostate specific antigen doubling time of ≤10 months; and
4. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy.

Yonsa® (Abiraterone Acetate) Approval Criteria:

1. A diagnosis of metastatic, castration-resistant prostate cancer (CRPC); and
2. Concomitant treatment with a gonadotropin-releasing hormone (GnRH) analog or prior history of bilateral orchiectomy.

Zytiga® (Abiraterone) Approval Criteria [Castration-Sensitive Prostate Cancer (CSPC) Diagnosis]:

1. A diagnosis of metastatic, high-risk, CSPC; and
2. Member must have high-risk disease defined as having at least two of the following risk factors:
   a. Total Gleason score of ≥8; or
   b. Presence of ≥3 lesions on bone scan; or
   c. Evidence of measurable visceral metastases; and
3. Abiraterone must be used in combination with a corticosteroid.

Utilization Details of Prostate Cancer Medications: Calendar Year 2017

Pharmacy Claims: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ CLAIM
ABIRATERONE PRODUCTS					
ZYTIGA TAB 250MG	25	5	$226,306.59	5	$9,052.26
SUBTOTAL	**25**	**5**	**$226,306.59**	**5**	**$9,052.26**
ENZALUTAMIDE PRODUCTS					
XTANDI CAP 40MG	14	6	$140,889.41	2.33	$10,063.53
SUBTOTAL	**14**	**6**	**$140,889.41**	**2.33**	**$10,063.53**
TOTAL	**39**	**10***	**$367,196.00**	**3.55**	**$9,415.28**

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

Medical Claims: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM
CABAZITAXEL PRODUCTS				
JEVTANA INJECTION (J9043)	2	1	$37,305.60	$18,652.80
TOTAL	**2**	**1**	**$37,305.60**	**$18,652.80**

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

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Appendix K

Calendar Year 2017 Annual Review of Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor Medications and Vote to Prior Authorize Austedo® (Deutetrabenazine) for Tardive Dyskinesia

Oklahoma Health Care Authority
June 2018

Current Prior Authorization Criteria

Austedo® (Deutetrabenazine) Approval Criteria [Huntington's Disease Diagnosis]:

1. An FDA approved diagnosis of chorea associated with Huntington's disease; and
2. Austedo® must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
3. A previous trial of Xenazine® (tetrabenazine) or a patient-specific, clinically significant reason why the member cannot use brand Xenazine® (tetrabenazine); and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Austedo® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter 2 (VMAT2) inhibitor (e.g., tetrabenazine, valbenazine) concurrently with Austedo®; and
9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Austedo® [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. The daily dose of Austedo® must not exceed 36mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) or if the member is a known poor CYP2D6 metabolizer; and
11. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea have decreased and the member is not showing worsening signs of depression.

Ingrezza® (Valbenazine) Approval Criteria:

1. An FDA approved diagnosis of tardive dyskinesia meeting the following DSM-5 criteria:
   a. Involuntary athetoid or choreiform movements; and
   b. History of treatment with dopamine receptor blocking agent (DRBA); and
   c. Symptom duration lasting longer than 4 to 8 weeks; and
2. Member must be 18 years of age or older; and

3. Ingrezza® must be prescribed by a neurologist or psychiatrist, or a mid-level practitioner with a supervising physician that is a neurologist or psychiatrist; and
4. Member must not be at significant risk for suicidal or violent behavior and must not have unstable psychiatric symptoms; and
5. The daily dose of Ingrezza® must not exceed 40mg per day if the member is taking strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, clarithromycin); and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs); and
7. Member must not be taking other vesicular monoamine transporter 2 (VMAT2) inhibitors (e.g., tetrabenazine, deutetrabenazine); and
8. Female members must not be pregnant or breastfeeding; and
9. Prescriber must document a baseline evaluation using the Abnormal Involuntary Movement Scale (AIMS); and
10. A quantity limit of one capsule per day will apply; and
11. Approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by an improvement from baseline in the AIMS total score (a negative change in score indicates improvement).

Xenazine® (Tetrabenazine) Approval Criteria:

1. Authorization of generic tetrabenazine (in place of brand Xenazine®) will require a patient-specific, clinically significant reason why the member cannot use the brand formulation (brand formulation is preferred); and
2. A diagnosis of one of the following:
    a. Chorea associated with Huntington's disease; or
    b. Tardive dyskinesia; or
    c. Tourette syndrome; and
3. Xenazine® must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Xenazine® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter 2 (VMAT2) inhibitor (e.g., deutetrabenazine, valbenazine) concurrently with Xenazine®; and
9. Member must not be taking medications that are known to prolong the QTc interval concomitantly with Xenazine® [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and
10. Patients who require doses of tetrabenazine greater than 50mg per day must be tested and genotyped to determine if they are poor metabolizers (PMs), intermediate

metabolizers (IMs), or extensive metabolizers (EMs) by their ability to express the drug metabolizing enzyme, CYP2D6. The following dose limits will apply based on patient metabolizer status:

   a. Extensive and Intermediate CYP2D6 Metabolizers: 100mg divided daily; or
   b. Poor CYP2D6 Metabolizers: 50mg divided daily; and

11. The daily dose of Xenazine® must not exceed 50mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion); and
12. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea, tardive dyskinesia, or Tourette syndrome have decreased and the member is not showing worsening signs of depression.

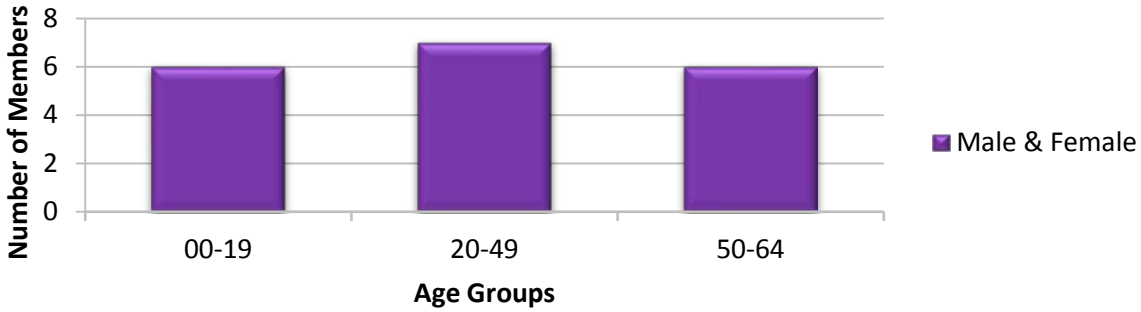
Utilization of VMAT2 Inhibitor Medications: Calendar Year 2017

Comparison of Calendar Years

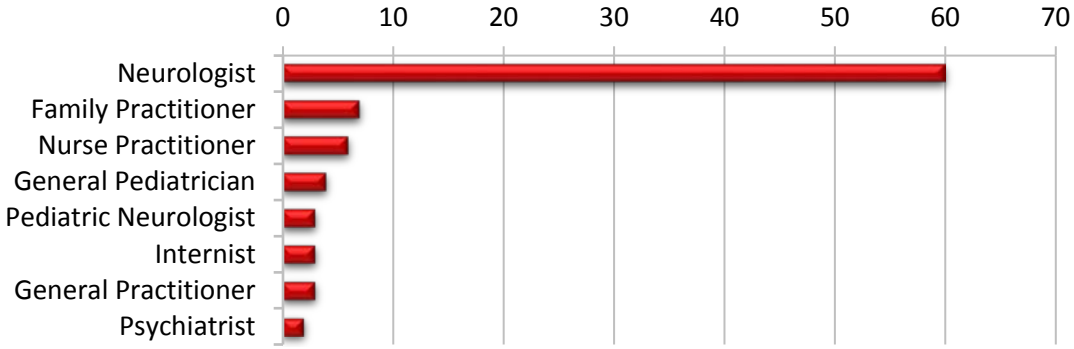
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	13	80	$960,736.25	$12,009.20	$360.77	6,536	2,663
2017	19	88	$740,121.60	$8,410.47	$282.38	5,546	2,621
% Change	**46.20%**	**10.00%**	**-23.00%**	**-30.00%**	**-21.70%**	**-15.10%**	**-1.60%**
Change	**6**	**8**	**-$220,614.65**	**-$3,598.73**	**-$78.39**	**-990**	**-42**

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

Demographics of Members Utilizing VMAT2 Inhibitor Medications



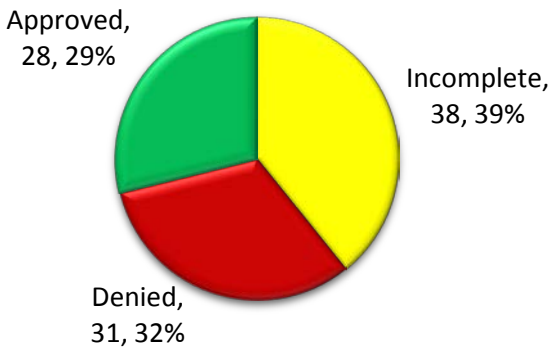
Top Prescriber Specialties of VMAT2 Inhibitor Medications by Number of Claims



Prior Authorization of VMAT2 Inhibitor Medications

There were 97 prior authorization requests submitted for VMAT2 inhibitor medications during calendar year 2017. The prior authorization for Xenazine® (tetrabenazine) was implemented on November 6, 2017. Members currently on Xenazine® (tetrabenazine) at the time of implementation were grandfathered. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



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

Anticipated Patent Expiration(s):

- Ingrezza® (valbenazine): October 2029
- Austedo® (deutetrabenazine): September 2033

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

- **August 2017:** The FDA approved Austedo® (deutetrabenazine) for the treatment of tardive dyskinesia (TD) in adults. Deutetrabenazine was FDA approved for the treatment of chorea associated with Huntington's disease in April 2017. The approval for TD was based on results from two Phase 3 randomized, double-blind, placebo-controlled studies (AIM-TD and ARM-TD) that evaluated the safety and efficacy of the medication in reducing abnormal involuntary movements associated with TD. The ARM-TD trial included 117 patients with TD. Patients who received deutetrabenazine for 12 weeks had a greater improvement in scores on the total Abnormal Involuntary Movement Scale (AIMS) and they also had improved scores on the scale's individual components compared with those who received matching placebo. Deutetrabenazine significantly reduced AIMS total score by 3.0 points vs. 1.6 points in the placebo arm at week 12 (P=0.019, treatment effect of -1.4 points). The AIM-TD trial included 222 patients with TD and showed that those who received deutetrabenazine had better quality of life scores on the modified 24-item Craniocervical Dystonia Questionnaire (mCDQ-24) than the placebo group. Deutetrabenazine significantly reduced AIMS total score by 3.3 points from baseline in the 36mg/day arm vs. 1.4 points in the placebo arm at week 12 (P<0.05, treatment effect of -1.9 points). The most common adverse reactions during clinical trials in patients with TD included nasopharyngitis and insomnia. Deutetrabenazine may increase the risk of depression and suicidality in patients with

Huntington's disease and is contraindicated in patients with Huntington's disease who are suicidal, or have untreated or inadequately treated depression.

- **October 2017:** Neurocrine Biosciences, Inc. announced that the FDA approved an 80mg Ingrezza® (valbenazine) capsule strength. Previously, Ingrezza® was only available as a 40mg capsule.

News:

- **December 2017:** The Institute for Clinical and Economic Review (ICER) released the Final Evidence Report and Report-at-a-Glance on VMAT2 inhibitors for the management of TD. The report was subject to public deliberation during a meeting of the New England Comparative Effectiveness Public Advisory Council (CEPAC). The majority of an independent council voted that evidence is sufficient to suggest a net health benefit in the treatment of TD for both valbenazine and deutetrabenazine. However, there is uncertainty of the long-term benefits and harms. Furthermore, the majority of the council voted that evidence is insufficient to show a net health benefit of tetrabenazine, or distinguish between the net benefit of valbenazine and deutetrabenazine. To fall within ICER's threshold value range of $100,000 to $150,000 per quality adjusted life year (QALY), valbenazine would require an 85 to 90% discount, while deutetrabenazine would require a discount of 90 to 93%. According to the report, one in five eligible Americans with TD could be treated with valbenazine and deutetrabenazine before crossing ICER's budget threshold of $915 million per year. ICER issued an *Affordability and Access Alert* as part of its final report on the VMAT2 inhibitors for the treatment of TD. The alert is intended to signal to manufacturers, insurers, patient groups, and other stakeholders that the amount of added health care costs associated with the new treatments may be difficult for the health care system to absorb over the short term without displacing other needed services or contributing to rapid growth in health care insurance costs.
- **April 2018:** According to a prospective multicenter study presented at the Academy of Managed Care Pharmacy (AMCP) Managed Care and Specialty Pharmacy 2018 annual meeting, TD can limit patient's ability to perform critical daily activities, including breathing and eating. Researchers examined involuntary movements and functioning among more than 700 patients receiving antipsychotic medications for psychiatric indications and found that more than 27% of the sampled patients with symptoms consistent with TD said that uncontrollable movements made eating difficult and approximately 9% stated TD symptoms affected their breathing. The clinical study lead was Charles Yonan, PharmD, the senior director of health economics and outcomes research at Neurocrine Biosciences, which manufactures Ingrezza® (valbenazine). The investigators administered two validated health-related quality of life scales, the EuroQol-5D-5L and the Sheehan Disability Scale, and found that patients with TD symptoms reported problems with mobility, usual activities, self-care, and had pain and discomfort.

Pipeline:

- **October 2017:** Neurocrine Biosciences, Inc. announced that valbenazine was granted Orphan Drug designation by the FDA for the treatment of pediatric patients with

Tourette syndrome. Tourette syndrome is a neurological disorder characterized by motor and vocal tics and becomes evident in early childhood or adolescence.

- **October 2017:** Neurocrine Biosciences, Inc. announced that it has initiated a Phase 2b clinical trial, known as T-Force GOLD, for valbenazine in children and adolescents with Tourette syndrome. The study is a multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the safety, efficacy, tolerability, and optimal dose of once-daily valbenazine in up to 120 pediatric patients with moderate-to-severe Tourette syndrome. Patients will receive either valbenazine or placebo over 12 weeks followed by two weeks off-drug. The primary endpoint is the change from baseline of the Yale Global Tic Severity Scale between placebo and active treatment groups at the end of week 12. Top-line data is expected in late 2018.
- **April 2018:** Researchers reported at the American Academy of Neurology annual meeting that an antisense oligonucleotide (ASO) for Huntington's disease, known as IONIS-HTT_{Rx}, lowered mutant huntingtin levels in cerebrospinal fluid (CSF) by 40 to 60%. According to Sarah Tabrizi, MBChB, PhD, of University College London, the magnitude of this reduction exceeds the amount needed for phenotypic reversal in animal models of Huntington's disease. IONIS-HTT_{Rx} is designed to bind to the huntingtin mRNA in a specific sequence that leads to its degradation. The drug was evaluated in a double-blind, Phase 1/2a trial of 46 patients with early Huntington's disease, randomized 3:1 to placebo. Five doses were tested ranging from 10mg to 120mg per day and administered through an intrathecal bolus injection. Study participants each had four IONIS-HTT_{Rx} doses, at day 1, 29, 57, and 85, over a 3-month period and were followed for 4 additional months. The primary objective of the trial was the safety and tolerability of the drug and a key exploratory objective was to measure CSF mutant huntingtin. No participants discontinued the study and most adverse effects were mild and unrelated to the study drug. The antisense drug produced dose-dependent reductions in CSF mutant huntingtin. The researchers reported no significant findings of any exploratory clinical measures among the group; however, the researchers stated they did not expect clinical change in a small study over 7 months. In a post-hoc analysis, they did observe that CSF mutant huntingtin lowering was associated with positive trends of several exploratory clinical measures. An open-label extension study is currently underway to investigate the effects of sustained long-term CSF mutant huntingtin lowering.

VMAT2 Inhibitor Cost Comparison

Medication	Cost Per Unit	Cost Per Month*	Cost Per Year*
Ingrezza® (valbenazine) 80mg	$207.50	$6,225.00	$74,700.00
Austedo® (deutetrabenazine) 12mg	$82.20	$9,864.00	$118,368.00
Xenazine® (tetrabenazine) 25mg	$229.09	$27,490.80	$329,889.60

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

*Cost per month and per year based on maximum recommended dose.

Recommendations

The College of Pharmacy recommends the prior authorization of Austedo® (deutetrabenazine) for TD with the following criteria:

Austedo® (Deutetrabenazine) Approval Criteria [Tardive Dyskinesia Diagnosis]:

1. An FDA approved diagnosis of tardive dyskinesia meeting the following DSM-5 criteria:
    a. Involuntary athetoid or choreiform movements; and
    b. History of treatment with dopamine receptor blocking agent (DRBA); and
    c. Symptom duration lasting longer than 4 to 8 weeks; and
2. Member must be 18 years of age or older; and
3. Austedo® must be prescribed by a neurologist or psychiatrist, or a mid-level practitioner with a supervising physician that is a neurologist or psychiatrist; and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Austedo® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter 2 (VMAT2) inhibitor (e.g., tetrabenazine, valbenazine) concurrently with Austedo®; and
9. For members requiring doses of Austedo® above 24mg per day, who are using Austedo® concomitantly with other medications that are known to prolong the QTc interval [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval] the prescriber must agree to assess the QTc interval before and after increasing the dose of Austedo® or other medications that are known to prolong the QTc interval; and
10. The member must not have congenital long QT syndrome or a history of cardiac arrhythmias; and
11. The daily dose of Austedo® must not exceed 36mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) or if they are a known poor CYP2D6 metabolizer; and
12. Female members must not be pregnant or breastfeeding; and
13. Prescriber must document a baseline evaluation using the Abnormal Involuntary Movement Scale (AIMS); and
14. Approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by an improvement from baseline in the AIMS total score (a negative change in score indicates improvement) or documentation of a positive clinical response to therapy.

The College of Pharmacy recommends the following changes to the current prior authorization criteria for Austedo® (deutetrabenazine) and Ingrezza® (valbenazine) as shown in red below:

Austedo® (Deutetrabenazine) Approval Criteria [Huntington's Disease Diagnosis]:

1. An FDA approved diagnosis of chorea associated with Huntington's disease; and
2. Austedo® must be prescribed by a neurologist, or a mid-level practitioner with a supervising physician that is a neurologist; and
3. A previous trial of Xenazine® (tetrabenazine) or a patient-specific, clinically significant reason why the member cannot use brand Xenazine® (tetrabenazine); and
4. Member must not be actively suicidal or have uncontrolled depression and prescriber must verify member will be monitored for depression prior to starting Austedo® therapy and throughout treatment; and
5. Member must not have hepatic impairment; and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs) or have taken an MAOI within the last 14 days; and
7. Member must not be taking reserpine or have taken reserpine within the last 20 days; and
8. Member must not use another vesicular monoamine transporter 2 (VMAT2) inhibitor (e.g., tetrabenazine, valbenazine) concurrently with Austedo®; and
9. ~~Member must not be taking medications that are known to prolong the QTc interval concomitantly with Austedo® [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval]; and~~
10. For members requiring doses of Austedo® above 24mg per day, who are using Austedo® concomitantly with other medications that are known to prolong the QTc interval [antipsychotic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antibiotics (e.g., moxifloxacin), Class 1A (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications, or any other medications known to prolong the QTc interval] the prescriber must agree to assess the QTc interval before and after increasing the dose of Austedo® or other medications that are known to prolong the QTc interval; and
11. The member must not have congenital long QT syndrome or a history of cardiac arrhythmias; and
12. The daily dose of Austedo® must not exceed 36mg per day if the member is taking strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) or if they are a known poor CYP2D6 metabolizer; and
13. Approvals will be for the duration of six months at which time the prescriber must document that the signs and symptoms of chorea have decreased and the member is not showing worsening signs of depression.

Ingrezza® (Valbenazine) Approval Criteria:

1. An FDA approved diagnosis of tardive dyskinesia meeting the following DSM-5 criteria:
    a. Involuntary athetoid or choreiform movements; and

   b. History of treatment with dopamine receptor blocking agent (DRBA); and
   c. Symptom duration lasting longer than 4 to 8 weeks; and
2. Member must be 18 years of age or older; and
3. Ingrezza® must be prescribed by a neurologist or psychiatrist, or a mid-level practitioner with a supervising physician that is a neurologist or psychiatrist; and
4. Member must not be at significant risk for suicidal or violent behavior and must not have unstable psychiatric symptoms; and
5. The daily dose of Ingrezza® must not exceed 40mg per day if the member is taking strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, clarithromycin); and
6. Member must not be taking monoamine oxidase inhibitors (MAOIs); and
7. Member must not be taking other vesicular monoamine transporter 2 (VMAT2) inhibitors (e.g., tetrabenazine, deutetrabenazine); and
8. The daily dose of Ingrezza® must not exceed 40mg per day for members with moderate or severe hepatic impairment (Child-Pugh score 7 to 15); and
9. The member must not have congenital long QT syndrome or a history of arrhythmias associated with a prolonged QT interval; and
10. Female members must not be pregnant or breastfeeding; and
11. Prescriber must document a baseline evaluation using the Abnormal Involuntary Movement Scale (AIMS); and
12. A quantity limit of one capsule per day will apply; and
13. Approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment as indicated by an improvement from baseline in the AIMS total score (a negative change in score indicates improvement) or documentation of a positive clinical response to therapy.

Utilization Details of VMAT2 Inhibitor Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/ MEMBER	COST/ DAY	COST/ CLAIM
TETRABENAZINE PRODUCTS						
XENAZINE TAB 25MG	29	4	$336,852.95	7.25	$387.19	$11,615.62
TETRABENAZINE TAB 25MG	29	6	$208,219.86	4.83	$235.54	$7,180.00
TETRABENAZINE TAB 12.5MG	12	6	$54,269.97	2	$155.06	$4,522.50
XENAZINE TAB 12.5MG	8	1	$75,100.48	8	$312.92	$9,387.56
SUBTOTAL	**78**	**17**	**$674,443.26**	**4.59**	**$287.73**	**$8,646.71**
VALBENAZINE PRODUCTS						
INGREZZA CAP 40MG	5	5	$34,504.59	1	$271.69	$6,900.92
INGREZZA CAP 80MG	5	3	$31,173.75	1.67	$207.82	$6,234.75
SUBTOTAL	**10**	**8**	**$65,678.34**	**1.25**	**$237.11**	**$6,567.83**
TOTAL	**88**	**19***	**$740,121.60**	**3.52**	**$282.38**	**$8,410.47**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
The prior authorization for Xenazine® (tetrabenazine) was implemented on November 6, 2017. Members currently on therapy at the time of implementation were grandfathered.

[1] U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 03/2018. Last accessed 04/23/2018.

[2] Austedo Prescribing Information. Teva. Available online at: https://www.austedo.com/hcp/renderpdf.aspx?file=PrescribingInformation.pdf. Last revised 08/2017. Last accessed 05/17/2018.

[3] Brooks M. FDA Oks Deutetrabenazine (Austedo) for Tardive Dyskinesia. *Medscape*. Available online at: https://www.medscape.com/viewarticle/885051. Issued 08/30/2017. Last accessed 04/23/2018.

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[5] Neurocrine Biosciences, Inc. Neurocrine Announces FDA Approval of 80mg Ingrezza® (valbenazine) Capsules for the Treatment of Adults with Tardive Dyskinesia (TD). *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/neurocrine-announces-fda-approval-of-80-mg-ingrezza-valbenazine-capsules-for-the-treatment-of-adults-with-tardive-dyskinesia-td-300531471.html. Issued 10/05/2017. Last accessed 04/27/2018.

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[8] Neurocrine Biosciences, Inc. Neurocrine Initiates Phase IIb Clinical Study of Once-daily Ingrezza® in Children and Adolescents with Tourette Syndrome. *PR Newswire*. Available online at: https://www.prnewswire.com/news-releases/neurocrine-initiates-phase-iib-clinical-study-of-once-daily-ingrezza-in-children-and-adolescents-with-tourette-syndrome-300543268.html. Issued 10/25/2017. Last accessed 04/26/2018.

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Appendix L

Calendar Year 2017 Annual Review of ADHD and Narcolepsy Medications and 30-Day Notice to Prior Authorize Cotempla XR-ODT™ [Methylphenidate Extended-Release (ER) Orally Disintegrating Tablet (ODT)], Mydayis® (Amphetamine/ Dextroamphetamine ER Capsule), and Adzenys ER™ (Amphetamine ER Suspension)

Oklahoma Health Care Authority
June 2018

Current Prior Authorization Criteria

ADHD Medications Tier-2 Approval Criteria:

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

ADHD Medications Tier-3 Approval Criteria:

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

a. An FDA approved diagnosis; and
b. Previously failed trials (within the last 180 days) with a long-acting Tier-1 stimulant, a long-acting Tier-2 stimulant, Intuniv®, and Strattera®, unless contraindicated, that did not yield adequate results; and
c. A patient-specific, clinically significant reason why the member cannot use clonidine immediate-release tablets.

ADHD Medications Special Prior Authorization (PA) Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra®, and Zenzedi® Approval 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, and Methylin® Chewable Tablets and Solution Approval Criteria:
   a. A covered diagnosis; and
   b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of stimulant medications that can be used for members who cannot swallow capsules or tablets; and
   c. An age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.

ADHD Medications Additional Criteria:

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

Narcolepsy Medications Approval Criteria:

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

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Placement of products shown in blue is based on net cost after rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.

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

ER = extended-release, SR = sustained-release, caps = capsules, ODT = orally disintegrating tablet, chew tabs = chewable tablets, soln = solution, susp = suspension

Utilization of ADHD & Narcolepsy Medications: Calendar Year 2017

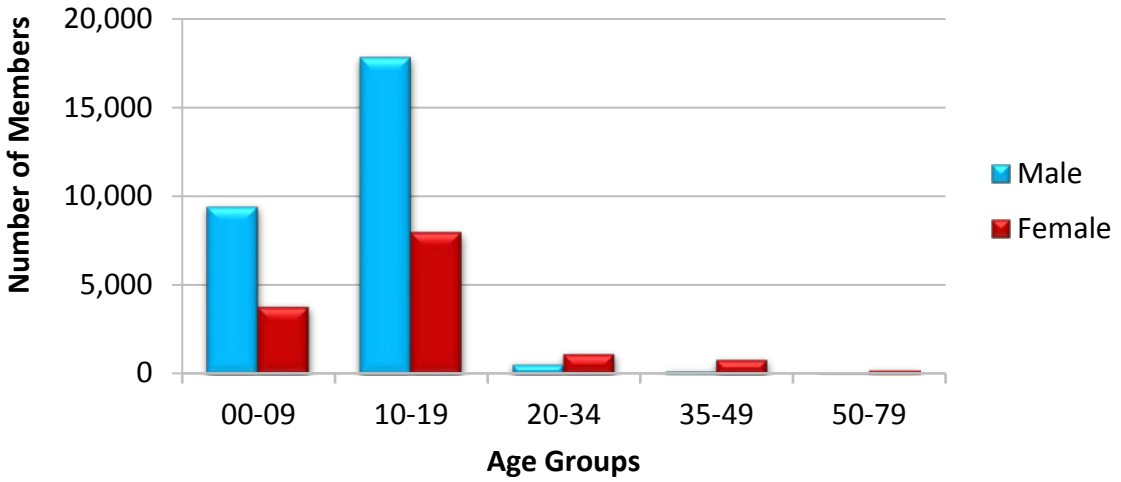
Comparison of Calendar Years: ADHD & Narcolepsy Medications

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	41,721	341,811	$62,239,928.55	$182.09	$6.13	12,072,942	10,158,517
2017	42,104	344,511	$55,680,227.98	$161.62	$5.45	12,149,984	10,224,700
% Change	**0.90%**	**0.80%**	**-10.50%**	**-11.20%**	**-11.10%**	**0.60%**	**0.70%**
Change	**383**	**2,700**	**-$6,559,700.57**	**-$20.47**	**-$0.68**	**77,042**	**66,183**

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

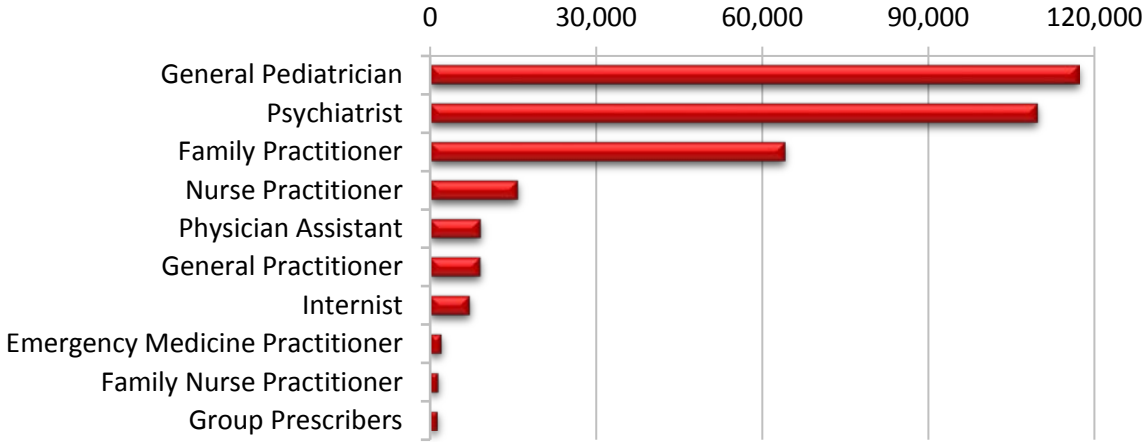
- Aggregate drug rebates collected during calendar year 2017 for attention deficit hyperactivity disorder (ADHD) and narcolepsy medications: $38,475,088.77[Δ]
- Please note, due to new federal regulations, a new pricing methodology for pharmacy claims reimbursement was implemented by SoonerCare on January 3, 2017. Ingredient reimbursement changed from an estimated acquisition cost (EAC) to an actual acquisition cost (AAC). In addition, the professional dispensing fee increased from $3.60 in 2016 to $10.55 effective January 2017; professional dispensing fees are included in the reimbursement totals in the following report. The impact of the pricing methodology and dispensing fee change are estimated to be budget neutral. This change in reimbursement should be considered when evaluating reimbursement changes from year to year. Medications with a very low cost per claim and large volume of claims will appear to increase in price due to the increase in dispensing fee; however, these increases will be neutralized by changes in ingredient reimbursement for higher cost medications.

Demographics of Members Utilizing ADHD & Narcolepsy Medications



[Δ] 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.

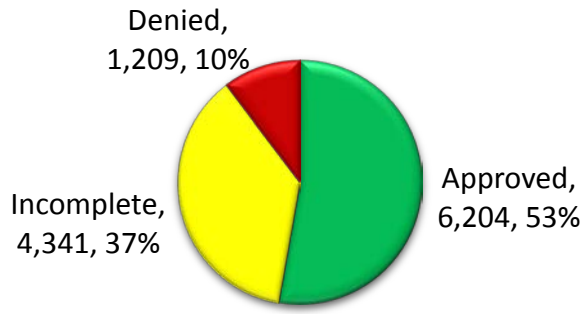
Top Prescriber Specialties of ADHD & Narcolepsy Medications by Number of Claims



Prior Authorization of ADHD & Narcolepsy Medications

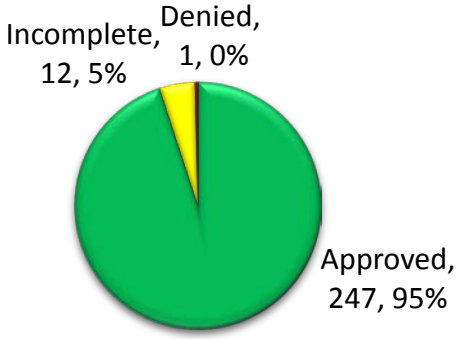
There were 11,754 prior authorization requests submitted for ADHD and narcolepsy medications during calendar year 2017. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



There were 260 prior authorization requests submitted for a total of 205 unique members for ADHD and narcolepsy medications during calendar year 2017 that were referred for a psychiatric consultation. Most requests were for children between 3 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations



Medicaid Drug Rebate Program[1,2,3]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Participation in the federal drug rebate program requires Medicaid coverage with limited exceptions (e.g., cosmetic medications, fertility medications). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any commercial payer. Best prices are reported to CMS by the manufacturer, but are not publicly available.

If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices. As average wholesale price (AWP) increases, the rebated amount per unit (RAPU) increases as well, resulting in minimal effect on Medicaid net cost. Until 2017, the CPI penalty only applied to brand medications; following a Senate vote in October 2015, the Medicaid CPI penalty was extended to generic drugs with an effective date of January 1, 2017.

Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. The ADHD and Narcolepsy Medications Product Based Prior Authorization (PBPA) category is heavily influenced by supplemental rebates. The ADHD and narcolepsy brand name products that are preferred over available generic products are preferred due to a lower net cost compared to generics, after taking into account federal and/or supplemental rebate participation. In calendar year 2017, the Oklahoma Health Care Authority (OHCA) collected $38,475,088.77 in aggregate drug rebates for ADHD and narcolepsy medications. These rebates are collected after reimbursement for the medication and are not reflected in this report. The costs included in this report do not reflect net costs.

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

Anticipated Patent Expiration(s):

- Aptensio XR® [methylphenidate extended-release (ER) capsule]: December 2019
- Vyvanse® (lisdexamfetamine capsule): February 2023
- Vyvanse® (lisdexamfetamine chewable tablet): February 2023
- Daytrana® (methylphenidate ER patch): October 2025
- Dyanavel® XR (amphetamine ER suspension): March 2029
- Quillivant XR® (methylphenidate ER suspension): February 2031
- Adzenys XR-ODT® [amphetamine ER orally disintegrating tablet (ODT)]: June 2032
- Xyrem® (sodium oxybate solution): March 2033
- QuilliChew ER® (methylphenidate ER chewable tablet): August 2033

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

- **May 2017:** The FDA approved Abbreviated New Drug Applications (ANDAs) for the first generic versions of Strattera® (atomoxetine). Four pharmaceutical companies received FDA approval in May 2017 to market generic atomoxetine, followed by one additional pharmaceutical company in February 2018. Additionally, there are currently ANDAs for generic atomoxetine submitted from another four pharmaceutical companies that are

awaiting FDA approval. Generic atomoxetine is currently available as a Tier-1 non-stimulant ADHD medication.

- **June 2017:** The FDA approved Cotempla XR-ODT™ (methylphenidate ER ODT), the first and only methylphenidate ER ODT, for the treatment of ADHD in patients 6 to 17 years of age. Cotempla XR-ODT™ is intended for once daily administration.
- **June 2017:** The FDA approved Mydayis® (amphetamine/dextroamphetamine ER capsule) for the treatment of ADHD in patients 13 years of age and older. Mydayis® is not for use in children 12 years of age and younger. Mydayis® is a once daily treatment that is comprised of three different types of drug-releasing beads.
- **September 2017:** The FDA approved Adzenys ER™ (amphetamine ER suspension) for the treatment of ADHD in patients 6 years of age and older. Adzenys ER™ is a once daily liquid medication that does not require refrigeration or reconstitution at the pharmacy level. Adzenys XR-ODT® (amphetamine ER ODT) was FDA approved in 2016 for the treatment of ADHD in patients 6 years of age and older.

Pipeline:

- **December 2016:** Highland Therapeutics submitted a New Drug Application (NDA) to the FDA for Benjorna™ (formerly referred to as HLD200) for the treatment of ADHD, with a Prescription Drug User Fee Act (PDUFA) goal date of July 30, 2017; however, the FDA has not yet approved Benjorna™ and there have been no updates published regarding the status of the NDA for Benjorna™. Benjorna™ is a novel formulation of long-acting methylphenidate that relies on Delexis® drug delivery technology for controlled-release of the drug; Benjorna™ is to be taken once daily in the evening with the objective of controlling symptoms of ADHD immediately upon awakening and throughout the day. The medication is coated with two layers of polymer that only permits release of the drug once it has reached the colon; thus, blood levels of methylphenidate do not begin to increase until 8 hours after the medication is taken. Highland Therapeutics also has a novel formulation of amphetamine in the pipeline based on Delexis® drug delivery technology, HLD-100, for the treatment of ADHD. HLD-100 is currently in Phase 2 clinical trials.
- **September 2017:** Supernus Pharmaceuticals announced the outcome of the planned interim analysis from the first Phase 3 clinical trial with SPN-810. The company is developing SPN-810 (molindone hydrochloride) as a novel treatment for impulsive aggression (IA) in patients 6 to 12 years of age who have ADHD. Molindone hydrochloride was previously marketed in the United States for the treatment of schizophrenia under the brand name Moban® at different strengths and dosage forms at higher daily doses than Supernus is using in their development program for the treatment of IA in patients with ADHD. SPN-810 is being tested in two Phase 3 clinical trials at total daily doses of 18mg and 36mg compared to placebo. The two trials are being conducted using an agreed-upon novel scale to measure IA that was developed by the company with the FDA under a Special Protocol Assessment (SPA). The two trials are of the same design except that under the SPA, an interim analysis was planned in the first trial when one-half of the patients (146 patients) reached randomization. The purpose of the interim analysis was to assess the doses being tested and allow for

optimization of the trial design of both trials. The interim analysis has been completed and both trials will continue through to completion. Based on the predefined criteria for dropping a dose arm, the lower dose of 18mg will be eliminated, and moving forward, all patients will be randomized to either the 36mg dose arm or placebo. The company expects enrollment in the Phase 3 trials to continue through mid-2018. If SPN-810 is effective for the treatment of IA in patients with ADHD, the company plans on developing it for the treatment of IA across other central nervous system (CNS) disorders where IA is widely prevalent. Supernus also has another product currently in Phase 2 clinical trials for the treatment of ADHD, SPN-812 (viloxazine hydrochloride), which would be a novel non-stimulant treatment option for ADHD. Viloxazine hydrochloride is a norepinephrine reuptake inhibitor that is currently marketed in Europe as an antidepressant, but was never developed in the United States for any indication.

- **November 2017:** Sunovion submitted an NDA to the FDA for dasotraline, a novel dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI), for the treatment of ADHD in children, adolescents, and adults. The NDA submission is supported by multiple placebo-controlled safety and efficacy studies, as well as two long-term studies that assessed the safety of dasotraline in patients with ADHD for up to one year. In total, approximately 2,500 patients with ADHD were evaluated in these studies, and dasotraline was generally well tolerated. Dasotraline has an extended half-life (47 to 77 hours) that supports the potential for stable plasma concentrations yielding a continuous therapeutic effect over the 24-hour dosing interval. The FDA has set a PDUFA goal date of August 31, 2018 for dasotraline for the treatment of ADHD. Dasotraline is also in development for the treatment of binge eating disorder (BED) and is currently in Phase 3 clinical trials.
- **March 2018:** Aevi Genomic Medicine is currently developing AEVI-001 (fasoracetam; formerly known as NFC-1), which is a metabotropic glutamate receptor (mGluR) activator, for the treatment of ADHD. The company is continuing screening and recruitment efforts for its Phase 2 ("ASCEND") clinical trial in an mGluR mutation positive genetic subset of pediatric and adolescent patients with ADHD to confirm genetic responders to AEVI-001. Patient enrollment is ongoing, with data expected by mid-2018. Additionally, the company is planning to initiate Phase 2 clinical trials in 2018 with AEVI-001 for an mGluR mutation positive genetic subset of patients with autism spectrum disorder (ASD). The mGluRs are family C G-protein-coupled receptors that participate in the modulation of synaptic transmission and neuronal excitability throughout the CNS. The mGluRs bind glutamate within a large extracellular domain and transmit signals through the receptor protein to intracellular signaling partners. The widespread expression of mGluRs makes these receptors particularly attractive drug targets, and recent studies continue to validate the therapeutic utility of mGluR ligands in neurological and psychiatric disorders.
- **March 2018:** Jazz Pharmaceuticals submitted an NDA to the FDA for solriamfetol (JZP-110), a selective DNRI, for the treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea (OSA). Solriamfetol has been granted Orphan Drug designation for the treatment of excessive sleepiness associated with narcolepsy.

The solriamfetol Phase 3 clinical program includes one study evaluating excessive sleepiness in adult patients with narcolepsy (TONES 2), two studies evaluating excessive sleepiness in adult patients with OSA (TONES 3 and TONES 4), and an open-label, long-term safety and maintenance of efficacy study in the treatment of excessive sleepiness in patients with narcolepsy or OSA (TONES 5). The FDA has set a PDUFA goal date of December 20, 2018 for solriamfetol. Solriamfetol is also in development for the treatment of excessive sleepiness in Parkinson's disease and is currently in Phase 2 clinical trials.

- **May 2018:** Jazz Pharmaceuticals submitted a supplemental New Drug Application (sNDA) for Xyrem® (sodium oxybate) to treat cataplexy and excessive daytime sleepiness in pediatric narcolepsy patients. Xyrem® was first FDA approved in 2002 for the treatment of cataplexy in narcolepsy and for the treatment of excessive daytime sleepiness in narcolepsy in adult patients. Xyrem® is the sodium salt of gamma hydroxybutyrate (GHB). Abuse of GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions. Because of the risks of CNS depression, abuse, and misuse, Xyrem® is available only through a restricted distribution program called the Xyrem® REMS Program. Jazz Pharmaceuticals is also developing JZP-258, an oral solution containing a mixture of oxybate salts with 90% less sodium content than Xyrem®, for the treatment of cataplexy and excessive daytime sleepiness in adult patients with narcolepsy. JZP-258 is currently in Phase 3 clinical trials.

Cotempla XR-ODT™ (Methylphenidate ER ODT) Product Summary[21,22]

Indications: Cotempla XR-ODT™ (methylphenidate ER ODT) is indicated for the treatment of ADHD in pediatric patients 6 to 17 years of age.

Dosing:

- Cotempla XR-ODT™ is available as grape-flavored methylphenidate ER ODTs in the following strengths: 8.6mg, 17.3mg, and 25.9mg, which is the same amount of methylphenidate (base equivalent) found, respectively, in 10mg, 20mg, and 30mg strength methylphenidate hydrochloride products.
- Cotempla XR-ODT™ contains approximately 25% immediate-release (IR) and 75% ER methylphenidate. Methylphenidate is ionically-bound to the sulfonate of polystyrene sulfonate particles.
- Cotempla XR-ODT™ should be administered orally once daily in the morning with or without food. Patients should take Cotempla XR-ODT™ consistently either with food or without food.
- Each ODT should remain in the child-resistant blister pack until the patient is ready to take it. After opening the blister pack, the whole ODT should be placed on the patient's tongue and allowed to disintegrate without chewing or crushing. The ODT will disintegrate in saliva so that it can be swallowed. No liquid is needed to take the ODT.
- The recommended starting dose of Cotempla XR-ODT™ is 17.3mg once daily in the morning. The dose may be titrated weekly in increments of 8.6mg to 17.3mg. Daily doses greater than 51.8mg have not been studied and are not recommended.

- The dose of Cotempla XR-ODT™ should be individualized according to the needs and responses of the patient. Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of Cotempla XR-ODT™ and adjust the dosage as needed.
- The safety and effectiveness of Cotempla XR-ODT™ in pediatric patients younger than 6 years of age have not been established.

National Average Drug Acquisition Cost (NADAC): The NADAC of Cotempla XR-ODT™ 25.9mg is $10.34 per ODT, which results in a monthly cost of $620.40, based on the maximum dose of 51.8mg per day (two 25.9mg ODTs per day).

Mydayis® (Amphetamine/Dextroamphetamine ER Capsule) Product Summary[23,24]

Indications: Mydayis® (amphetamine/dextroamphetamine ER capsule) is indicated for the treatment of ADHD in patients 13 years of age and older.

- Limitations of Use: Pediatric patients 12 years of age and younger experienced higher plasma exposure than patients 13 years of age and older at the same dose of Mydayis® and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite.

Dosing:

- Mydayis® is available as amphetamine/dextroamphetamine ER capsules in the following strengths: 12.5mg, 25mg, 37.5mg, and 50mg.
- Mydayis® capsules contain three types of drug-releasing beads, an IR and two different types of delayed release (DR) beads. The first DR bead releases amphetamine at pH 5.5 and the other DR bead releases amphetamine at pH 7.0.
- Because the effects of Mydayis® may last up to 16 hours and there is potential for insomnia, Mydayis® should be administered orally once daily in the morning upon awakening. In the event of a missed dose, Mydayis® should not be administered later in the day, and additional medication should not be administered to make up for the missed dose.
- Mydayis® can be administered with or without food. Patients should take Mydayis® consistently either with food or without food.
- Mydayis® capsules should either be swallowed whole or the capsules may be opened and the entire contents sprinkled over a spoonful of applesauce, to be consumed immediately in its entirety without chewing. The dose of a single capsule should not be divided.
- The recommended starting dose of Mydayis® is 12.5mg once daily in the morning upon awakening. The dose may be adjusted in increments of 12.5mg no sooner than weekly, up to a recommended maximum dose of 25mg once daily (pediatric patients ages 13 to 17 years) or 50mg once daily (adult patients ages 18 to 55 years). Doses greater than 25mg daily have not been evaluated in clinical trials in pediatric patients, and doses greater than 50mg daily have shown no additional clinically meaningful benefit in adult patients.

- If switching from another medication or any other amphetamine products, treatment with the other product should be discontinued, and the patient should be titrated with Mydayis® using the recommended dosing and titration schedule (*see above*). Mydayis® 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 dose of Mydayis® should be individualized according to the needs and responses of the patient. Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of Mydayis® and adjust the dosage as needed.
- The safety and effectiveness of Mydayis® in pediatric patients 12 years of age and younger have not been established. In clinical trials, pediatric patients 6 to 12 years of age experienced higher rates of adverse reactions in some cases compared to patients 13 years of age and older, including higher rates of insomnia (30% vs. 8%) and decreased appetite (43% vs. 22%). In addition, amphetamine systemic exposure in patients 6 to 12 years of age following a single dose were higher than those observed in adults at the same dose [72 to 79% higher C_{max} and approximately 83% higher area under the curve (AUC)] (*see Limitations of Use*).

NADAC: The NADAC of Mydayis® ranges from $8.54 to $8.66 per capsule, depending on strength, which results in a monthly cost of $256.20 to $259.80, based on the recommended dosing of one capsule per day.

Adzenys ER™ (Amphetamine ER Suspension) Product Summary[25,26]

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

Dosing:

- Adzenys ER™ is available as an orange-flavored amphetamine 1.25mg/mL ER oral suspension. Adzenys ER™ suspension does not require refrigeration, does not require reconstitution at the pharmacy level, and is available in a 450mL bottle.
- Adzenys ER™ contains approximately equal amounts of IR and DR amphetamine.
- Adzenys ER™ should be administered orally once daily in the morning with or without food. Patients or caregivers should be instructed to shake the bottle of Adzenys ER™ before administering the dose. Adzenys ER™ should not be added to foods or mixed with other liquids before consuming.
- The recommended starting dose of Adzenys ER™ for patients 6 to 17 years of age is 6.3mg (5mL) once daily in the morning. The dose may be increased in increments of 3.1mg (2.5mL) or 6.3mg (5mL) at weekly intervals. The maximum dose is 18.8mg (15mL) daily for patients 6 to 12 years of age, and 12.5mg (10mL) daily for patients 13 to 17 years of age.
- The recommended dose of Adzenys ER™ for adults is 12.5mg (10mL) daily.
- If switching from Adderall XR®, patients may be switched to Adzenys ER™ at the equivalent dose taken once daily (*refer to Adzenys ER™ prescribing information for a*

complete table of equivalent doses). If switching from any other amphetamine products, treatment with the other product should be discontinued, and the patient should be titrated with Adzenys ER™ using the recommended dosing and titration schedule (*see above*). Adzenys ER™ 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 dose of Adzenys ER™ should be individualized according to the needs and responses of the patient.
- The safety and effectiveness of Adzenys ER™ in pediatric patients younger than 6 years of age with ADHD have not been established.

Wholesale Acquisition Cost (WAC): The WAC of Adzenys ER™ is $1.42 per milliliter, which results in a monthly cost of $639.00, based on the maximum dose of 18.8mg per day (15mL per day) for patients 6 to 12 years of age, or $426.00 per month, based on the maximum dose of 12.5mg per day (10mL per day) for patients 13 years of age and older.

Recommendations

The College of Pharmacy recommends the placement of Cotempla XR-ODT™ (methylphenidate ER ODT), Mydayis® (amphetamine/dextroamphetamine ER capsule), and Adzenys ER™ (amphetamine ER suspension) into the Special Prior Authorization (PA) Tier of the ADHD and Narcolepsy Medications PBPA category, based on net costs, with the following criteria (changes noted in red):

ADHD Medications Special Prior Authorization (PA) Approval Criteria:

1. Desoxyn®, Dexedrine®, Dexedrine Spansules®, Evekeo®, ProCentra®, and Zenzedi® Approval 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®, Adzenys ER™, Cotempla XR-ODT™, Daytrana®, Dyanavel® XR, and Methylin® Chewable Tablets and Solution Approval Criteria:
    a. A covered diagnosis; and
    b. A patient-specific, clinically significant reason why the member cannot use all other available formulations of stimulant medications that can be used for members who cannot swallow capsules or tablets; and
    c. An age restriction of ten years and younger will apply. Members older than ten years of age will require a patient-specific, clinically significant reason why a special formulation product is needed.
3. Mydayis® Approval Criteria:
    a. A covered diagnosis; and
    b. Member must be 13 years of age or older; and
    c. A patient-specific, clinically significant reason why the member cannot use all other available stimulant medications.

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

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Placement of products shown in blue is based on net cost after rebates, and products may be moved to a higher tier if the net cost changes in comparison to other available products.

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

ER = extended-release, SR = sustained-release, caps = capsules, ODT = orally disintegrating tablet, chew tabs = chewable tablets, soln = solution, susp = suspension

Utilization Details of ADHD & Narcolepsy Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
LISDEXAMFETAMINE PRODUCTS						
VYVANSE CAP 30MG	24,154	6,159	$6,115,646.47	$8.52	$253.19	10.98%
VYVANSE CAP 20MG	18,580	5,807	$4,684,392.42	$8.52	$252.12	8.41%
VYVANSE CAP 40MG	17,991	4,174	$4,558,084.90	$8.51	$253.35	8.19%
VYVANSE CAP 50MG	12,529	2,652	$3,182,634.39	$8.54	$254.02	5.72%
VYVANSE CAP 60MG	7,779	1,528	$1,977,853.58	$8.52	$254.26	3.55%
VYVANSE CAP 70MG	7,685	1,265	$1,948,056.89	$8.50	$253.49	3.50%
VYVANSE CAP 10MG	6,645	22	$1,656,762.95	$8.52	$249.32	2.98%
VYVANSE CHW 10MG	288	180	$77,593.24	$9.16	$269.42	0.14%
VYVANSE CHW 20MG	231	135	$56,322.82	$8.39	$243.82	0.10%
VYVANSE CHW 30MG	134	79	$34,793.39	$8.78	$259.65	0.06%
VYVANSE CHW 40MG	62	30	$16,414.68	$9.03	$264.75	0.03%
VYVANSE CHW 50MG	24	13	$6,062.74	$9.00	$252.61	0.01%
VYVANSE CHW 60MG	13	8	$3,210.62	$8.23	$246.97	0.01%
SUBTOTAL	**96,115**	**22,052**	**$24,317,829.09**	**$8.52**	**$253.01**	**43.67%**
METHYLPHENIDATE PRODUCTS						
METHYLPHENID TAB 10MG	9,883	2,329	$328,525.02	$1.12	$33.24	0.59%
METHYLPHENID TAB 5MG	8,023	2,263	$214,722.33	$0.90	$26.76	0.39%
METHYLPHENID TAB 36MG ER	5,180	988	$1,589,345.72	$10.27	$306.82	2.85%
METADATE CD CAP 20MG	4,623	1,945	$1,023,849.91	$7.51	$221.47	1.84%
METHYLPHENID CAP 20MG	4,509	1,773	$450,683.55	$3.38	$99.95	0.81%
METHYLPHENID TAB 54MG ER	4,430	797	$968,908.50	$7.32	$218.72	1.74%
METHYLPHENID TAB 20MG	4,265	872	$193,776.85	$1.52	$45.43	0.35%
METHYLPHENID CAP 30MG	3,897	1,393	$368,756.98	$3.19	$94.63	0.66%
METADATE CD CAP 30MG	3,865	1,447	$840,822.29	$7.37	$217.55	1.51%
METHYLPHENID TAB 36MG ER	2,956	566	$556,919.69	$6.28	$188.40	1.00%
METHYLPHENID TAB 54MG ER	2,856	485	$411,940.57	$4.83	$144.24	0.74%
METHYLPHENID CAP 40MG	2,595	819	$322,605.80	$4.18	$124.32	0.58%
METADATE CD CAP 10MG	2,390	1,116	$526,108.91	$7.50	$220.13	0.94%
METADATE CD CAP 40MG	2,387	859	$707,605.56	$10.03	$296.44	1.27%
METHYLPHENID TAB 20MG ER	2,034	546	$295,837.30	$4.89	$145.45	0.53%
METHYLPHENID CAP 10MG	1,733	886	$162,717.34	$3.19	$93.89	0.29%
METHYLPHENID TAB 27MG ER	1,696	381	$330,680.35	$6.54	$194.98	0.59%
METADATE CD CAP 50MG	1,133	342	$421,488.91	$12.51	$372.01	0.76%
METHYLPHENID CAP 50MG	1,086	351	$173,973.11	$5.37	$160.20	0.31%
METHYLPHENID TAB 18MG ER	995	250	$195,611.27	$6.60	$196.59	0.35%
METADATE CD CAP 60MG	874	228	$320,504.90	$12.31	$366.71	0.58%
METHYLPHENID TAB 27MG ER	822	190	$107,189.81	$4.37	$130.40	0.19%
METHYLPHENID CAP 60MG	816	230	$121,415.52	$4.99	$148.79	0.22%
METHYLPHENID TAB 10MG ER	694	202	$102,113.87	$4.88	$147.14	0.18%
METHYLPHENID TAB 18MG ER	506	134	$66,433.94	$4.40	$131.29	0.12%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
METHYLPHENID CAP 20MG ER	444	227	$53,431.45	$4.08	$120.34	0.10%
METHYLPHENID SOL 5MG/5ML	400	124	$80,717.38	$6.77	$201.79	0.14%
APTENSIO XR CAP 30MG	392	206	$84,226.12	$7.31	$214.86	0.15%
APTENSIO XR CAP 40MG	391	176	$84,595.08	$7.26	$216.36	0.15%
APTENSIO XR CAP 20MG	376	228	$80,387.41	$7.29	$213.80	0.14%
METADATE TAB 20MG ER	370	117	$26,158.34	$2.38	$70.70	0.05%
RITALIN LA CAP 30MG	366	97	$108,770.38	$10.00	$297.19	0.20%
APTENSIO XR CAP 10MG	364	258	$78,597.86	$7.34	$215.93	0.14%
APTENSIO XR CAP 60MG	352	125	$74,130.87	$7.03	$210.60	0.13%
RITALIN LA CAP 40MG	345	76	$102,867.05	$9.95	$298.17	0.18%
QUILLIVANT SUS 25MG/5ML	333	71	$101,415.19	$10.16	$304.55	0.18%
RITALIN LA CAP 20MG	328	111	$87,732.47	$8.99	$267.48	0.16%
APTENSIO XR CAP 50MG	297	100	$63,079.56	$7.08	$212.39	0.11%
METHYLPHENID SOL 10MG/5ML	244	62	$68,599.70	$9.44	$281.15	0.12%
METHYLPHENID CAP 30MG ER	239	131	$30,064.15	$4.24	$125.79	0.05%
RITALIN LA CAP 10MG	218	104	$56,342.27	$8.72	$258.45	0.10%
METHYLPHENID CHW 5MG	207	83	$31,188.67	$5.15	$150.67	0.06%
DAYTRANA DIS 30MG/9HR	201	29	$53,387.61	$8.85	$265.61	0.10%
METHYLPHENID CAP 40MG ER	190	93	$23,735.68	$4.19	$124.92	0.04%
APTENSIO XR CAP 15MG	182	107	$40,510.66	$7.44	$222.59	0.07%
METHLPHENIDA CHW 2.5MG	157	60	$18,610.94	$4.02	$118.54	0.03%
METHYLIN SOL 5MG/5ML	132	38	$7,625.22	$1.96	$57.77	0.01%
METHYLPHENID CHW 10MG	97	23	$25,798.61	$9.00	$265.97	0.05%
METHYLIN SOL 10MG/5ML	95	21	$8,292.33	$2.88	$87.29	0.01%
CONCERTA TAB 54MG	81	26	$19,071.40	$7.87	$235.45	0.03%
DAYTRANA DIS 20MG/9HR	70	14	$18,947.16	$9.02	$270.67	0.03%
CONCERTA TAB 36MG	60	27	$15,321.21	$8.61	$255.35	0.03%
QUILLICHEW CHW 20MG ER	32	19	$9,499.69	$9.60	$296.87	0.02%
DAYTRANA DIS 15MG/9HR	32	12	$11,771.73	$12.26	$367.87	0.02%
DAYTRANA DIS 10MG/9HR	19	9	$6,089.31	$10.68	$320.49	0.01%
CONCERTA TAB 27MG	19	8	$3,429.63	$6.02	$180.51	0.01%
QUILLICHEW CHW 40MG ER	15	4	$4,574.67	$10.17	$304.98	0.01%
QUILLICHEW CHW 30MG ER	14	6	$4,806.90	$11.45	$343.35	0.01%
RITALIN TAB 10MG	12	1	$1,207.43	$3.35	$100.62	0.00%
METHYLPHENID CAP 60MG LA	7	1	$2,152.08	$10.25	$307.44	0.00%
RITALIN TAB 20MG	5	1	$806.10	$5.37	$161.22	0.00%
CONCERTA TAB 18MG	2	1	$587.34	$9.79	$293.67	0.00%
SUBTOTAL	**81,336**	**24,188**	**$12,291,067.65**	**$5.09**	**$151.11**	**22.07%**
AMPHETAMINE/DEXTROAMPHETAMINE PRODUCTS						
AMPHET/DEXTR TAB 10MG	12,719	2,933	$395,147.72	$1.04	$31.07	0.71%
AMPHET/DEXTR TAB 20MG	8,811	1,707	$308,718.39	$1.17	$35.04	0.55%
AMPHET/DEXTR TAB 5MG	8,446	2,344	$285,276.78	$1.14	$33.78	0.51%
AMPHET/DEXTR TAB 30MG	4,379	734	$162,283.18	$1.24	$37.06	0.29%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
ADDERALL XR CAP 30MG	4,230	660	$892,816.87	$7.08	$211.07	1.60%
ADDERALL XR CAP 20MG	3,948	804	$875,337.93	$7.44	$221.72	1.57%
AMPHET/DEXTR TAB 15MG	3,815	821	$130,305.65	$1.15	$34.16	0.23%
ADDERALL XR CAP 15MG	1,868	448	$390,751.58	$7.02	$209.18	0.70%
ADDERALL XR CAP 10MG	1,862	511	$384,104.32	$6.97	$206.29	0.69%
ADDERALL XR CAP 25MG	1,517	280	$311,602.42	$6.91	$205.41	0.56%
AMPHET/DEXTR TAB 7.5MG	763	232	$32,067.64	$1.42	$42.03	0.06%
ADDERALL XR CAP 5MG	382	125	$80,365.81	$7.10	$210.38	0.14%
AMPHET/DEXTR TAB 12.5MG	264	70	$10,790.62	$1.39	$40.87	0.02%
AMPHET/DEXTR CAP 20MG ER	29	9	$2,342.63	$2.52	$80.78	0.00%
AMPHET/DEXTR CAP 30MG ER	21	6	$765.71	$1.25	$36.46	0.00%
AMPHET/DEXTR CAP 5MG ER	9	1	$899.45	$3.33	$99.94	0.00%
AMPHET/DEXTR CAP 15MG ER	6	3	$328.11	$1.82	$54.69	0.00%
AMPHET/DEXTR CAP 25MG ER	4	3	$365.77	$3.05	$91.44	0.00%
MYDAYIS CAP 37.5MG	1	1	$270.40	$9.01	$270.40	0.00%
SUBTOTAL	**53,074**	**11,692**	**$4,264,540.98**	**$2.70**	**$80.35**	**7.66%**
GUANFACINE PRODUCTS						
GUANFACINE TAB 2MG ER	16,232	3,771	$435,566.47	$0.91	$26.83	0.78%
GUANFACINE TAB 1MG ER	11,464	3,886	$311,734.01	$0.94	$27.19	0.56%
GUANFACINE TAB 3MG ER	11,076	2,134	$311,062.91	$0.94	$28.08	0.56%
GUANFACINE TAB 4MG ER	8,580	1,349	$238,002.14	$0.93	$27.74	0.43%
INTUNIV TAB 3MG	61	8	$17,703.42	$9.67	$290.22	0.03%
INTUNIV TAB 2MG	56	8	$16,102.42	$9.58	$287.54	0.03%
INTUNIV TAB 4MG	56	7	$15,760.67	$9.56	$281.44	0.03%
INTUNIV TAB 1MG	24	3	$6,979.44	$9.69	$290.81	0.01%
SUBTOTAL	**47,549**	**11,166**	**$1,352,911.48**	**$0.96**	**$28.45**	**2.43%**
DEXMETHYLPHENIDATE PRODUCTS						
DEXMETHYLPH TAB 10MG	8,095	1,608	$386,209.10	$1.60	$47.71	0.69%
DEXMETHYLPH TAB 5MG	6,079	1,468	$223,134.12	$1.24	$36.71	0.40%
DEXMETHYLPHE CAP 20MG ER	3,631	780	$608,371.21	$5.63	$167.55	1.09%
DEXMETHYLPH CAP 30MG ER	2,553	489	$339,603.43	$4.47	$133.02	0.61%
DEXMETHYLPH CAP 15MG ER	2,354	566	$304,888.26	$4.34	$129.52	0.55%
DEXMETHYLPHE CAP 10MG ER	1,907	497	$308,018.63	$5.45	$161.52	0.55%
DEXMETHYLPH TAB 2.5MG	1,191	352	$35,347.84	$1.01	$29.68	0.06%
DEXMETHYLPHE CAP 25MG ER	975	246	$180,306.54	$6.23	$184.93	0.32%
DEXMETHYLPH CAP 40MG ER	922	166	$151,311.08	$5.55	$164.11	0.27%
FOCALIN XR CAP 25MG	869	238	$303,129.76	$11.68	$348.83	0.54%
FOCALIN XR CAP 20MG	662	206	$223,162.41	$11.32	$337.10	0.40%
FOCALIN XR CAP 15MG	614	174	$209,192.53	$11.45	$340.70	0.38%
DEXMETHYLPHE CAP 5MG ER	571	190	$81,924.33	$4.89	$143.48	0.15%
FOCALIN XR CAP 30MG	441	130	$140,102.23	$10.63	$317.69	0.25%
FOCALIN XR CAP 10MG	408	125	$131,317.29	$10.76	$321.86	0.24%
DEXMETHYLPHE CAP 35MG ER	275	66	$63,532.81	$7.76	$231.03	0.11%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
FOCALIN XR CAP 35MG	245	63	$89,613.66	$12.37	$365.77	0.16%
FOCALIN XR CAP 40MG	156	48	$57,582.10	$12.30	$369.12	0.10%
FOCALIN TAB 10MG	154	44	$11,705.86	$2.53	$76.01	0.02%
FOCALIN XR CAP 5MG	141	42	$44,070.92	$10.52	$312.56	0.08%
FOCALIN TAB 5MG	96	28	$4,858.99	$1.70	$50.61	0.01%
FOCALIN TAB 2.5MG	16	11	$626.86	$1.37	$39.18	0.00%
SUBTOTAL	**32,355**	**7,537**	**$3,898,009.96**	**$4.05**	**$120.48**	**7.00%**
ATOMOXETINE PRODUCTS						
STRATTERA CAP 40MG	4,378	1,606	$1,863,601.14	$14.44	$425.67	3.35%
ATOMOXETINE CAP 40MG	4,327	1,620	$603,279.06	$4.72	$139.42	1.08%
ATOMOXETINE CAP 25MG	3,771	1,515	$503,216.84	$4.57	$133.44	0.90%
STRATTERA CAP 25MG	3,685	1,433	$1,466,259.43	$13.66	$397.90	2.63%
STRATTERA CAP 60MG	2,778	850	$1,121,170.30	$13.53	$403.59	2.01%
ATOMOXETINE CAP 60MG	2,670	855	$353,554.21	$4.43	$132.42	0.63%
ATOMOXETINE CAP 18MG	1,806	804	$237,797.47	$4.60	$131.67	0.43%
STRATTERA CAP 18MG	1,739	769	$716,403.81	$14.53	$411.96	1.29%
STRATTERA CAP 80MG	1,700	538	$747,015.24	$14.13	$439.42	1.34%
ATOMOXETINE CAP 80MG	1,573	488	$226,139.75	$4.64	$143.76	0.41%
ATOMOXETINE CAP 10MG	1,391	667	$184,768.44	$4.67	$132.83	0.33%
STRATTERA CAP 10MG	1,285	599	$539,371.63	$14.86	$419.74	0.97%
STRATTERA CAP 100MG	540	153	$240,929.24	$14.41	$446.17	0.43%
ATOMOXETINE CAP 100MG	455	134	$62,899.61	$4.50	$138.24	0.11%
SUBTOTAL	**32,098**	**12,031**	**$8,866,406.17**	**$9.37**	**$276.23**	**15.92%**
CLONIDINE EXTENDED-RELEASE PRODUCTS						
CLONIDINE TAB 0.1MG ER	937	144	$189,729.86	$6.73	$202.49	0.34%
KAPVAY TAB 0.1MG	18	2	$13,482.02	$23.65	$749.00	0.02%
SUBTOTAL	**955**	**146**	**$203,211.88**	**$7.06**	**$212.79**	**0.36%**
AMPHETAMINE PRODUCTS						
ADZENYS XR TAB 6.3MG	140	62	$40,490.53	$9.80	$289.22	0.07%
ADZENYS XR TAB 12.5MG	79	30	$23,015.55	$9.74	$291.34	0.04%
ADZENYS XR TAB 9.4MG	71	26	$19,090.23	$8.96	$268.88	0.03%
ADZENYS XR TAB 15.7MG	33	11	$9,763.91	$9.86	$295.88	0.02%
ADZENYS XR TAB 3.1MG	29	17	$8,432.11	$9.69	$290.76	0.02%
ADZENYS XR TAB 18.8MG	10	4	$2,377.33	$7.92	$237.73	0.00%
EVEKEO TAB 10MG	8	1	$2,882.88	$12.01	$360.36	0.01%
DYANAVEL XR SUS 2.5MG/ML	6	2	$2,762.04	$15.43	$460.34	0.00%
EVEKEO TAB 5MG	3	1	$1,125.09	$12.50	$375.03	0.00%
SUBTOTAL	**379**	**154**	**$109,939.67**	**$9.74**	**$290.08**	**0.20%**
MODAFINIL PRODUCTS						
MODAFINIL TAB 200MG	259	39	$18,729.46	$2.42	$72.31	0.03%
MODAFINIL TAB 100MG	22	6	$1,823.43	$2.77	$82.88	0.00%
PROVIGIL TAB 200MG	8	1	$21,720.51	$90.50	$2,715.06	0.04%
SUBTOTAL	**289**	**46**	**$42,273.40**	**$4.89**	**$146.27**	**0.08%**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
DEXTROAMPHETAMINE PRODUCTS						
DEXTROAMPHET CAP 15MG ER	67	7	$13,279.06	$6.61	$198.19	0.02%
DEXTROAMPHET TAB 10MG	45	9	$4,960.55	$3.67	$110.23	0.01%
DEXTROAMPHET CAP 5MG ER	19	3	$1,081.03	$1.90	$56.90	0.00%
DEXTROAMPHET CAP 10MG ER	17	3	$668.62	$1.31	$39.33	0.00%
DEXTROAMPHET TAB 5MG	13	4	$710.43	$1.82	$54.65	0.00%
ZENZEDI TAB 30MG	10	1	$3,966.00	$13.22	$396.60	0.01%
DEXTROAMPHET SOL 5MG/5ML	6	1	$9,823.51	$54.58	$1,637.25	0.02%
SUBTOTAL	**177**	**28**	**$34,489.20**	**$6.50**	**$194.85**	**0.06%**
ARMODAFINIL PRODUCTS						
ARMODAFINIL TAB 250MG	52	9	$9,220.97	$5.91	$177.33	0.02%
NUVIGIL TAB 250MG	38	7	$24,642.11	$21.62	$648.48	0.04%
ARMODAFINIL TAB 150MG	36	6	$5,054.19	$4.68	$140.39	0.01%
NUVIGIL TAB 150MG	12	6	$9,835.79	$27.32	$819.65	0.02%
ARMODAFINIL TAB 200MG	10	1	$1,464.29	$4.98	$146.43	0.00%
NUVIGIL TAB 200MG	1	1	$646.22	$21.54	$646.22	0.00%
SUBTOTAL	**149**	**30**	**$50,863.57**	**$11.39**	**$341.37**	**0.09%**
SODIUM OXYBATE PRODUCTS						
XYREM SOL 500MG/ML	24	2	$239,127.70	$332.12	$9,963.65	0.43%
SUBTOTAL	**24**	**2**	**$239,127.70**	**$332.12**	**$9,963.65**	**0.43%**
METHAMPHETAMINE PRODUCTS						
METHAMPHETAM TAB 5MG	8	1	$5,475.22	$23.81	$684.40	0.01%
DESOXYN TAB 5MG	3	1	$4,082.01	$45.36	$1,360.67	0.01%
SUBTOTAL	**11**	**2**	**$9,557.23**	**$29.87**	**$868.84**	**0.02%**
TOTAL	**344,511**	**42,104***	**$55,680,227.98**	**$5.45**	**$161.62**	**100%**

*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 Crysvita® (Burosumab-twza)

Oklahoma Health Care Authority
June 2018

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

X-linked hypophosphatemia (XLH) is an inherited, X-linked disorder caused by mutations in the *PHEX* gene. Mutations in *PHEX* result in increased concentrations of fibroblast growth factor 23 (FGF23), a protein produced by osteocytes in bones that regulates serum phosphate levels. Excess FGF23 inhibits renal sodium/phosphate cotransporters resulting in inhibition of phosphate reabsorption and causing subsequent hypophosphatemia. Chronic hypophosphatemia leads to poor bone mineralization and fractures. XLH is inherited in an X-linked dominant pattern; therefore, both males and females can develop XLH. While the majority of cases are inherited, de novo mutations in *PHEX* can occur in a person with no family history of the disease. It is estimated that XLH occurs in approximately 1 in 20,000 live births.

XLH is a progressive disorder; however, age of onset, disease severity, and rate of progression vary significantly among affected individuals. Some patients with XLH will only have hypophosphatemia and no bone-related symptoms while others may have more severe symptoms. In most patients, symptoms become apparent in the first 2 years of life when a child begins walking. Initial symptoms include bowing of the legs, short stature, and slowed growth. Additional findings include osteomalacia, bone pain, muscle pain and weakness, waddling gait, joint pain (a result of calcification of tendons and ligaments), abnormal tooth development, tooth abscesses, rickets, fractures, and impaired physical function. In some cases, symptoms of XLH will not appear until adulthood. Adults with XLH have overlapping symptoms including non-healing fractures, reduced mobility, pain, and functional limitations.

Diagnosis of XLH is based on clinical and laboratory findings. Clinical findings such as slow growth rate, bowing of the legs, or other skeletal abnormalities often prompt initial evaluation. Family history of XLH can also prompt evaluation. Patients with XLH will have low levels of phosphate, high levels of FGF23, and normal serum calcium and 25-hydroxy vitamin D. Genetic testing can confirm an XLH diagnosis.

Treatment of XLH focuses on reducing discomfort and correcting bone deformation. Children are generally treated from time of diagnosis until closure of growth plates. The mainstay of pediatric treatment is oral phosphate three to five times daily in combination with high-dose calcitriol. Prepubertal children treated with this regimen can show improved radiological signs of rickets, improved growth, correction of deformities in lower limbs, and reduced bone or joint pain. Complications of this regimen may include nephrocalcinosis and hyperparathyroidism. Additional therapies employed include growth hormone and epihysiodesis (growth plate clamping) to mechanically straighten lower extremities during growth. Treatment in adults is less established. Phosphate and calcitriol treatment is generally reserved for adults with

skeletal pain, an upcoming orthopedic surgery, evidence of osteomalacia with an elevated alkaline phosphatase, or recurrent pseudofractures or stress fractures. Some patients may also require surgeries to correct bone deformities. Additionally, total hip and knee arthroplasty is sometimes required as a result of degenerative joint disease.

In April 2018, the U.S. Food and Drug Administration (FDA) approved Crysvita® (burosumab-twza), an FGF23 blocking antibody, for the treatment of XLH in adult and pediatric patients 1 year of age and older. Burosumab-twza is the first therapy directed toward correction of renal phosphate wasting, and has efficacy data in repairing skeletal abnormalities including fractures and osteomalacia.

Market News and Updates[5,7]

New FDA Approval(s):

- **April 2018:** The FDA approved Crysvita® (burosumab-twza), a FGF23 blocking antibody, for the treatment of XLH in adult and pediatric patients 1 year of age and older. Crysvita® was granted Breakthrough Therapy designation under which the FDA expedites its review of drugs that are intended to treat serious conditions where the drug may represent an improvement over other available therapies. Crysvita® also received Orphan Drug designation and Ultragenyx Pharmaceutical, Inc. received a Rare Pediatric Disease Priority Review voucher. The voucher can be redeemed at a later date to receive priority review of a subsequent marketing application for a different product.

News:

- **April 2018:** Ultragenyx Pharmaceutical, Inc. estimated that, after taking into account rebates that the company plans to negotiate, burosumab will cost approximately $160,000 per patient annually for children and $200,000 per patient annually for adults, depending on body weight. Ultragenyx also indicated that it does not plan to increase costs in the initial years of the drug's availability. Steven B. Miller, MD, chief medical officer of Express Scripts, a national pharmacy benefit manager (PBM), stated "It's not inexpensive, but I do believe the right word is responsible," adding that the cost of the drug is "going to be a very reasonable tradeoff" when surgical interventions currently required for XLH patients are taken in to account.

Crysvita® (Burosumab-twza) Product Summary[8,9,10,11,12,13,14,15,16,17]

Indication(s): Crysvita® (burosumab-twza) is a FGF23 blocking antibody indicated for the treatment of XLH in adult and pediatric patients 1 year of age and older.

Dosing:

- Crysvita® (burosumab-twza) is available as single-dose vials intended for subcutaneous (SC) injection in the following strengths: 10mg/mL, 20mg/mL, or 30mg/mL.
- Burosumab-twza is administered via SC injection and should be administered by a health care provider.
- Prior to initiation of burosumab-twza, fasting serum phosphorus concentration should be below the reference range for age.

- Oral phosphate and active vitamin D analogs should be discontinued 1 week prior to initiation of treatment with burosumab-twza.
- Pediatric Patients (1 to 17 years of age):
  - The recommended starting dose regimen is 0.8mg/kg of body weight, rounded to the nearest 10mg, administered every two weeks. The minimum starting dose is 10mg up to a maximum dose of 90mg.
  - After initiation of treatment, fasting serum phosphorus should be measured every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is above the lower limit of the reference range for age and below 5mg/dL, treatment should be continued with the same dose.
- Adult patients (18 years of age and older):
  - The recommended dose regimen in adults is 1mg/kg of body weight, rounded to the nearest 10mg up to a maximum dose of 90mg, administered every four weeks.
  - After initiation of treatment, fasting serum phosphorus should be assessed on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate.
- Dose adjustments should follow the recommendations in the burosumab-twza *Prescribing Information*. Dose adjustments should not be made more frequently than every 4 weeks.

Mechanism of Action: XLH is a result of excess FGF23 and subsequent suppression of renal tubular phosphate reabsorption and the renal production of 1,25 dihydroxy vitamin D. Burosumab-twza inhibits the biological activity of FGF23; therefore, restoring renal phosphate reabsorption and increasing the serum concentration of 1,25 dihydroxy vitamin D.

Contraindication(s):
- Concomitant use with oral phosphate and active vitamin D analogs
- Initiation of burosumab-twza treatment if serum phosphorus is within or above the normal range for age
- Patients with severe renal impairment or end-stage renal disease (ESRD) because these conditions are associated with abnormal mineral metabolism

Safety:
- Hypersensitivity: Hypersensitivity reactions (e.g., rash, urticaria) have been reported in patients treated with burosumab-twza.
- Hyperphosphatemia and Risk of Nephrocalcinosis: Increases in serum phosphorus to above the upper limit of normal may be associated with an increased risk of nephrocalcinosis. Dose interruption and/or dose reduction may be required based on a patient's serum phosphorus levels.
- Injection Site Reactions: Administration of burosumab-twza may result in local injection site reactions. Burosumab-twza should be discontinued if severe injection site reactions occur.

Use in Specific Populations:

- Pregnancy: There are no available data on burosumab-twza use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. In utero, burosumab-twza exposure in cynomolgus monkeys did not result in teratogenic effects. Late fetal loss and preterm birth were observed in pregnant cynomolgus monkeys at 64-fold human exposure at the adult human dose of 1mg/kg every 4 weeks. Serum phosphorus levels should be monitored throughout pregnancy.
- Lactation: There is no information regarding the presence of burosumab-twza in human milk, or the effects of burosumab-twza on milk production or the breastfed infant. Maternal IgG is present in breast milk. However, the effects of local gastrointestinal exposure and limited systemic exposure to burosumab-twza in the breastfed infant are unknown.
- Pediatric Use: The safety and efficacy of burosumab-twza have been established in pediatric patients 1 year of age and older. Efficacy in pediatric patients 1 year of age and older with XLH is based on open-label studies of 52 pediatric patients 5 to 12 years of age with XLH, and in 13 pediatric patients 1 to 4 years of age with XLH evaluating serum phosphorus and radiographic findings. Efficacy in adolescents is supported by studies in pediatric patients less than 13 years of age. Dosing in this age group was derived using modeling and simulation of adult and pediatric pharmacokinetic and pharmacodynamic data.
- Geriatric Use: Clinical studies of burosumab-twza did not include sufficient numbers of patients 65 years and older to determine whether they respond differently from younger patients.

Adverse Reactions: The most common adverse reactions (pediatric incidence >10%) experienced during treatment with burosumab-twza in clinical trials include the following: headache, injection site reaction, vomiting, pyrexia, pain in extremity, decreased vitamin D, rash, toothache, myalgia, tooth abscess, and dizziness.

Efficacy in Pediatric XLH: Burosumab-twza has been evaluated in 65 pediatric patients with XLH.

- Study 1: Study 1 compared treatment with burosumab-twza administered every 2 weeks (Q2W) versus every 4 weeks (Q4W) in a randomized, open-label study in 52 prepubescent XLH patients 5 to 12 years of age with open growth plates and Tanner stage 2 or less based on breast and testicular development. XLH was confirmed by *PHEX* mutation in the patient or a direct family member or by a serum FGF23 level >30pg/mL. For inclusion, patients were required to have a serum phosphorous ≤2.8mg/dL, a standing height <50th percentile for age and gender, and radiographic evidence of active bone disease. Following a 16-week dose titration phase, patients completed 48-weeks of treatment with burosumab-twza. The burosumab-twza dose was adjusted to target a fasting serum phosphorus concentration of 3.5mg/dL to 5.0mg/dL. A total of 26 patients received burosumab-twza Q2W up to a maximum dose of 2mg/kg. The remaining 26 patients received burosumab-twza Q4W. The mean dose at week 40 was 0.98mg/kg in the Q2W group and 1.50mg/kg in the Q4W group. At study entry, the mean age of

patients was 8.5 years and 46% were male. Approximately, 96% had received oral phosphate and active vitamin D analogs for a mean duration of 7 years. Oral phosphate and active vitamin D analogs were discontinued prior to study enrollment; 94% of patients had radiographic evidence of rickets at baseline. Burosumab-twza increased mean serum phosphorus levels from 2.4mg/dL at baseline to 3.3mg/dL and 3.4mg/dL at week 40 and 64 in the Q2W group. The ratio of renal tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) increased from mean of 2.2mg/dL at baseline to 3.3mg/dL and 3.4mg/dL at week 40 and 64. Treatment for 64 weeks increased standing mean height Z score from -1.72 at baseline to -1.54 in the Q2W group [least squares (LS) mean change of +0.19; 95% confidence interval (CI) 0.09 to 0.29].

- Study 2: Study 2 was a 64-week open-label study in 13 pediatric XLH patients 1 to 4 years of age. Patients received burosumab-twza at a dose of 0.8mg/kg Q2W with titration up to 1.2mg/kg based on serum phosphorus measurements. The diagnosis of XLH was supported by either confirmed *PHEX* mutation in the patient or a direct family member or by a serum FGF23 >30pg/mL. Patients were required to have biochemical findings associated with XLH including serum phosphorus <3.0mg/dL and serum creatinine within an age-adjusted normal range. At study entry, the mean age of patients was 2.9 years and 69% were male. All patients had radiographic evidence of rickets at baseline and had received oral phosphate and active vitamin D analogs for a mean duration of 16.9 months. Oral phosphate and active vitamin D analogs were discontinued prior to study enrollment. Burosumab-twza increased mean serum phosphorus levels from 2.5mg/dL at baseline to 3.5mg/dL at week 40 (P<0.001).
- Radiographs from 52 burosumab-twza-treated patients in Study 1 and 13 patients in Study 2 were examined to assess XLH-related rickets using the 10-point Thacher Rickets Severity Score (RSS) and the 7-point Radiographic Global Impression of Change (RGI-C). The RSS score is assigned based on images of the wrist and knee from a single timepoint, with higher scores indicating greater rickets severity. The RGI-C score is assigned based on side-by-side comparisons of wrist and knee radiographs from two timepoints, with higher scores indicating greater improvement in radiographic evidence of rickets. A RGI-C score of +2.0 was defined as radiographic evidence of substantial healing.
    - Study 1: After 40 weeks of treatment, mean RSS decreased from 1.9 to 0.8 (LS mean change of -1.1; 95% CI -1.28 to -0.85), and mean RGI-C score was +1.7 (95% CI +1.48 to +1.84) in patients receiving burosumab-twza Q2W. A total of 18 out of 26 patients achieved an RGI-C score of ≥ +2.0. These findings were maintained at week 64.
    - Study 2: After 40 weeks of treatment with burosumab-twza, mean RSS decreased from 2.9 to 1.2 (LS mean change of -1.7; 95% CI -2.03 to -1.44) and mean RGI-C global score was +2.3 (95% CI +2.16 to +2.51). All 13 patients achieved a RGI-C global score ≥ +2.0. The mean lower limb deformity as assessed by RGI-C using standing long leg radiographs was +1.3 (P<0.001).

Efficacy in Adult XLH:

- Study 3: Study 3 was a 24-week randomized, double-blind, placebo-controlled study in 134 adult XLH patients who received burosumab-twza 1mg/kg Q4W or placebo. XLH was confirmed by classic clinical features of adult XLH (e.g., short stature, bowed legs) and either *PHEX* mutation in the patient or a direct family member or by a serum FGF23 level >30pg/mL. In addition, participants were required to have biochemical and clinical findings consistent with XLH including serum phosphorus and TmP/GFR <2.5mg/dL and presence of skeletal pain attributed to XLH. A total of 93% of subjects had received prior phosphate and 95% had received prior vitamin D analogs. Oral phosphate and vitamin D analogs were not allowed during the study. At study entry, the mean age of patients was 40 years (range 19 to 66 years) and 35% were male. Baseline, mean serum phosphorus were 1.9mg/dL and 2.0mg/dL in the placebo and burosumab-twza groups, respectively. During the initial 24 weeks of treatment, mean serum phosphorus across the midpoints of dose intervals were 2.1mg/dL and 3.2mg/dL and across the ends of dose intervals were 2.0mg/dL and 2.7mg/dL in the placebo and burosumab-twza groups, respectively. A total of 94% of burosumab-twza-treated patients achieved a serum phosphorus level above the lower limit of normal (LLN) at mid-point of the dose interval compared to 8% in the placebo group through week 24 (P<0.0001). Change from baseline to week 24 in brief pain inventory (BPI) question 3 (Q3; worst pain in past 24 hours) score (P=0.09) and change from baseline to week 24 in Western Ontario and McMaster University Osteoarthritis (WOMAC) physical function score (P=0.05) were not statistically significantly different compared to placebo; however, change from baseline to week 24 in WOMAC stiffness score (P=0.01) was statistically significant compared to placebo.
    - In Study 3, a skeletal survey was conducted at baseline to identify osteomalacia-related fractures and pseudofractures. Osteomalacia-related fractures are defined as atraumatic lucencies extending across both bone cortices and pseudofractures are defined as atraumatic lucencies extending across one cortex. Approximately 52% of patients had either active (unhealed) fractures (12%) or active pseudofractures (47%) at baseline. Assessment of active fracture/pseudofracture sites at week 24 demonstrated a higher rate of complete healing in the burosumab-twza group compared to placebo (fractures healed: 0% placebo vs. 50% burosumab-twza; pseudofractures healed: 9% placebo vs. 41% burosumab-twza). During treatment through week 24, a total of 6 new fractures or pseudofractures appeared in 68 patients receiving burosumab-twza, compared to 8 new abnormalities in 66 patients receiving placebo.
- Study 4: Study 4 was a 48-week, open-label, single-arm study in 14 adult XLH patients to assess the effects of burosumab-twza on improvement of osteomalacia as determined by histologic and histomorphometric evaluation of iliac crest bone biopsies. Patients received 1mg/kg burosumab-twza Q4W. At study entry, the mean age of patients was 40 years (range 25 to 52 years) and 43% were male. Oral phosphate and vitamin D analogs were not allowed during the study. After 48 weeks of treatment, healing of osteomalacia was observed in 10 patients as demonstrated by decreases in osteoid volume/bone volume (OV/BV) from a mean score of 26% at baseline to 11%, a change

of -57%. Osteoid thickness declined in 11 patients from a mean of 17 micrometers to 12 micrometers, a change of -33%. Mineralization lag time declined in 6 patients from a mean of 594 days to 156 days, a change of -74%.

Cost: The wholesale acquisition cost (WAC) of burosumab-twza is $3,400 per 10mg/mL single-dose vial, $6,800 per 20mg/mL single-dose vial, and $10,200 per 30mg/mL single-dose vial.

Patient Weight	Dosing Regimen	Vials Per Dose	Cost Per Dose	Cost Per Year
Pediatric Patient Dosing				
10kg	0.8 to 2mg/kg Q2W	(1) 10mg to (1) 20mg	$3,400 to $6,800	$88,400 to $176,800
20kg	0.8 to 2mg/kg Q2W	(1) 20mg to (2) 20mg	$6,800 to $13,600	$176,800 to $353,600
40kg	0.8 to 2mg/kg Q2W	(1) 30mg to (2) 30mg + (1) 20mg	$10,200 to $27,200	$265,200 to $707,200
Max	90mg every Q2W	(3) 30mg	$30,600	$795,600
Adult Patient Dosing				
60kg	1mg/kg Q4W	(2) 30mg	$20,400	$265,200
70kg	1mg/kg Q4W	(2) 30mg + (1) 10mg	$23,800	$309,400
Max	90mg Q4W	(3) 30mg	$30,600	$397,800

Costs based on WAC and do not reflect rebated prices or net costs.
Max = maximum recommended dose for age regardless of patient weight
Costs per year based on 26 infusions (Q2W dosing) or 13 infusions (Q4W dosing).

Specialist Recommendation(s): The College of Pharmacy received input from a geneticist regarding XLH genetic testing. The specialist recommended prior authorization of burosumab-twza to ensure appropriate usage; however, requiring genetic testing as proof of XLH diagnosis was not recommended, but rather it could be use an option to confirm diagnosis. Laboratory evidence of elevated FGF23 was recommended as an alternative to confirm an XLH diagnosis.

Recommendations

The College of Pharmacy recommends the prior authorization of Crysvita® (burosumab-twza) with the following criteria:

Crysvita® (Burosumab-twza) Approval Criteria:

1. An FDA approved indication for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older. Diagnosis of XLH must be confirmed by one of the following:
    a. Genetic testing; or
    b. Elevated serum fibroblast growth factor 23 (FGF23) level >30pg/mL; and
2. Member's serum phosphorus level must be below the normal range for member age; and
3. Member's XLH symptoms must not be adequately controlled on phosphate and calcitriol supplements. Members experiencing adverse effects related to these treatments may

also be considered for approval. Detailed information regarding adverse effects must be documented on the prior authorization request; and

4. Member must not have any contraindications to taking Crysvita® including the following:
    a. Concomitant use with oral phosphate and active vitamin D analogs; and
    b. Serum phosphorus within or above the normal range for member age; and
    c. Severe renal impairment or end-stage renal disease; and
5. Crysvita® must be administered by a health care professional. Approvals will not be granted for self-administration. Prior authorization requests must indicate how Crysvita® will be administered; and
    a. Crysvita® must be shipped to the facility where the member is scheduled to receive treatment; and
6. Member must have clinical signs and symptoms of XLH (symptoms beyond hypophosphatemia alone); and
7. Every two week dosing will not be approved for members 18 years of age or older; and
8. The prescriber must agree to assess serum phosphorus levels on a monthly basis for the first 3 months of treatment, and thereafter as appropriate; and
9. Crysvita® must be prescribed by a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH (or be an advanced care practitioner with a supervising physician who is a nephrologist, endocrinologist, or specialist with expertise in the treatment of XLH); and
10. Initial authorizations will be for the duration of 6 months, at which time the prescriber must verify the member is responding to the medication as demonstrated by serum phosphorus levels within the normal range for member age or clinically significant improvement in bone-related symptoms; and
11. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

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Appendix N

Calendar Year 2017 Annual Review of Various Special Formulations and 30-Day Notice to Prior Authorize Baclofen 5mg Tablet, Esomep-EZS™ (Esomeprazole Kit), Lyrica® CR (Pregabalin Extended-Release), Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion), Sinuva™ (Mometasone Furoate Sinus Implant), Xepi™ (Ozenoxacin 1% Cream), Xhance™ (Fluticasone Propionate Nasal Spray), and ZTlido™ (Lidocaine 1.8% Topical System)

Oklahoma Health Care Authority
June 2018

Introduction

Multiple formulations of medications are made for ease of administration, to increase bioavailability, or as new technologies are 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

GoNitro™ (Nitroglycerin Sublingual Powder) Approval Criteria:

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

Gralise® (Gabapentin Extended-Release Tablets) Approval Criteria:

1. An FDA-approved indication of postherpetic neuralgia; and
2. Documented treatment attempts at recommended dosing with at least one agent from two of the following drug classes that did not yield adequate relief:
    a. Tricyclic antidepressants; or
    b. Anticonvulsants; or
    c. Topical or oral analgesics; and
3. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

Horizant® (Gabapentin Enacarbil Extended-Release Tablets) Approval Criteria:

1. For the FDA-approved indication of restless leg syndrome:
    a. Member must be 18 years of age or older; and

b. Documented treatment attempts at recommended dosing with at least two of the following that did not yield adequate relief:
    i. Carbidopa/levodopa; or
    ii. Pramipexole; or
    iii. Ropinirole; and
c. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

2. For the FDA-approved indication of postherpetic neuralgia:
    a. Member must be 18 years of age or older; and
    b. Documented treatment attempts at recommended dosing with at least one agent from two of the following drug classes that did not yield adequate relief:
        i. Tricyclic antidepressants; or
        ii. Anticonvulsants; or
        iii. Topical or oral analgesics; and
    c. A patient-specific, clinically significant reason why the member cannot take the immediate-release formulation of gabapentin.

Kristalose® (Lactulose Packets for Oral Solution) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the liquid lactulose formulation.

Metozolv® ODT [Metoclopramide Orally Disintegrating Tablets (ODT)] Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use the metoclopramide oral tablet formulation.

Nuvessa™ (Metronidazole Vaginal Gel 1.3%) Approval Criteria:

1. An FDA approved diagnosis of bacterial vaginosis in non-pregnant women; and
2. A patient-specific, clinically significant reason why the member cannot use MetroGel-Vaginal® 0.75% (metronidazole vaginal gel 0.75%) or the generic metronidazole oral tablets.

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 applies. Members 10 years of age and younger do not require prior authorization for Purixan® therapy; and
3. Members older than 10 years of age require a patient-specific, clinically significant reason why the oral tablet formulation cannot be used.

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 nonsteroidal anti-inflammatory drugs (NSAIDs); and
3. A patient-specific, clinically significant reason why the oral tablets or the generic injectable formulation cannot be used.

Rayos® (Prednisone Delayed-Release Tablets) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use immediate-release corticosteroid medications.

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

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

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

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

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

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

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

1. An FDA approved indication of one of the following:
    a. Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen; or

b. Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy; and

2. A patient-specific, clinically significant reason why the oral tablets or generic injectable formulation cannot be used.

Utilization of Special Formulations: Calendar Year 2017

Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	20	101	$71,532.82	$708.25	$25.65	5,392	2,789
2017	37	148	$116,497.69	$787.15	$28.15	9,624	4,138
% Change	**85.00%**	**46.50%**	**62.90%**	**11.10%**	**9.70%**	**78.50%**	**48.40%**
Change	**17**	**47**	**$44,964.87**	**$78.90**	**$2.50**	**4,232**	**1,349**

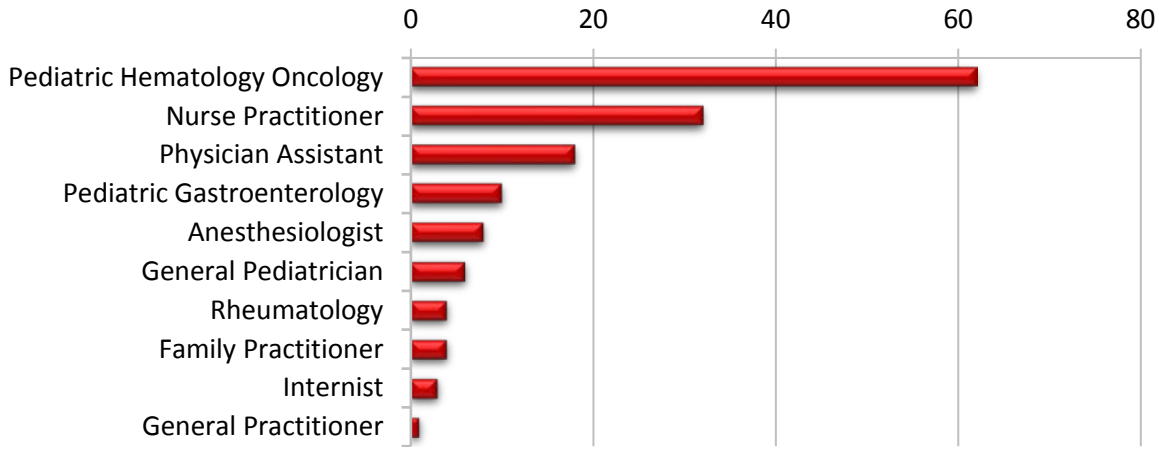
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Due to the evolving nature of this category, calendar year comparisons may not reflect the same product utilization from year to year.

Demographics of Members Utilizing Special Formulations

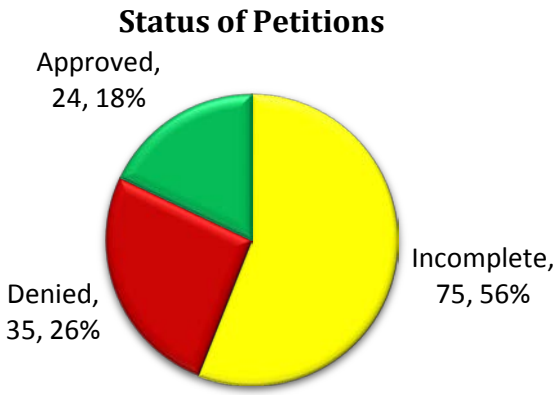
- Due to the small number of members utilizing special formulations, detailed demographic information could not be provided.

Top Prescriber Specialties of Special Formulations by Number of Claims



Prior Authorization of Special Formulations

There were 134 prior authorization requests submitted for special formulations during calendar year 2017. The following chart shows the status of the submitted petitions for calendar year 2017.



Baclofen 5mg Tablet Product Summary[1]

Indication(s): Baclofen 5mg tablet is a muscle relaxant indicated for muscle spasticity. It may be useful for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis or spinal cord injuries, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity.

Dosing and Administration:

- The determination of optimal dosage requires individual titration.
- It is recommended to start therapy at a low dosage (5mg three times daily) and increase gradually until optimum effect is achieved (usually between 40 to 80mg daily). The total daily dose should not exceed 80mg.

Other Formulation(s) Available:

- Baclofen 10mg Tablets:
  - The indications and dosing recommendations for baclofen 10mg tablets are the same as those of baclofen 5mg tablets.
  - Baclofen 10mg tablets are supplied as white, round, flat-faced, beveled edge tablets that are scored on one side.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days*
baclofen 5mg tablets	**$0.93**	**$223.20**
baclofen 10mg tablets	$0.10	$12.00

Unit = tablet
Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per 30 days based on usual effective dosing of 40mg daily.

Calendar Year 2017 Utilization: There was no utilization of baclofen 5mg tablets during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
BACLOFEN TAB 10MG	12,539	3,797	$223,533.63	$0.64	3.3	$17.83
TOTAL	**12,539**	**3,797***	**$223,533.63**	**$0.64**	**3.3**	**$17.83**

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

ESOMEP-EZS™ (Esomeprazole Kit) Product Summary[2,3,4]

Indication(s): ESOMEP-EZS™ (esomeprazole kit) is a proton pump inhibitor indicated for treatment of gastroesophageal reflux disease (GERD), risk reduction of nonsteroidal anti-inflammatory drug (NSAID)-associated gastric ulcer(s), *Helicobacter pylori* (*H. pylori*) eradication to reduce the risk of duodenal ulcer recurrence, and pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

Dosing and Administration:

- ESOMEP-EZS™ is supplied in a kit containing a quantity of 30 esomeprazole magnesium 20mg delayed-release (DR) capsules along with 59mL of PharmapureRx® Pill Swallowing Spray™.
- The recommended dose of ESOMEP-EZS™ varies according to diagnosis. For GERD, the recommended dose is 20mg to 40mg once daily for 4 to 8 weeks. For risk reduction of NSAID-associated gastric ulcer, the recommended dose is 20mg to 40mg once daily for up to six months. For *H. pylori* eradication, the recommended dose is 40mg once daily for 10 days as part of triple therapy, and for pathological hypersecretory conditions, the recommended dose is 40mg twice daily.
- It is recommended to use one to two sprays of PharmapureRx® Pill Swallowing Spray™ to coat the tongue and throat, then place the capsule on the tongue and swallow immediately with water.

Other Formulation(s) Available:

- Esomeprazole DR Capsules, Nexium® Oral Suspension, and Omeprazole DR Capsules:
  - The indications and dosing recommendations for esomeprazole DR capsules and Nexium® oral suspension granules are the same as those of ESOMEP-EZS™. Omeprazole DR capsules have the same indications with an additional indication of treatment and maintenance of healing of erosive esophagitis. The recommended doses are diagnosis dependent.
  - Esomeprazole DR capsules are supplied in two strengths: 20mg and 40mg. Nexium® oral suspension granules are supplied in a dose packet containing esomeprazole DR granules and are supplied in five strengths: 2.5mg, 5mg, 10mg, 20mg, and 40mg. Omeprazole DR capsules are supplied in three strengths: 10mg, 20mg, and 40mg.
  - Both esomeprazole DR capsules and omeprazole DR capsules can be swallowed whole or opened and mixed with applesauce prior to administration. Nexium® oral suspension granules are mixed with water prior to administration.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days
ESOMEP-EZS™ (esomeprazole kit)	**$358.30**	**$358.30**
esomeprazole DR capsules 20mg	$0.56	$16.80
Nexium® (esomeprazole) oral suspension granules 20mg	$8.67	$260.10
omeprazole DR capsules 20mg	$0.04	$1.20

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

Calendar Year 2017 Utilization: There was no utilization of ESOMEP-EZS™ during calendar year 2017. For other products including esomeprazole DR capsules, Nexium® oral suspension granules, and omeprazole DR capsules there were 70,267 claims for 21,528 members with a total cost of $913,838.82. The cost per day was $0.34 with a cost per claim of $13.01. These costs do not reflect rebated prices or net costs.

Lyrica® CR (Pregabalin Extended-Release) Product Summary[5,6,7]

Indication(s): Lyrica® CR [pregabalin extended-release (ER)] is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN). Efficacy of Lyrica® CR has not been established for the management of fibromyalgia or as adjunctive therapy for adult patients with partial-onset seizures.

Dosing and Administration:

- Lyrica® CR is supplied as an oral tablet in three strengths: 82.5mg, 165mg, and 330mg.
- The recommended starting dose for DPN pain is 165mg daily with a maximum dose of 330mg daily. For PHN, the recommended starting dose is 165mg daily and may be increased to 330mg daily within one week, if needed. After two to four weeks at 330mg daily, the dose may be increased to the maximum dose of 660mg once daily.
- Lyrica® CR should be taken once daily after an evening meal. It should be swallowed whole and should not be split, crushed, or chewed.
- When switching from Lyrica® to Lyrica® CR, patients should be instructed to take the scheduled morning dose of Lyrica® and start Lyrica® CR after an evening meal.

Other Formulation(s) Available:

- Lyrica® Capsules, Gabapentin Capsules, and Gabapentin Tablets:
  - Lyrica® capsules are indicated for management of neuropathic pain associated with DPN, management of PHN, adjunctive therapy for adults with partial-onset seizures, management of fibromyalgia, and management of neuropathic pain associated with spinal cord injury.
    - Lyrica® is supplied as oral capsules in eight strengths: 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, and 300mg.
    - For Lyrica®, the recommended dose for DPN is 100mg three times daily; and for PHN, the recommended dose is 150mg to 300mg per day in divided doses.
  - Gabapentin is indicated for PHN and adjunctive therapy in the treatment of partial-onset seizures, with and without secondary generalization, in adult and pediatric patients 3 years of age and older with epilepsy.
    - Gabapentin is supplied as oral capsules in three strengths: 100mg, 300mg, and 400mg. It is also supplied as oral tablets in two strengths: 600mg and 800mg.
    - For gabapentin, the recommended starting dose for PHN is 300mg/day titrated to 900mg/day over 3 days and as needed up to 1,800mg/day.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days*
Lyrica® CR (pregabalin ER) 165mg	**$12.77**	**$383.10**
Lyrica® (pregabalin) 150mg	$7.14	$428.40
gabapentin 300mg capsules	$0.04	$3.60

Unit = tablet or capsule
Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per 30 days based on recommended dose for PHN.

Calendar Year 2017 Utilization: There was no utilization of Lyrica® CR during calendar year 2017. For other products including Lyrica® capsules, gabapentin capsules, and gabapentin tablets, there were 101,503 claims for 20,565 members with a total cost of $5,507,864.44. The cost per day was $1.73 with a cost per claim of $54.26. These costs do not reflect rebated prices or net costs.

Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion) Product Summary[8,9]

Indication(s): Restasis MultiDose® (cyclosporine 0.05% ophthalmic emulsion) is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

Dosing and Administration:

- Restasis MultiDose® is supplied as cyclosporine 0.05% ophthalmic emulsion packaged in a sterile, multi-dose, preservative-free 10mL bottle containing 5.5mL of emulsion. Each bottle contains a unidirectional valve and air filter.
- Restasis MultiDose® should be administered as one drop in each eye twice daily, approximately 12 hours apart.
- Restasis MultiDose® can be used by contact lens wearers; however, contact lenses should be removed before use and replaced 15 minutes after administration of Restasis MultiDose®.

Other Formulation(s) Available:

- Restasis® (Cyclosporine 0.05% Single-Use Vials):
  - Restasis® single-use vials have the same indication and recommended dosing as Restasis MultiDose®.
  - Restasis® is packaged in sterile, preservative-free single-use vials. Each vial contains 0.4mL in a 0.9mL vial. The vials are packaged in trays containing either 30 or 60 vials. The entire contents of each tray must be dispensed intact.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days
Restasis MultiDose® (cyclosporine 0.05%)	**$88.12**	**$484.60**
Restasis® (cyclosporine 0.05% single-use vial)	$8.15	$489.00

Unit = single-use vial or mL
Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Calendar Year 2017 Utilization: There were 20 claims for 13 members utilizing Restasis MultiDose® (cyclosporine 0.05% ophthalmic emulsion) during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
RESTASIS EMU 0.05%	843	309	$287,881.49	$13.64	2.73	$341.50
RESTASIS MUL EMU 0.05%	20	13	$9,125.13	$14.15	1.54	$456.26
TOTAL	**863**	**317***	**$297,006.62**	**$13.66**	**2.72**	**$344.16**

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

Sinuva™ (Mometasone Furoate Sinus Implant) Product Summary[10,11,12,13]

Indication(s): Sinuva™ (mometasone furoate sinus implant) is a corticosteroid-eluting implant indicated for the treatment of nasal polyps in adults 18 years of age and older who have had ethmoid sinus surgery.

Dosing and Administration:

- Sinuva™ implant system contains 1,350mcg of mometasone furoate in a sterile, disposable delivery system. The implant is 20mm in length and 34mm in expanded diameter.
- Sinuva™ is loaded into a delivery system and placed in the ethmoid sinus under endoscopic visualization by a physician trained in otolaryngology. The implant may be left in the sinus to gradually release the corticosteroid over 90 days. The implant can be removed at day 90 or earlier at the physician's discretion using standard surgical instruments.
- Repeat administration of Sinuva™ has not been studied.

Other Formulation(s) Available:

- <u>Mometasone Furoate Nasal Spray:</u>
  - Mometasone furoate nasal spray is indicated for the treatment of nasal symptoms of allergic rhinitis and nasal congestion associated with seasonal allergic rhinitis in patients 2 years of age or older, prophylaxis of seasonal allergic rhinitis in patients 12 years of age or older, and the treatment of nasal polyps in patients 18 years of age or older.
  - For treatment of nasal polyps, the recommended dose is two sprays in each nostril twice daily (400mcg/day).

- Mometasone nasal spray is supplied in a bottle with a manual spray pump containing 17g of product formulation that delivers 120 sprays of 50mcg mometasone furoate per actuation.

Specialist Recommendation(s): The College of Pharmacy received input from an otolaryngology specialist regarding corticosteroid trials. The specialist recommended prior authorization of Sinuva™ to ensure appropriate usage, and recommended a minimum of a three-month trial of intranasal corticosteroids. The specialist also recommended a trial of systemic corticosteroids, if not medically contraindicated, and that the member have recurrent or chronic sinusitis and recurrent nasal obstruction due to nasal polyps.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 90 Days
Sinuva™ (mometasone furoate sinus implant) 1,350mcg	**$1,275.00**	**$2,550.00***
mometasone furoate nasal spray 50mcg	$3.74	$381.48[+]

Unit = implant or gram
Costs do not reflect rebated prices or net costs.
Costs based on National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
*Cost per 90 days includes bilateral implants and based on usual treatment duration of Sinuva™.
[+]Cost per 90 days for mometasone furoate nasal spray based on recommended dosing for nasal polyps.

Calendar Year 2017 Utilization: There was no utilization of Sinuva™ during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
MOMETASONE SPR 50MCG	52	21	$4,821.29	$2.30	2.48	$92.72
NASONEX SPR 50MCG	2	2	$487.67	$8.13	1	$243.84
TOTAL	**54**	**21***	**$5,308.96**	**$2.46**	**2.57**	**$98.31**

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

Xepi™ (Ozenoxacin 1% Cream) Product Summary[14,15,16]

Indication(s): Xepi™ (ozenoxacin 1% cream) is a quinolone antimicrobial indicated for the topical treatment of impetigo due to *Staphylococcus aureus* (*S. aureus*) or *Streptococcus pyogenes* (*S. pyogenes*) in adult and pediatric patients 2 months of age and older.

Dosing and Administration:

- Xepi™ is a 1% pale yellow cream supplied in 10g, 30g, and 45g tubes. Each gram of cream contains 10mg of ozenoxacin.
- Xepi™ is to be applied topically in a thin layer to the affected area(s) twice daily for 5 days.
- The affected area may be up to 100cm^2 in adult and pediatric patients 12 years of age and older or 2% of the total body surface area and not exceeding 100cm^2 in pediatric patients younger than 12 years of age.

Other Formulation(s) Available:

- Gentamicin 0.1% Cream and Mupirocin 2% Ointment:

- Gentamicin cream is indicated for primary skin infections including: impetigo contagiosa, superficial folliculitis, ecthyma, furunculosis, sycosis barbae, and pyoderma gangrenosum. It is also indicated for various secondary skin infections. It is indicated for adults and pediatric patients 1 year of age and older.
    - Gentamicin cream is effective against sensitive strains of streptococci (group A beta-hemolytic, alpha-hemolytic), *S. aureus*, and various strains of gram-negative bacteria.
    - Gentamicin cream is to be applied to the affected area(s) three to four times daily.
    - Gentamicin cream is supplied in a 15g tube containing 1mg gentamicin in each gram.
- Mupirocin ointment, like Xepi™, is indicated for topical treatment of impetigo due to *S. aureus* and *S. pyogenes.* Mupirocin ointment is indicated for adults and pediatric patients 2 months of age and older.
    - Mupirocin ointment is to be applied to the affected area(s) three times daily for up to 10 days.
    - Mupirocin ointment is supplied in a 22g tube containing 20mg of mupirocin in each gram of ointment.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per Treatment
Xepi™ (ozenoxacin 1% cream)	**Unknown**	**Unknown**
gentamicin 0.1% cream	$2.18	$65.40
mupirocin 2% ointment	$0.22	$4.84

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

Calendar Year 2017 Utilization: There was no utilization of Xepi™ during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
MUPIROCIN OIN 2%	42,990	36,488	$680,846.60	$1.51	1.18	$15.84
GENTAMICIN CRE 0.1%	97	64	$5,485.86	$3.65	1.52	$56.56
TOTAL	**43,087**	**36,542***	**$686,332.46**	**$1.51**	**1.18**	**$15.93**

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

Xhance™ (Fluticasone Propionate Nasal Spray) Product Summary[17,18,19]

Indication(s): Xhance™ (fluticasone propionate nasal spray) is a corticosteroid indicated for the treatment of nasal polyps in patients 18 years of age or older.

Dosing and Administration:

- Xhance™ is supplied in an amber glass bottle fitted with a metered-dose manual spray pump unit inside the device with a nasal applicator, valve mechanism, asymmetrical

cone-shaped nosepiece, flexible mouthpiece, and cap. Each bottle contains 16mL of product formulation that delivers 120 sprays of 93mcg fluticasone propionate per spray.

- Xhance™ is delivered into the nose by actuating the pump spray into one nostril while simultaneously blowing into the mouthpiece of the device.
- The recommended dose is one spray per nostril twice daily (total daily dose of 372mcg). A dose of two sprays per nostril twice daily may also be effective in some patients (total daily dose of 744mcg).

Other Formulation(s) Available:

- Fluticasone Propionate Nasal Spray and Mometasone Furoate Nasal Spray:
  - Fluticasone propionate nasal spray is indicated for the management of the nasal symptoms of perennial nonallergic rhinitis in adult and pediatric patients 4 years of age and older.
    - Fluticasone propionate is supplied in an amber glass bottle fitted with a white metering atomizing pump, white nasal adapter, and dust cover. Each bottle contains 16g and provides 120 actuations. Each actuation delivers 50mcg of fluticasone propionate.
    - Fluticasone propionate is dosed as two sprays per nostril once daily (200mcg per day) for adults and one spray per nostril once daily (100mcg per day) for children 4 years of age and older.
    - Multiple randomized trials have found that fluticasone (200mcg twice daily) is superior to placebo in reducing symptoms of nasal obstruction in patients with nasal polyps.
  - Mometasone furoate nasal spray is indicated for the treatment of nasal symptoms of allergic rhinitis and nasal congestion associated with seasonal allergic rhinitis in patients 2 years of age or older, prophylaxis of seasonal allergic rhinitis in patients 12 years of age or older, and the treatment of nasal polyps in patients 18 years of age or older.
    - Mometasone nasal spray is supplied in bottles with a manual spray pump containing 17g of product formulation that delivers 120 sprays of 50mcg mometasone furoate per actuation.
    - For treatment of nasal polyps, the recommended dose is two sprays in each nostril twice daily (400mcg/day).

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days*
Xhance™ (fluticasone propionate nasal spray) 93mcg	**$26.56**	**$424.96**
fluticasone propionate nasal spray 50mcg	$0.24	$7.68
mometasone furoate nasal spray 50mcg	$3.74	$127.16

Unit = gram or mL

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

*Cost per 30 days based on dosing for nasal polyps.

Calendar Year 2017 Utilization: There was no utilization of Xhance™ during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
FLUTICASONE SPR 50MCG	98,678	53,410	$1,414,119.30	$0.39	1.85	$14.33
MOMETASONE SPR 50MCG	52	21	$4,821.29	$2.30	2.48	$92.72
NASONEX SPR 50MCG/AC	2	2	$487.67	$8.13	1	$243.84
TOTAL	**98,732**	**53,427***	**$1,419,428.26**	**$0.39**	**1.85**	**$14.38**

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

ZTlido™ (Lidocaine 1.8% Topical System) Product Summary[20,21,22]

Indication(s): ZTlido™ (lidocaine 1.8% topical system) contains lidocaine, an amide local anesthetic, and is indicated for relief of pain associated with PHN.

Dosing and Administration:

- ZTlido™ is supplied as a carton of 30 single-use topical systems in individual child-resistant envelopes.
- ZTlido™ is recommended to be applied to intact skin to cover the most painful area. The prescribed number of topical systems (maximum of three per day) should be applied once for up to 12 hours within a 24-hour period (12 hours on and 12 hours off).
- Because of the difference in bioavailability, one ZTlido™ provides lidocaine exposure equivalent to one Lidoderm® (lidocaine patch 5%).

Other Formulation(s) Available:

- Lidocaine 5% Topical Patch:
  - Lidocaine 5% topical patch is indicated for relief of pain associated with PHN.
  - The recommended dosing is the same as that of ZTlido™.
  - Lidocaine 5% topical patch is also supplied in a carton containing 30 patches in individual child-resistant envelopes.

Specialist Recommendation(s): The National Institute for Health and Care Excellence (NICE) recommends the use of amitriptyline, duloxetine, gabapentin, or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia). The use of topical treatment is recommended for people with localized neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.

Formulation Cost Comparison:

Product	Cost Per Unit	Cost Per 30 Days
ZTlido™ (lidocaine 1.8% topical system)	**Unknown**	**Unknown**
lidocaine 5% topical patch	$2.74	$82.20

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

Calendar Year 2017 Utilization: There was no utilization of ZTlido™ during calendar year 2017.

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
LIDOCAINE PAD 5%	43	20	$5,344.02	$4.36	2.15	$124.28
TOTAL	**43**	**20***	**$5,344.02**	**$4.36**	**2.15**	**$124.28**

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

Recommendations

The College of Pharmacy recommends the placement of baclofen 5mg tablets into the Special Prior Authorization (PA) Tier of the Muscle Relaxant Medications Product Based Prior Authorization (PBPA) category with the following criteria:

Baclofen 5mg Tablet Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use other appropriate Tier-1 products including splitting a baclofen 10mg tablet to achieve a 5mg dose must be provided.

Muscle Relaxant Medications		
Tier-1	**Tier-2**	**Special PA***
baclofen 10mg, 20mg (Lioresal®)	metaxalone (Skelaxin®)	**baclofen 5mg (Lioresal®)**
chlorzoxazone (Parafon Forte®)		carisoprodol 250mg (Soma®)
cyclobenzaprine (Flexeril®)		carisoprodol 350mg (Soma®)
methocarbamol (Robaxin®)		carisoprodol/ASA
orphenadrine (Norflex®)		carisoprodol/ASA/codeine
tizanidine tablets (Zanaflex®)		chlorzoxazone (Lorzone®)
		cyclobenzaprine (Fexmid®)
		cyclobenzaprine ER (Amrix®)
		tizanidine capsules (Zanaflex®)

PA = prior authorization; ASA = aspirin; ER = extended-release
*Medications in the Special Prior Authorization Tier have individual criteria.

The College of Pharmacy also recommends the placement of ESOMEP-EZS™ (esomeprazole kit) into the Special PA Tier of the Anti-Ulcer Medications PBPA category with the following criteria:

ESOMEP-EZS™ (Esomeprazole Kit) Approval Criteria:

1. A previous 14-day trial of esomeprazole magnesium and a patient-specific, clinically significant reason why other lower tiered proton pump inhibitors including esomeprazole are not appropriate for the member must be provided; and
2. Current Tier structure rules will also apply.

Anti-Ulcer Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA***
omeprazole (Prilosec® caps)	dexlansoprazole (Dexilant® caps)	esomeprazole (Nexium® caps, I.V.)	cimetidine tabs (Tagamet®)
pantoprazole (Protonix® tabs)	esomeprazole (Nexium® packets)	esomeprazole strontium caps	**esomeprazole kit (ESOMEP-EZS™)**

Anti-Ulcer Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA***
	lansoprazole (Prevacid® caps, ODT)	dexlansoprazole (Dexilant® SoluTab)	famotidine (Pepcid® susp)
	pantoprazole (Protonix® I.V.)	omeprazole (Prilosec® susp, powder)	nizatidine caps & sol (Axid®)
	rabeprazole sodium (Aciphex® tabs)	pantoprazole (Protonix® susp)	omeprazole/sodium bicarbonate (Zegerid®)
		rabeprazole sodium (Aciphex® Sprinkles)	ranitidine caps
			sucralfate susp unit dose cups

*Medications in the Special Prior Authorization Tier have individual criteria.
PA = prior authorization; susp = suspension; I.V. = intravenous; tabs = tablets; caps = capsules; ODT = orally disintegrating tablet; sol = solution
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Additionally, the College of Pharmacy recommends the prior authorization of Lyrica® CR [pregabalin extended-release (ER)], Restasis MultiDose® (cyclosporine 0.05% ophthalmic emulsion), Sinuva™ (mometasone furoate sinus implant), and ZTlido™ (lidocaine 1.8% topical system) with the following criteria:

Lyrica® CR (Pregabalin Extended-Release) Approval Criteria:

1. An FDA approved diagnosis of one of the following:
   a. Neuropathic pain associated with diabetic peripheral neuropathy (DPN); or
   b. Neuropathic pain associated with postherpetic neuralgia (PHN); and
2. A patient-specific, clinically significant reason (beyond convenience) why the member cannot use the immediate-release formulation must be provided; and
3. For a diagnosis of DPN, current Lyrica® immediate-release criteria will also apply; and
4. Requests exceeding once daily dosing will not be approved.

Restasis MultiDose® (Cyclosporine 0.05% Ophthalmic Emulsion) Approval Criteria:

1. A patient-specific, clinically significant reason why the member cannot use Restasis® in the individual dosage formulation (single-use vials) must be provided.

Sinuva™ (Mometasone Furoate Sinus Implant) Approval Criteria:

1. An FDA approved indication of nasal polyps in adults 18 years of age and older who have had ethmoid sinus surgery; and
2. Date of ethmoid sinus surgery must be provided; and
3. Sinuva™ must be prescribed and implanted by a physician specializing in otolaryngology; and
4. Failure of nasal corticosteroids after at least a six week three month trial at the maximum recommended dose in combination with a 14-day trial of oral corticosteroids within the last six months (if not contraindicated); and

5. Prescriber must confirm the member has recurrent nasal obstruction/congestion symptoms and recurrent bilateral sinusitis or chronic sinusitis sinus obstruction due to nasal polyps; and
6. A quantity limit of 2 implants per member will apply.

ZTlido™ (Lidocaine 1.8% Topical System) Approval Criteria:

1. An FDA approved diagnosis of pain due to postherpetic neuralgia (PHN); and
2. Documented treatment attempts, at recommended dosing, of at least one agent from two of the following drug classes that failed to provide adequate relief or contraindication(s) to all of the following classes:
   a. Tricyclic antidepressants; or
   b. Anticonvulsants; or
   c. Topical or oral analgesics; and
3. A patient-specific, clinically significant reason why the member cannot use lidocaine 5% patch(es), which are available without prior authorization, must be provided; and
4. A quantity limit of 3 patches per day with a maximum of 90 patches per month will apply.

The College of Pharmacy recommends the placement of Xhance™ (fluticasone propionate nasal spray) into Tier-3 of the Nasal Allergy Medications PBPA category with the following criteria:

Xhance™ (Fluticasone Propionate Nasal Spray) Approval Criteria:

1. An FDA approved diagnosis of nasal polyps; and
2. A patient-specific, clinically significant reason why the member cannot use intranasal fluticasone, budesonide, mometasone, and/or other cost-effective therapeutic equivalent medication(s) must be provided; and
3. Current Tier structure rules will also apply.

Nasal Allergy Medications		
Tier-1	**Tier-2**	**Tier-3**
beclomethasone (Beconase® AQ)	azelastine (Astelin®)	azelastine (Astepro®)
fluticasone (Flonase®)	beclomethasone (Qnasl® 80mcg)	azelastine/fluticasone (Dymista®)
		beclomethasone (Qnasl® 40mcg)
		budesonide (Rhinocort AQ®)
		ciclesonide (Omnaris®, Zetonna®)
		flunisolide (Nasalide®, Nasarel®)
		fluticasone (Veramyst®)
		fluticasone (Xhance™)
		mometasone (Nasonex®)
		olopatadine (Patanase®)

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

Finally, the College of Pharmacy recommends the placement of Xepi™ (ozenoxacin 1% cream) into Tier-2 of the Topical Antibiotic Products PBPA category. Current Tier-2 criteria will apply.

Topical Antibiotic Tier-2 Approval Criteria:

1. Documented five-day trial of a Tier-1 product within the last 30 days.
2. Clinical exceptions apply for adverse effects with all Tier-1 products, or a unique indication not covered by Tier-1 products.
3. Approvals will be for the duration of ten days.

Topical Antibiotics	
Tier-1	**Tier-2**
gentamicin cream 0.1% (Garamycin®)	mupirocin cream 2% (Bactroban®)
gentamicin ointment 0.1% (Garamycin®)	mupirocin kit 2% (Centany®)
gentamicin powder	mupirocin nasal ointment 2% (Bactroban®)
neomycin/polymixin B sulfates/ bacitracin zinc/hydrocortisone ointment 1% (Cortisporin®)	**ozenoxacin 1% cream (Xepi™)**
neomycin/polymixin B sulfates/hydrocortisone cream 0.5% (Cortisporin®)	retapamulin ointment 1% (Altabax®)
mupirocin ointment 2% (Bactroban®)	

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

Utilization Details of Special Formulations: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	CLAIMS/ MEMBER	COST/ CLAIM
GABAPENTIN PRODUCTS						
HORIZANT TAB 600MG	13	3	$7,526.91	$19.30	4.33	$578.99
SUBTOTAL	**13**	**3**	**$7,526.91**	**$19.30**	**4.33**	**$578.99**
LACTULOSE PRODUCTS						
KRISTALOSE PAK 20GM	13	3	$3,673.64	$9.42	4.33	$282.59
KRISTALOSE PAK 10GM	11	4	$2,650.15	$11.04	2.75	$240.92
SUBTOTAL	**24**	**7**	**$6,323.79**	**$10.04**	**3.43**	**$263.49**
MERCAPTOPURINE PRODUCTS						
PURIXAN SUS 20MG/ML	86	23	$84,668.73	$34.56	3.74	$984.52
SUBTOTAL	**86**	**23**	**$84,668.73**	**$34.56**	**3.74**	**$984.52**
METHOTREXATE PRODUCTS						
OTREXUP INJ 15MG	9	1	$5,487.78	$21.78	9	$609.75
OTREXUP INJ 17.5MG	4	1	$2,383.72	$21.28	4	$595.93
XATMEP SOL 2.5MG/ML	11	4	$9,912.05	$32.71	2.75	$901.10
SUBTOTAL	**24**	**6**	**$17,783.55**	**$26.66**	**4**	**$740.98**
METRONIDAZOLE PRODUCTS						
NUVESSA GEL 1.3%	1	1	$194.71	$194.71	1	$194.71
SUBTOTAL	**1**	**1**	**$194.71**	**$194.71**	**1**	**$194.71**
TOTAL	**148**	**37***	**$116,497.69**	**$28.15**	**4**	**$787.15**

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

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Appendix O

Calendar Year 2017 Annual Review of Atypical Antipsychotic Medications

Oklahoma Health Care Authority
June 2018

Current Prior Authorization Criteria

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

ER = extended-release; susp = suspension
Tier structure based on supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.
[◊] Does not count toward a Tier-1 trial
*Special formulation criteria for suspension and ODT formulations apply.
**Use of Invega® Trinza® requires members to have been adequately treated with the 1-month paliperidone extended-release injection (Invega® Sustenna®) for at least four months.
[¥]Aripiprazole (Abilify®) orally disintegrating tablets (ODT) are considered a special formulation, and approval will require a patient-specific, clinically significant reason why a special formulation product is needed in place of the regular tablet formulation.
[α]In addition to the Tier-3 criteria requirements, approval requires a patient-specific, clinically significant reason why the member cannot use olanzapine and fluoxetine as individual components.

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

Atypical Antipsychotic Tier-2 Approval Criteria:

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

Atypical Antipsychotic Tier-3 Approval Criteria:

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

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

1. Authorization of 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 [a selective serotonin reuptake inhibitor (SSRI) and duloxetine] and a trial of aripiprazole tablets that did not yield adequate response. Tier structure rules apply.
2. Authorization of Symbyax® (olanzapine/fluoxetine) for a diagnosis of major depressive disorder requires previous trials with at least two other antidepressants from both categories [a selective serotonin reuptake inhibitor (SSRI) and duloxetine], a trial of aripiprazole tablets that did not yield adequate response, and a patient-specific, clinically significant reason why the member cannot use olanzapine and fluoxetine as individual components. Tier structure rules apply.

Utilization of Atypical Antipsychotic Medications: Calendar Year 2017

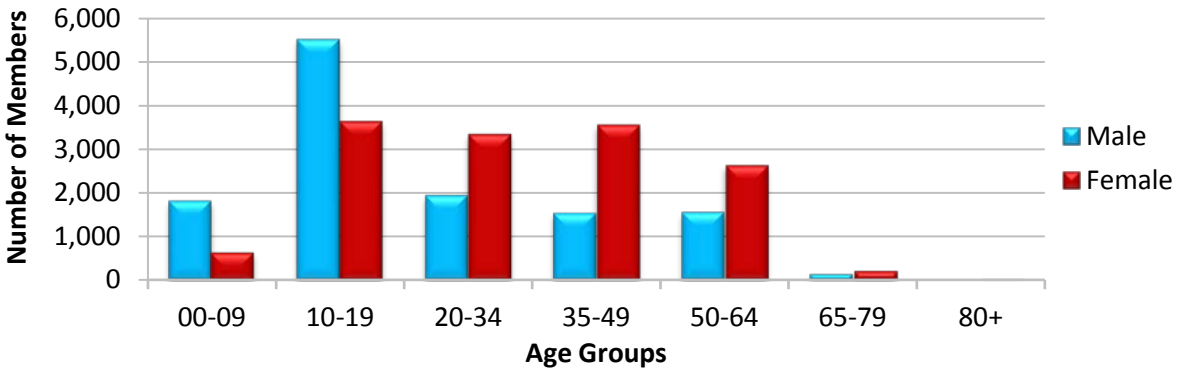
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2016	25,380	181,463	$42,763,898.54	$235.66	$7.69	7,448,494	5,557,944
2017	26,591	187,758	$37,748,516.50	$201.05	$6.50	7,604,673	5,810,013
% Change	**4.80%**	**3.50%**	**-11.70%**	**-14.70%**	**-15.50%**	**2.10%**	**4.50%**
Change	**1,211**	**6,295**	**-$5,015,382.04**	**-$34.61**	**-$1.19**	**156,179**	**252,069**

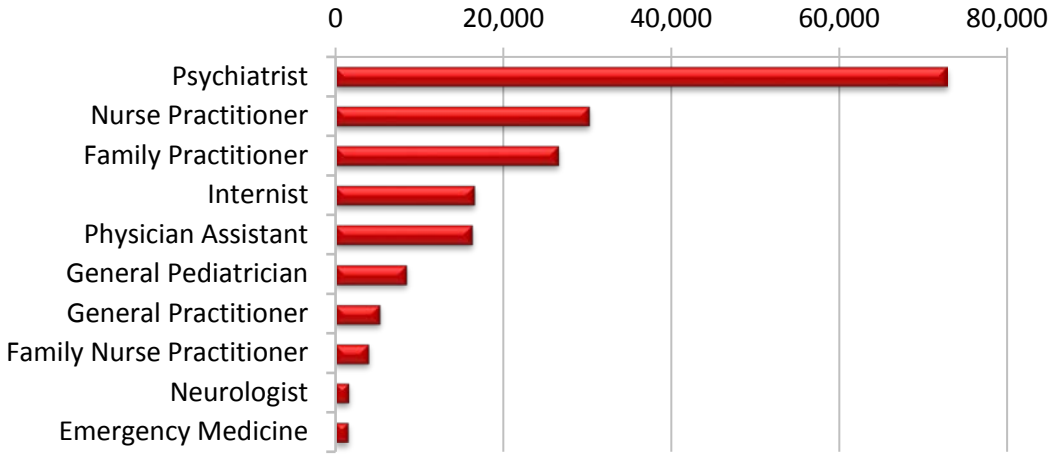
*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.

- Aggregate drug rebates collected during calendar year 2017 for atypical antipsychotics: $18,838,626.32[Δ]
- Please note, due to new federal regulations, a new pricing methodology for pharmacy claims reimbursement was implemented by SoonerCare on January 3, 2017. Ingredient reimbursement changed from an estimated acquisition cost (EAC) to an actual acquisition cost (AAC). In addition, the professional dispensing fee increased from $3.60 in 2016 to $10.55 effective January 2017; professional dispensing fees are included in the reimbursement totals in the following report. The impact of the pricing methodology and dispensing fee change are estimated to be budget neutral. This change in reimbursement should be considered when evaluating reimbursement changes from year to year. Medications with a very low cost per claim and large volume of claims will appear to increase in price due to the increase in dispensing fee; however, these increases will be neutralized by changes in ingredient reimbursement for higher cost medications.

Demographics of Members Utilizing Atypical Antipsychotic Medications



Top Prescriber Specialties of Atypical Antipsychotic Medications by Number of Claims

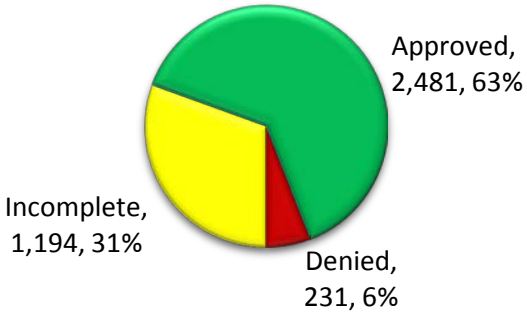


[Δ] Important considerations: Aggregate drug rebates are based on the date the claim is paid rather than the date dispensed. Claims data are based on the date dispensed.

Prior Authorization of Atypical Antipsychotic Medications

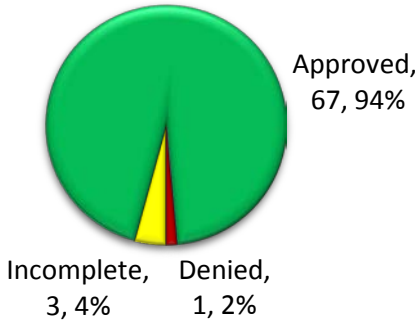
There were 3,906 prior authorization requests submitted for atypical antipsychotic medications during calendar year 2017. Computer edits are in place to detect lower tiered medications in a member's recent claims history and generate automated prior authorizations where possible. The following chart shows the status of the submitted petitions for calendar year 2017.

Status of Petitions



There were 71 prior authorization requests submitted for a total of 61 unique members for atypical antipsychotic medications during calendar year 2017 that were referred for a psychiatric consultation. Most requests were for children between 3 and 4 years of age. The following chart shows the status of the submitted petitions.

Status of Psychiatric Consultations



Medicaid Drug Rebate Program[1,2,3]

Medicaid coverage of a drug requires the manufacturer to have a federal rebate agreement with the Secretary of Health and Human Services (HHS). Participation in the federal drug rebate program requires Medicaid coverage with limited exceptions (e.g., cosmetic medications, fertility medications). Rebate amounts are based on the "best price" for each drug. Best price refers to the lowest price paid to a manufacturer for a drug by any commercial payer. Best prices are reported to CMS by the manufacturer, but are not publicly available.

If a drug's price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices. As average wholesale price (AWP) increases, the rebated amount per unit (RAPU) increases as well, resulting in minimal effect on Medicaid net cost. Until 2017, the CPI penalty

only applied to brand medications; following a Senate vote in October 2015, the Medicaid CPI penalty was extended to generic drugs with an effective date of January 1, 2017.

Additionally, many states have negotiated supplemental rebate agreements with manufacturers to produce added rebates. The Atypical Antipsychotic Medications Product Based Prior Authorization (PBPA) category is heavily influenced by supplemental rebates. In calendar year 2017, the Oklahoma Health Care Authority (OHCA) collected $18,838,626.32 in aggregate drug rebates for atypical antipsychotic medications. These rebates are collected after reimbursement for the medication and are not reflected in this report. The costs included in this report do not reflect net costs.

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

Anticipated Patent Expiration(s):

- Saphris® (asenapine sublingual tablets): October 2026
- Rexulti® (brexpiprazole tablets): February 2027
- Vraylar® (cariprazine capsules): December 2028
- Invega® Sustenna® [paliperidone extended release (ER) injection]: January 2031
- Latuda® (lurasidone tablets): November 2031
- Fanapt® (iloperidone tablets): December 2031
- Aristada® (aripiprazole lauroxil injection): March 2035

News:

- **November 2017:** Investigators at the University of Buenos Aires in Argentina found that older adult patients taking second-generation antipsychotics who experienced an intermediate or high level of metabolic changes had an almost threefold increased risk of experiencing a cardiovascular (CV) event, especially stroke, compared to those on medications that were associated with a lower risk for metabolic changes.
- **January 2018:** The U.S. Food and Drug Administration (FDA) approved the inclusion of Phase 3 study data from the randomized Paliperidone Research in Demonstrating Effectiveness (PRIDE) trial in the product label of Invega® Sustenna® (paliperidone ER injection). The trial included patients not typically included in clinical research consisting of 444 adult patients with schizophrenia that had been taken into custody and jailed at least once in the previous two years. The results showed that for those who received the study drug, the time to relapse was significantly delayed, as well as time to psychiatric hospitalization or repeated arrest and/or incarceration compared to a group of patients who received one of seven commonly prescribed oral antipsychotic medications.

New FDA Approval(s):

- **July 2017:** The FDA approved Abilify Maintena® (aripiprazole ER injection) for the maintenance monotherapy treatment of bipolar I disorder in adults. This indication is in addition to the 2013 original approval for the treatment of adults with schizophrenia.
- **November 2017:** The FDA approved Vraylar® (cariprazine) for the maintenance treatment of schizophrenia. Vraylar® was previously approved for use in adults for the

acute treatment of schizophrenia and the acute treatment of manic or mixed episodes of bipolar I disorder.

- **November 2017:** The FDA approved Abilify Mycite® (aripiprazole tablets and sensor), the first drug in the United States with a digital ingestion tracking system. Abilify Mycite® contains an ingestible sensor embedded in the tablet, that once in contact with stomach fluid, communicates to a wearable sensor known as the Mycite® Patch. The patch transmits the date and time of tablet ingestion via Bluetooth to the Mycite® APP, a smartphone application. Abilify Mycite® is FDA approved for the treatment of schizophrenia, the acute treatment of manic and mixed episodes associated with bipolar I disorder, and for use as an add-on treatment for depression in adults. The use of Abilify Mycite® to track drug ingestion in "real-time" or during an emergency is not recommended because detection may be delayed or not occur. Abilify Mycite® is not yet available on the market and will be reviewed with the Drug Utilization Review (DUR) Board once cost and launch information become available.
- **May 2018:** The FDA approved a supplemental New Drug Application (sNDA) for Latuda® (lurasidone) for the treatment of major depressive episodes associated with bipolar I disorder (bipolar depression) in children and adolescents 10 to 17 years of age. This is in addition to Latuda's® FDA approved indications for the treatment of adults with bipolar depression as monotherapy and as adjunctive therapy with lithium or valproate, and for the treatment of schizophrenia in adults and children 13 to 17 years of age.

Pipeline:

- **November 2016:** ACADIA Pharmaceuticals announced the initiation of ENHANCE-1, a six-week, randomized, double blind, placebo-controlled, multicenter, outpatient Phase 3 study to evaluate Nuplazid® (pimavanserin) for adjunctive treatment of schizophrenia in patients with an inadequate response to current antipsychotic therapy. The study is currently recruiting as of April 2018. Nuplazid® is currently approved for the treatment of Parkinson's disease psychosis.
- **April 2017:** Braeburn Pharmaceuticals announced that a 6-month study of the safety, tolerability, and pharmacokinetics of transferring patients diagnosed with schizoaffective disorder or schizophrenia and stabilized on oral risperidone to BB0817 (risperidone 6-month implant) met its primary endpoint. The enrolled patients received three risperidone implants just under the skin in their upper arm. The study met its objectives and demonstrated that plasma concentrations of oral risperidone and 9-hydroxy-risperidone were comparable to the plasma levels of BB0817 and remained consistent throughout the 6-month study. During the 6-month study, 100% of patients remained stable with no clinically meaningful change in Positive and Negative Symptom Scale (PANSS) scores from baseline. The systemic adverse events were similar to those of oral risperidone and included akathisia (9%), extrapyramidal symptoms (6%), and anxiety (6%). Implant site pain was the most common adverse event related to the procedure (11%), and was generally mild in intensity. A total of 94% of patients chose to enroll in an extension phase of the study to receive a second set of implants.
- **June 2017:** Alkermes announced positive preliminary topline results from ENLIGHTEN-1, the first of two Phase 3 antipsychotic efficacy studies of ALKS 3831 (olanzapine/

samidorphan) for the treatment of schizophrenia. The oral antipsychotic candidate combines olanzapine with an opioid antagonist, samidorphan, which is designed to alleviate some of olanzapine's metabolic side effects including weight gain. ENLIGHTEN-1 was a four-week, hospital-based study that compared ALKS 3831 to placebo and olanzapine in patients with acute schizophrenia. ALKS 3831 demonstrated statistically significant reductions from baseline in PANSS scores compared to placebo ($P<0.001$). The most common adverse events for both the ALKS 3831 and olanzapine treatment groups were weight gain, somnolence, and dry mouth. ENLIGHTEN-2, a six-month Phase 3 study evaluating the weight gain profile of olanzapine compared to ALKS 3831, is ongoing with data expected in the fourth quarter of 2018.

- **December 2017:** Allergan and Gedeon Richter announced positive topline results from their Phase 3 study of Vraylar® (cariprazine) for the treatment of bipolar I depression. Participants in both the 1.5mg and 3mg cariprazine dose groups showed a significantly greater improvement compared to placebo in change from baseline to week 6 on Montgomery-Asberg Depression Rating Scale (MADRS) total score. Vraylar® (cariprazine) is currently FDA approved for the treatment of schizophrenia and for the treatment of acute manic or mixed episodes associated with bipolar I disorder. The companies plan to submit an sNDA to the FDA for the treatment of bipolar depression in the second half of 2018.
- **December 2017:** Indivior announced that the FDA has accepted an NDA for RBP-7000, an investigational, once-monthly injectable risperidone in the Atrigel® delivery system for the treatment of schizophrenia. The NDA, which was submitted on September 28, 2017, is based on data from a pivotal Phase 3 study assessing clinical efficacy and safety, and from the long-term safety study of RBP-7000. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of July 28, 2018.
- **January 2018:** Hisamitsu Pharmaceutical Co., Ltd. and Noven Pharmaceuticals, Inc. announced that the investigational transdermal patch for treatment of schizophrenia known as HP-3070 (asenapine transdermal) achieved the primary endpoint in a Phase 3 clinical trial. The study results showed that when compared to placebo the investigational product achieved statistically significant improvement from baseline in the change of the total PANSS score at week six. Based on these study results, Hisamitsu Pharmaceutical will schedule a pre-NDA meeting with the FDA and expects to submit the NDA for the investigational product in 2018.
- **May 2018:** NeuroRX was awarded a Special Protocol Agreement (SPA) letter and received Fast Track designation from the FDA in September 2017 for NRX-101, an investigational, oral, fixed-dose combination of cycloserine and lurasidone being developed as the first drug regimen to treat severe bipolar depression in patients with acute suicidal ideation and behavior (ASIB). A Phase 2b/3 clinical trial is planned to begin in the third quarter of 2018.

Recommendations

The College of Pharmacy does not recommend any changes to the Atypical Antipsychotic Medication Product Based Prior Authorization (PBPA) criteria or tier chart at this time.

Utilization Details of Atypical Antipsychotic Medications: Calendar Year 2017

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
TIER-1 PRODUCTS						
ARIPIPRAZOLE INJECTABLE PRODUCTS						
ABILIFY MAIN INJ 400MG	767	136	$1,426,628.06	$65.79	$1,860.01	3.78%
ABILIFY MAIN INJ 400MG	436	100	$799,568.56	$63.36	$1,833.87	2.12%
ABILIFY MAIN INJ 300MG	119	23	$165,719.48	$48.23	$1,392.60	0.44%
ABILIFY MAIN INJ 300MG	57	17	$79,177.39	$49.06	$1,389.08	0.21%
SUBTOTAL	**1,379**	**276**	**$2,471,093.49**	**$62.79**	**$1,791.95**	**6.55%**
ARIPIPRAZOLE LAUROXIL INJECTABLE PRODUCTS						
ARISTADA INJ 882MG/3.2ML	169	50	$364,362.63	$74.70	$2,155.99	0.97%
ARISTADA INJ 662MG/2.4ML	86	19	$129,729.32	$52.23	$1,508.48	0.34%
ARISTADA INJ 441MG/1.6ML	27	7	$29,397.12	$37.21	$1,088.78	0.08%
ARISTADA INJ 1064MG/3.9ML	1	1	$2,757.65	$45.96	$2,757.65	0.01%
SUBTOTAL	**283**	**77**	**$526,246.72**	**$64.08**	**$1,859.53**	**1.40%**
ARIPIPRAZOLE ORAL PRODUCTS						
ARIPIPRAZOLE TAB 5MG	9,783	3,290	$402,256.24	$1.33	$41.12	1.07%
ARIPIPRAZOLE TAB 10MG	8,244	2,573	$357,336.42	$1.37	$43.35	0.95%
ARIPIPRAZOLE TAB 15MG	5,138	1,443	$222,200.89	$1.36	$43.25	0.59%
ARIPIPRAZOLE TAB 20MG	3,487	882	$192,166.57	$1.73	$55.11	0.51%
ARIPIPRAZOLE TAB 2MG	3,125	1,161	$132,863.40	$1.37	$42.52	0.35%
ARIPIPRAZOLE TAB 30MG	2,040	422	$117,073.67	$1.72	$57.39	0.31%
ARIPIPRAZOLE SOL 1MG/ML	108	23	$84,248.66	$24.63	$780.08	0.22%
ABILIFY TAB 5MG	16	3	$18,998.40	$28.79	$1,187.40	0.05%
ABILIFY TAB 10MG	13	3	$11,299.40	$28.97	$869.18	0.03%
ABILIFY TAB 15MG	6	1	$5,220.06	$29.00	$870.01	0.01%
ABILIFY TAB 20MG	4	1	$14,586.54	$40.52	$3,646.64	0.04%
ARIPIPRAZOLE TAB 10MG ODT	2	2	$2,318.72	$38.65	$1,159.36	0.01%
SUBTOTAL	**31,966**	**9,804**	**$1,560,568.97**	**$1.55**	**$48.82**	**4.14%**
CLOZAPINE PRODUCTS						
CLOZAPINE TAB 100MG	5,460	448	$357,693.33	$3.04	$65.51	0.95%
CLOZAPINE TAB 200MG	1,866	167	$157,643.20	$4.23	$84.48	0.42%
CLOZAPINE TAB 50MG	1,506	144	$67,488.73	$2.27	$44.81	0.18%
CLOZAPINE TAB 25MG	1,080	111	$30,356.50	$1.49	$28.11	0.08%
CLOZARIL TAB 100MG	43	4	$68,548.94	$54.19	$1,594.16	0.18%
SUBTOTAL	**9,955**	**874**	**$681,730.70**	**$3.30**	**$68.48**	**1.81%**
OLANZAPINE PRODUCTS						
OLANZAPINE TAB 20MG	6,020	1,154	$118,152.79	$0.61	$19.63	0.31%
OLANZAPINE TAB 10MG	5,989	1,643	$87,733.98	$0.47	$14.65	0.23%
OLANZAPINE TAB 5MG	3,679	1,197	$51,768.65	$0.45	$14.07	0.14%
OLANZAPINE TAB 15MG	2,959	701	$54,829.23	$0.59	$18.53	0.15%
OLANZAPINE TAB 2.5MG	1,081	359	$15,228.63	$0.46	$14.09	0.04%
OLANZAPINE TAB 7.5MG	583	170	$8,784.35	$0.50	$15.07	0.02%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
OLANZAPINE TAB 20MG	427	108	$40,533.31	$2.34	$94.93	0.11%
OLANZAPINE TAB 10MG	425	129	$22,342.90	$1.56	$52.57	0.06%
OLANZAPINE TAB 5MG	224	90	$9,527.01	$1.48	$42.53	0.03%
OLANZAPINE TAB 15MG	209	52	$15,487.12	$2.08	$74.10	0.04%
ZYPREXA TAB 20MG	22	2	$23,608.14	$35.77	$1,073.10	0.06%
ZYPREXA TAB 5MG	22	2	$8,483.56	$12.10	$385.62	0.02%
ZYPREXA TAB 15MG	11	1	$8,093.50	$24.53	$735.77	0.02%
ZYPREXA TAB 10MG	9	1	$5,941.90	$18.01	$660.21	0.02%
OLANZAPINE INJ 10MG	2	2	$219.30	$36.55	$109.65	0.00%
SUBTOTAL	**21,662**	**5,611**	**$470,734.37**	**$0.68**	**$21.73**	**1.25%**
PALIPERIDONE INJECTABLE PRODUCTS						
INVEGA SUST INJ 234MG	3,429	648	$7,725,160.91	$78.90	$2,252.89	20.46%
INVEGA SUST INJ 156MG	1,451	400	$2,188,261.54	$52.76	$1,508.11	5.80%
INVEGA TRINZ INJ 819MG	537	195	$3,597,818.17	$77.10	$6,699.85	9.53%
INVEGA SUST INJ 117MG	328	84	$370,088.29	$39.66	$1,128.32	0.98%
INVEGA TRINZ INJ 546MG	232	86	$1,037,739.72	$51.08	$4,473.02	2.75%
INVEGA TRINZ INJ 410MG	92	32	$323,815.86	$40.70	$3,519.74	0.86%
INVEGA SUST INJ 78MG	51	9	$38,325.22	$25.98	$751.47	0.10%
INVEGA TRINZ INJ 273MG	14	7	$33,046.04	$26.87	$2,360.43	0.09%
INVEGA SUST INJ 39MG	4	2	$1,545.31	$13.32	$386.33	0.00%
SUBTOTAL	**6,138**	**1,463**	**$15,315,801.06**	**$67.63**	**$36.90**	**40.57%**
QUETIAPINE PRODUCTS						
QUETIAPINE TAB 100MG	11,492	3,169	$161,734.64	$0.45	$14.07	0.43%
QUETIAPINE TAB 50MG	8,795	2,673	$120,581.68	$0.44	$13.71	0.32%
QUETIAPINE TAB 200MG	8,119	2,046	$139,508.07	$0.54	$17.18	0.37%
QUETIAPINE TAB 300MG	7,383	1,593	$148,595.54	$0.63	$20.13	0.39%
QUETIAPINE TAB 400MG	5,905	1,135	$113,807.89	$0.60	$19.27	0.30%
QUETIAPINE TAB 25MG	5,042	1,590	$65,935.77	$0.42	$13.08	0.17%
QUETIAPINE TAB 400MG ER	648	137	$267,156.44	$12.04	$412.28	0.71%
QUETIAPINE TAB 300MG ER	636	153	$203,976.82	$9.90	$320.72	0.54%
QUETIAPINE TAB 50MG ER	307	120	$34,749.60	$3.45	$113.19	0.09%
QUETIAPINE TAB 150MG ER	269	115	$50,357.55	$5.63	$187.20	0.13%
QUETIAPINE TAB 200MG ER	216	68	$47,643.82	$6.45	$220.57	0.13%
SEROQUEL XR TAB 300MG	118	39	$103,132.54	$28.16	$874.00	0.27%
SEROQUEL XR TAB 400MG	87	34	$86,222.33	$30.17	$991.06	0.23%
SEROQUEL XR TAB 200MG	46	13	$21,609.82	$15.91	$469.78	0.06%
SEROQUEL XR TAB 150MG	45	15	$22,735.12	$15.14	$505.22	0.06%
SEROQUEL XR TAB 50MG	24	10	$9,955.29	$11.06	$414.80	0.03%
SEROQUEL TAB 400MG	12	1	$13,553.16	$37.65	$1,129.43	0.04%
SEROQUEL TAB 300MG	8	1	$11,534.40	$48.06	$1,441.80	0.03%
SUBTOTAL	**49,152**	**12,912**	**$1,622,790.48**	**$1.04**	**$33.02**	**4.30%**
RISPERIDONE INJECTABLE PRODUCTS						
RISPERDAL INJ 50MG	356	45	$558,985.71	$57.62	$1,570.18	1.48%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
RISPERDAL INJ 25MG	180	35	$106,709.74	$28.32	$592.83	0.28%
RISPERDAL INJ 37.5MG	118	21	$138,418.85	$43.15	$1,173.04	0.37%
RISPERDAL INJ 12.5MG	38	6	$15,311.54	$14.69	$402.94	0.04%
SUBTOTAL	**692**	**107**	**$819,425.84**	**$46.24**	**$1,184.14**	**2.17%**
RISPERIDONE ORAL PRODUCTS						
RISPERIDONE TAB 1MG	13,157	3,000	$168,540.63	$0.42	$12.81	0.45%
RISPERIDONE TAB 0.5MG	11,010	2,699	$141,237.00	$0.42	$12.83	0.37%
RISPERIDONE TAB 2MG	7,345	1,557	$96,586.92	$0.42	$13.15	0.26%
RISPERIDONE TAB 0.25MG	5,825	1,444	$75,404.47	$0.42	$12.94	0.20%
RISPERIDONE TAB 3MG	3,554	680	$46,259.28	$0.42	$13.02	0.12%
RISPERIDONE TAB 4MG	1,978	344	$28,704.81	$0.45	$14.51	0.08%
RISPERIDONE SOL 1MG/ML	892	167	$34,474.66	$1.17	$38.65	0.09%
RISPERIDONE TAB 0.5MG	268	69	$13,501.67	$1.77	$50.38	0.04%
RISPERIDONE TAB 1MG ODT	144	50	$9,658.27	$2.28	$67.07	0.03%
RISPERIDONE TAB 2MG ODT	143	31	$12,371.32	$2.65	$86.51	0.03%
RISPERIDONE TAB 0.25 ODT	45	12	$7,966.56	$6.05	$177.03	0.02%
RISPERIDONE TAB 3MG ODT	36	14	$5,828.20	$6.10	$161.89	0.02%
RISPERDAL SOL 1MG/ML	15	2	$14,278.09	$31.73	$951.87	0.04%
RISPERIDONE TAB 4MG ODT	13	6	$2,606.72	$5.26	$200.52	0.01%
RISPERDAL TAB 2MG	13	1	$11,484.20	$29.45	$883.40	0.03%
RISPERDAL TAB 3MG	12	1	$12,561.84	$34.89	$1,046.82	0.03%
RISPERDAL TAB 4MG	3	1	$5,324.49	$59.16	$1,774.83	0.01%
SUBTOTAL	**44,453**	**10,078**	**$686,789.13**	**$0.50**	**$15.45**	**1.83%**
ZIPRASIDONE PRODUCTS						
ZIPRASIDONE CAP 40MG	2,635	726	$95,955.82	$1.19	$36.42	0.25%
ZIPRASIDONE CAP 80MG	2,587	442	$118,286.92	$1.48	$45.72	0.31%
ZIPRASIDONE CAP 20MG	2,060	706	$80,540.50	$1.29	$39.10	0.21%
ZIPRASIDONE CAP 60MG	1,809	409	$78,608.89	$1.42	$43.45	0.21%
GEODON INJ 20MG	4	4	$672.23	$51.71	$168.06	0.00%
GEODON CAP 20MG	1	1	$337.61	$24.12	$337.61	0.00%
GEODON CAP 80MG	1	1	$563.73	$18.79	$563.73	0.00%
SUBTOTAL	**9,097**	**2,289**	**$374,965.70**	**$1.34**	**$41.22**	**0.98%**
TIER-1 SUBTOTAL	**174,777**	**43,491**	**$24,530,146.46**	**$4.54**	**$140.35**	**65.00%**
TIER-2 PRODUCTS						
LURASIDONE PRODUCTS						
LATUDA TAB 40MG	2,353	729	$2,624,168.96	$35.45	$1,115.24	6.95%
LATUDA TAB 80MG	1,649	399	$2,063,970.97	$39.38	$1,251.65	5.47%
LATUDA TAB 20MG	1,294	442	$1,349,026.04	$33.90	$1,042.52	3.57%
LATUDA TAB 60MG	1,130	334	$1,228,375.98	$34.60	$1,087.06	3.25%
LATUDA TAB 120MG	840	197	$1,462,553.91	$52.28	$1,741.14	3.87%
SUBTOTAL	**7,266**	**2,101**	**$8,728,095.86**	**$38.00**	**$1,201.22**	**23.11%**
ASENAPINE PRODUCTS						
SAPHRIS SUB 10MG	650	125	$560,885.21	$27.96	$862.90	1.49%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
SAPHRIS SUB 5MG	361	102	$289,005.81	$25.76	$800.57	0.77%
SAPHRIS SUB 2.5MG	85	24	$53,300.27	$21.80	$627.06	0.14%
SUBTOTAL	**1,096**	**251**	**$903,191.29**	**$26.78**	**$824.08**	**2.40%**
TIER-2 SUBTOTAL	**8,362**	**2,352**	**$9,631,287.15**	**$41.88**	**$1,151.79**	**25.51%**
TIER-3 PRODUCTS						
BREXPIPRAZOLE PRODUCTS						
REXULTI TAB 2MG	139	46	$145,926.12	$31.88	$1,049.83	0.39%
REXULTI TAB 1MG	71	25	$67,423.74	$32.43	$949.63	0.18%
REXULTI TAB 4MG	68	20	$75,294.84	$31.37	$1,107.28	0.20%
REXULTI TAB 3MG	43	17	$42,283.09	$30.84	$983.33	0.11%
REXULTI TAB 0.5MG	21	8	$20,238.62	$32.12	$963.74	0.05%
REXULTI TAB 0.25MG	6	1	$5,946.86	$33.04	$991.14	0.02%
SUBTOTAL	**348**	**117**	**$357,113.27**	**$31.78**	**$1,026.19**	**0.95%**
CARIPRAZINE PRODUCTS						
VRAYLAR CAP 3MG	167	53	$178,845.97	$34.62	$1,070.93	0.47%
VRAYLAR CAP 6MG	76	21	$80,519.59	$34.13	$1,059.47	0.21%
VRAYLAR CAP 1.5MG	55	24	$60,833.24	$34.37	$1,106.06	0.16%
VRAYLAR CAP 4.5MG	54	14	$56,945.35	$34.26	$1,054.54	0.15%
SUBTOTAL	**352**	**112**	**$377,144.15**	**$34.42**	**$1,071.43**	**0.99%**
CLOZAPINE ORALLY DISINTEGRATING PRODUCTS						
CLOZAPINE TAB 100MG ODT	225	23	$138,720.28	$21.50	$616.53	0.37%
CLOZAPINE TAB 150MG ODT	70	10	$74,556.42	$36.85	$1,065.09	0.20%
FAZACLO TAB 100MG ODT	62	6	$88,026.39	$52.90	$1,419.78	0.23%
CLOZAPINE TAB 25MG ODT	46	6	$8,504.46	$6.73	$184.88	0.02%
CLOZAPINE TAB 200MG ODT	44	11	$57,426.55	$47.54	$1,305.15	0.15%
FAZACLO TAB 200MG ODT	22	4	$32,144.67	$53.40	$1,461.12	0.09%
FAZACLO TAB 25MG ODT	19	2	$11,800.64	$20.70	$621.09	0.03%
FAZACLO TAB 150MG ODT	13	2	$24,919.08	$63.90	$1,916.85	0.07%
SUBTOTAL	**501**	**64**	**$436,098.49**	**$30.77**	**$870.46**	**1.16%**
ILOPERIDONE PRODUCTS						
FANAPT TAB 12MG	194	27	$321,632.27	$56.60	$1,657.90	0.85%
FANAPT TAB 6MG	170	33	$175,133.89	$35.48	$1,030.20	0.46%
FANAPT TAB 8MG	155	22	$138,828.52	$32.85	$895.67	0.37%
FANAPT TAB 4MG	127	22	$97,826.50	$25.87	$770.29	0.26%
FANAPT TAB 10MG	85	13	$145,945.30	$58.03	$1,717.00	0.39%
FANAPT TAB 2MG	45	12	$35,440.29	$28.02	$787.56	0.09%
FANAPT TAB 1MG	3	3	$1,748.18	$19.87	$582.73	0.00%
FANAPT TITRATION PAK	1	1	$143.88	$35.97	$143.88	0.00%
SUBTOTAL	**780**	**133**	**$916,698.83**	**$40.74**	**$1,175.25**	**2.42%**
OLANZAPINE/FLUOXETINE COMBINATION PRODUCTS						
OLANZA/FLUOX CAP 12-50MG	24	3	$15,582.64	$18.55	$649.28	0.04%
OLANZA/FLUOX CAP 3-25MG	18	2	$3,097.60	$5.74	$172.09	0.01%
OLANZA/FLUOX CAP 12-25MG	9	2	$5,003.57	$15.16	$555.95	0.01%

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
OLANZA/FLUOX CAP 6-25MG	8	2	$3,026.18	$8.41	$378.27	0.01%
OLANZA/FLUOX CAP 6-50MG	6	1	$1,822.54	$10.13	$303.76	0.00%
SUBTOTAL	**65**	**10**	**$28,532.53**	**$12.68**	**$438.96**	**0.07%**
PALIPERIDONE ORAL PRODUCTS						
PALIPERIDONE TAB ER 6MG	1,232	262	$691,687.38	$18.46	$561.43	1.83%
PALIPERIDONE TAB ER 9MG	651	120	$466,022.07	$21.50	$715.86	1.23%
PALIPERIDONE TAB ER 3MG	605	151	$273,871.98	$14.15	$452.68	0.73%
PALIPERIDONE TAB ER 1.5MG	82	23	$37,015.67	$14.80	$451.41	0.10%
INVEGA TAB 3MG	2	2	$1,990.10	$33.17	$995.05	0.01%
INVEGA TAB 6MG	1	1	$908.42	$30.28	$908.42	0.00%
SUBTOTAL	**2,573**	**559**	**$1,471,495.62**	**$18.15**	**$571.90**	**3.90%**
TIER-3 SUBTOTAL	**4,619**	**995**	**$3,587,082.89**	**$25.23**	**$776.59**	**9.49%**
TOTAL	**187,758**	**26,591***	**$37,748,516.50**	**$6.50**	**$201.05**	**100%**

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

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Appendix P

Industry News and Updates

Oklahoma Health Care Authority
June 2018

Introduction

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

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

News:

- **Sodium-Glucose Cotransporter-2 (SGLT-2) Inhibitors:** According to a large meta-analysis of clinical trials that compared the newer classes of diabetes medications head-to-head in terms of mortality, cardiovascular, and safety endpoints, SGLT-2 inhibitors came out on top. Dipeptidyl peptidase-4 (DPP-4) inhibitors did the worst in the analysis and glucagon-like peptide-1 (GLP-1) agonists were in the middle. Compared with control groups, SGLT-2 inhibitors were associated with reduced all-cause mortality [hazard ratio (HR) 0.80, 95% confidence interval (CI) 0.71 to 0.89], as were GLP-1 agonists (HR 0.88, 95% CI 0.81 to 0.94); however, DPP-4 inhibitors were not associated with reduced all-cause mortality (HR 1.02, 95% CI 0.94 to 1.11). Additionally, compared with DPP-4 inhibitors, SGLT-2 inhibitors and GLP-1 agonists were associated with reduced all-cause mortality (SGLT-2 inhibitors: HR 0.78, 95% CI 0.68 to 0.90; GLP-1 agonists: HR 0.86, 95% CI 0.77 to 0.96). There was no statistically significant difference between SGLT-2 inhibitors and GLP-1 agonists when they were compared to each other. The systematic review and meta-analysis included 236 clinical trials with more than 176,000 patients. The randomized clinical trials included patients with type 2 diabetes and compared GLP-1 agonists, DPP-4 inhibitors, and SGLT-2 inhibitors to each other, placebo, or no treatment. Cardiovascular outcomes trials, such as OUTCOME, LEADER, and TECOS, were also included. The study only analyzed outcomes by drug class and not by individual medications within each class. Dr. Robert Eckel, MD, of the University of Colorado Denver, who was not involved in the study, noted that the contribution of glycemic lowering was not assessed in the meta-analysis and only a small number of trials directly compared outcomes between diabetes drugs. “Nevertheless, if the price of the three classes of agents were identical, the SGLT-2 inhibitors should be the next choice beyond metformin for most patients, and perhaps considered as the drug of choice (but metformin is cheap),” said Dr. Eckel.
- **Male Contraceptive:** A new study published in the journal *PLOS ONE* in April 2018 shows that in a preclinical trial, a new form of male contraceptive can immobilize sperm temporarily without side effects. The compound, EP055, binds to sperm to significantly slow the overall mobility without affecting hormones. There are hormonal drugs in clinical trials, which target the production of sperm; however, these usually affect the

natural hormones in men. Male rhesus macaques, a type of monkey, were given a high-dose intravenous infusion during the study. Researchers found no indication of normal sperm motility thirty hours after the dose and no physical side effects were observed. According to the study's co-investigator Mary Zelinski, "At 18 days post-infusion, all macaques showed signs of complete recovery, suggesting that the EP055 compound is indeed reversible." Further work is needed before the compound will become available for human use, but the research team has started to test a pill form and will eventually conduct a mating trial to determine its effectiveness against pregnancy.

- **Unit-Dose Packaging:** When compared to other opioid analgesics, buprenorphine accounts for the most opioid-related pediatric hospitalizations. Since 2010, several manufacturers of buprenorphine began distributing their products in unit-dose packaging. An observational surveillance study evaluated the impact of unit-dose packaging on unintentional pediatric buprenorphine-naloxone poison center exposures. The Researched Abuse, Diversion, and Addiction-Related Surveillance System Poison Center Program was used in the study and the main outcome was the number of unintentional ingestions of buprenorphine-naloxone products involving children younger than 6 years of age. The study was split into three periods: pre-unit-dose packaging (first quarter 2008 through fourth quarter 2010), transition to unit-dose packaging (first quarter 2011 through fourth quarter 2012), and post-unit-dose packaging (first quarter 2013 through fourth quarter 2016). There were 6,217 total exposures to combination buprenorphine-naloxone products. In the pre-unit-dose packaging period, there were 20.57 pediatric unintentional exposures per 100,000 prescriptions; in the transition period to unit-dose-packaging, there were 8.77 pediatric unintentional exposures per 100,000 prescriptions; and in the post-unit-dose packaging period, there were 4.36 pediatric unintentional exposures per 100,000 prescriptions. This represents a 78.8% (95% CI: 76.1% to 81.3%; $P<0.001$) relative decrease from the pre-unit-dose packaging period. The shift from non-unit-dose packaging to unit-dose packaging in over 80% of buprenorphine-naloxone products was associated with a significant decrease in unintentional pediatric exposures reported to poison centers.
- **Gabapentin:** According to the prescription tracker GoodRx, gabapentin is one of the most prescribed medications in the United States. According to the U.S. Food and Drug Administration (FDA) Commissioner, Scott Gottlieb, the FDA is now studying patterns of prescribing and illicit use of gabapentin. Rachel Vickers Smith of the University of Louisville stated that many doctors are not aware of gabapentin's potential for abuse, particularly among those with a history of misusing drugs. Medical journal articles estimate between 15 and 25% of opioid abusers also use gabapentin. Emerging research suggests that the combination of gabapentin and opioids heightens the overdose risk. According to poison center data analyzed by RADARS research group within the Denver Health and Hospital Authority, the abuse rate increased nearly 400% between 2006 and 2015. Last year, Kentucky became the first state to classify the drug as a "scheduled substance". In 2016, gabapentin was detected in a third of fatal overdose cases analyzed by Kentucky medical examiners. Alyssa Peckham, a researcher at Midwestern University in Arizona, believes a more comprehensive federal response is needed. Peckham says gabapentin is not dangerous on its own, but can be dangerous when combined with

opioids and other drugs that suppress breathing. There is little consensus on the next steps or even the scope of the problem. Given recent restrictions on opioids by hospitals, insurers, and government authorities, many physicians are wary of limiting other medications that can help with the treatment of pain. The Centers for Disease Control and Prevention's (CDC) prescribing guidelines endorse gabapentin as a good choice for nerve pain. However, there are questions about how much is prescribed for proven uses and to what extent patients are benefiting from treatment. Historically, the vast majority of prescriptions have been for uses that are not FDA approved. In a recent article in the *Journal of the American Medical Association*, Dr. Joseph Ross, a researcher at Yale University's school of medicine, called for new studies of gabapentin's real-world use.

- **Repurposing Drugs:** Researchers at Broad Institute, a nonprofit biomedical institute, are seeking to acquire samples of every drug ever developed. Researchers plan to see if any of these drugs can be used to treat diseases besides those for which they were intended. Researchers state the Drug Repurposing Hub will be home to the largest collection of drugs ever assembled to find new possible uses. Since many of these medications are already FDA approved, they could get to the market faster as the approval process is shorter when the therapy has already been deemed safe. So far, Broad has acquired approximately 4,700 compounds and nearly 2,000 of those drugs were approved by the FDA or foreign drug regulators. Broad Institute researchers plan to test each compound on a variety of disease cells, including many strains of cancer at once.

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Appendix Q

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

FDA NEWS RELEASE

For Immediate Release: May 21st, 2018

FDA approves new drug for patients with chronic liver disease who have low blood platelets and are undergoing a medical procedure

The U.S. Food and Drug Administration (FDA) approved Doptelet® (avatrombopag) tablets to treat low blood platelet count (thrombocytopenia) in adults with chronic liver disease who are scheduled to undergo a medical or dental procedure. This is the first drug approved by the FDA for this use.

"Patients with chronic liver disease who have low platelet counts and require a procedure are at increased risk of bleeding," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Doptelet® was demonstrated to safely increase the platelet count. This drug may decrease or eliminate the need for platelet transfusions, which are associated with risk of infection and other adverse reactions."

Platelets (thrombocytes) are colorless cells produced in the bone marrow that help form blood clots in the vascular system and prevent bleeding. Thrombocytopenia is a condition in which there is a lower-than-normal number of circulating platelets in the blood. When patients have moderately to severely reduced platelet counts, serious or life-threatening bleeding can occur, especially during invasive procedures. Patients with significant thrombocytopenia typically receive platelet transfusions immediately prior to a procedure to increase the platelet count.

The safety and efficacy of Doptelet® was studied in two trials (ADAPT-1 and ADAPT-2) involving 435 patients with chronic liver disease and severe thrombocytopenia who were scheduled to undergo a procedure that would typically require platelet transfusion. The trials investigated two dose levels of Doptelet® administered orally over five days as compared to placebo (no treatment). The trial results showed that for both dose levels of Doptelet®, a higher proportion of patients had increased platelet counts and did not require platelet transfusion or any rescue therapy on the day of the procedure and up to seven days following the procedure as compared to those treated with placebo.

The most common side effects reported by clinical trial participants who received Doptelet® were fever, stomach (abdominal) pain, nausea, headache, fatigue, and swelling in the hands or feet (edema). People with chronic liver disease and people with certain blood clotting conditions may have an increased risk of developing blood clots when taking Doptelet®.

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

The FDA granted this approval to AkaRx, Inc.

FDA NEWS RELEASE

For Immediate Release: May 24th, 2018

FDA approves a new treatment for PKU, a rare and serious genetic disease

The FDA approved Palynziq™ (pegvaliase-pqpz) for adults with a rare and serious genetic disease known as phenylketonuria (PKU). Patients with PKU are born with an inability to break down phenylalanine (Phe), an amino acid present in protein-containing foods and high-intensity sweeteners used in a variety of foods and beverages. Palynziq™ is a novel enzyme therapy for adult PKU patients who have uncontrolled blood Phe concentrations on current treatment.

"This is a novel enzyme substitution therapy that helps address a significant unmet need in PKU patients who have been unable to control their blood Phe levels with current treatment options," said Julie Beitz, M.D., director of the Office of Drug Evaluation III in FDA's Center for Drug Evaluation and Research. "This new approval demonstrates our commitment to approving advancements in treatment that will give patients living with PKU different options for care."

PKU affects about 1 in 10,000 to 15,000 people in the United States. If untreated, PKU can cause chronic intellectual, neurodevelopmental and psychiatric disabilities. Lifelong restriction of phenylalanine intake through the diet is needed to prevent buildup of Phe in the body, which can cause long-term damage to the central nervous system.
The safety and efficacy of Palynziq™ were studied in two clinical trials in adult patients with PKU with blood phenylalanine concentrations greater than 600µmol/L on existing management. Most PKU patients in the Palynziq™ trials were on an unrestricted diet prior to and during the trials. The first trial was a randomized, open-label trial in patients treated with increasing doses of Palynziq™ administered as a subcutaneous injection up to a target dose of either 20mg once daily or 40 g once daily. The second trial was an 8-week, placebo-controlled, randomized withdrawal trial in patients who were previously treated with Palynziq™. Patients treated with Palynziq™ achieved statistically significant reductions in blood phenylalanine concentrations from their pre-treatment baseline blood Phe concentrations.
The most common adverse events reported in the Palynziq™ trials included injection site reactions, joint pain, hypersensitivity reactions, headache, generalized skin reactions lasting at least 14 days, pruritus (itchy skin), nausea, dizziness, abdominal pain, throat pain, fatigue, vomiting, cough, and diarrhea. Hypersensitivity reactions occurred in most patients, likely due to formation of antibodies to the product.
The most serious adverse reaction in the Palynziq™ trials was anaphylaxis, which occurred most frequently during upward titration of the dose within the first year of treatment. Because of this serious risk, the labeling for Palynziq™ includes a Boxed Warning and the product is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Palynziq™ REMS Program. Notable requirements of the Palynziq™ REMS Program include the following:

- Prescribers must be certified by enrolling in the REMS program and completing training
- Prescribers must prescribe auto-injectable epinephrine with Palynziq™
- Pharmacies must be certified with the program and must dispense only to patients who are authorized to receive Palynziq™

Patients must enroll in the program and be educated about the risk of anaphylaxis by a certified prescriber to ensure they understand the risks and benefits of treatment with Palynziq™
Patients must have auto-injectable epinephrine available at all times while taking Palynziq™
The FDA granted approval of Palynziq™ to BioMarin Pharmaceutical Inc.

Safety Announcements

FDA Alerts Health Care Professionals and Oncology Clinical Investigators about an Efficacy Issue Identified in Clinical Trials for Some Patients Taking Keytruda® (pembrolizumab) or Tecentriq® (atezolizumab) as Monotherapy to Treat Urothelial Cancer with Low Expression of PD-L1

[05/18/2018] The FDA is alerting health care professionals, oncology clinical investigators, and the public about decreased survival associated with the use of Keytruda® (pembrolizumab) or Tecentriq® (atezolizumab) as single therapy (monotherapy) in clinical trials to treat patients with metastatic urothelial cancer who have not received prior therapy and who have low expression of the protein programmed death ligand 1 (PD-L1).
In two ongoing clinical trials (KEYNOTE-361 and IMVIGOR-130), the Data Monitoring Committees' (DMC) early reviews found patients in the monotherapy arms of both trials with PD-L1 low status had decreased survival compared to patients who received cisplatin- or carboplatin-based chemotherapy. There was no change in the adverse event profile of Keytruda® or Tecentriq®. Both Merck, manufacturer of Keytruda®, and Genentech, manufacturer of Tecentriq®, have stopped enrolling patients whose tumors have PD-L1 low status to the Keytruda® or Tecentriq® monotherapy arms per the DMCs' recommendations.
The clinical trials compare platinum-based chemotherapy combined with Keytruda® or Tecentriq® to platinum-based chemotherapy alone. Both trials enrolled a third arm of monotherapy with Keytruda® or Tecentriq® to compare to platinum-based chemotherapy alone. The monotherapy arms remain open only to patients whose tumors have PD-L1 high status. The combination arms and the chemotherapy arms of both studies also remain open. The FDA is reviewing the findings of the ongoing clinical trials and will communicate new information as necessary.
Both Keytruda® and Tecentriq® are currently approved under accelerated approval for the treatment of locally advanced or metastatic urothelial carcinoma patients who are not eligible for cisplatin-containing

chemotherapy, irrespective of PD-L1 status. Patients taking Keytruda® or Tecentriq® for other approved uses should continue to take their medication as directed by their health care professional.
Health care professionals should be aware that the populations enrolled in the ongoing clinical trials were eligible for platinum-containing chemotherapy, and therefore differ from those enrolled in the trials that led to the accelerated approvals of both Keytruda® and Tecentriq® in the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. The FDA recommends providers select patients for the treatment of locally advanced or metastatic urothelial cancer using the criteria described in Section 14 of each label. These criteria supported the approvals for Keytruda® and Tecentriq® for initial monotherapy in cisplatin-ineligible patients. Keytruda® and Tecentriq® are also currently approved by the FDA for the treatment of multiple types of other cancers.
Patients should talk to their doctor if they have questions or concerns about either drug. Health care professionals and patients are encouraged to report any adverse events or side effects related to the use of these products and other similar products to FDA's MedWatch Adverse Event Reporting program.

Safety Announcements

FDA Drug Safety Communication: FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca®, Tivicay®, Triumeq®)

[05/18/2018] The FDA is alerting the public that serious cases of neural tube birth defects involving the brain, spine, and spinal cord have been reported in babies born to women treated with dolutegravir used to treat human immunodeficiency virus (HIV). Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appear to be at higher risk for these defects.
Neural tube defects are birth defects that can occur early in pregnancy when the spinal cord, brain, and related structures do not form properly. To date, in this observational study there are no reported cases of babies born with neural tube defects to women starting dolutegravir later in pregnancy. The FDA is investigating this new safety issue and will update the public when they have more information.
Dolutegravir is an FDA-approved antiretroviral medicine used in combination with other antiretroviral medicines to treat HIV, the virus that can cause acquired immunodeficiency syndrome (AIDS). Dolutegravir works by blocking integrase, an HIV enzyme, to prevent the virus from multiplying and can reduce the amount of HIV in the body. Stopping dolutegravir without first talking to a prescriber can cause the HIV infection to become worse. Approved in 2013, dolutegravir has been on the market for 5 years, and is available as a single ingredient product under the brand name Tivicay® and as a fixed dose combination tablet with other HIV medicines under the brand names Juluca® and Triumeq®.
Patients should not stop taking dolutegravir without first talking to their health care professional because stopping their medicine can cause the HIV infection to worsen. In addition:

- If patients are already pregnant, stopping a dolutegravir-containing regimen without switching to alternative HIV medicines could cause the amount of virus to increase and spread HIV to the baby.
- If patients take a dolutegravir-containing regimen at the time of becoming pregnant and during the first trimester of pregnancy, there is a risk that the baby may develop neural tube defects. Neural tube defects happen early in pregnancy, before many women even know they are pregnant. For this reason, women of childbearing age should talk to their health care professional about other non-dolutegravir-containing antiretroviral medicines.
- Patients should tell their health care professional if they are pregnant or are planning to become pregnant before they start a dolutegravir-containing regimen. Health care professional may discuss other treatment options with patients.
- Women of childbearing age who decide to take a dolutegravir-containing regimen should consistently use effective birth control (contraception) while on HIV treatment. Women should talk to their health care professionals about an effective birth control method to use while taking a dolutegravir-containing regimen.
- Before patients start a dolutegravir-containing regimen they will need a pregnancy test to determine if they are already pregnant.

Health care professionals should inform women of childbearing age about the potential risk of neural tube defects when a dolutegravir-containing regimen is used at the time of conception and early in pregnancy. In addition:

- Health care professionals should weigh the benefits and the risks of dolutegravir when prescribing antiretroviral medicines to women of childbearing age. Alternative antiretroviral medicines should be

considered. The relative risks and benefits of appropriate alternative antiretroviral therapies should be discussed.

- If the decision is made to use dolutegravir in women of childbearing age, health care professionals should reinforce the consistent use of effective birth control.
- Pregnancy testing should be performed before initiating a dolutegravir-containing regimen in women of childbearing age to exclude pregnancy.

Ongoing monitoring will continue as part of the observational study in Botswana. Additional birth outcomes are projected from pregnant women who were exposed to dolutegravir at the time of becoming pregnant. The FDA will conduct a comprehensive review of the results and any other data that becomes available. The FDA will update the public with any new information. To monitor birth outcomes of pregnant women, report pregnancy exposures to the Antiretroviral Pregnancy Registry at 1-800-258-4263.

Safety Announcements

Risk of serious and potentially fatal blood disorder prompts FDA action on oral over-the-counter benzocaine products used for teething and mouth pain and prescription local anesthetics

[05/23/2018] The FDA is warning that over-the-counter (OTC) oral drug products containing benzocaine should not be used to treat infants and children younger than 2 years. The FDA is also warning that benzocaine oral drug products should only be used in adults and children 2 years and older if they contain certain warnings on the drug label. These products carry serious risks and provide little to no benefits for treating oral pain, including sore gums in infants due to teething. Benzocaine, a local anesthetic, can cause a condition in which the amount of oxygen carried through the blood is greatly reduced. This condition, called methemoglobinemia, can be life-threatening and result in death.

Due to the significant safety risk of methemoglobinemia, the FDA has urged manufacturers that they should stop marketing OTC oral drug products for treating teething in infants and children younger than 2 years. If companies do not comply, the FDA will take action to remove these products from the market. The FDA has also urged manufacturers of OTC oral drug products containing benzocaine for adults and children 2 years and older to make the following changes to the labels of their products:

- Adding a warning about methemoglobinemia;
- Adding contraindications, the FDA's strongest warnings, directing parents and caregivers not to use the product for teething, and not to use in infants and children younger than 2 years; and
- Revising the directions to direct parents and caregivers not to use the product in infants and children younger than 2 years.

The FDA will continue to monitor the safety and effectiveness of OTC benzocaine products and intends to take additional actions in the future as needed. The FDA will notify the public about any updates. In addition to the FDA's recent actions regarding OTC benzocaine products, the FDA is also requiring a standardized methemoglobinemia warning to be included in the prescribing information of all prescription local anesthetics.

Parents and caregivers should follow the American Academy of Pediatrics' recommendations for treating teething pain:

- Gently rub or massage the child's gums with one of your fingers.
- Use a firm rubber teething ring.

Topical pain relievers and medications that are rubbed on the gums are not useful because they wash out of a baby's mouth within minutes. The FDA has previously cautioned parents and caregivers to not give certain homeopathic teething tablets to children.

Alternative treatments for adults who experience mouth pain may include dilute salt water mouth rinse and OTC pain relief medications. Adults should follow the American Dental Association's recommendations for mouth sores and spots:

- Schedule regular oral health checkups
- Keep a diary of what you eat and drink
- Keep a list of oral hygiene products you have been using
- Avoid all tobacco products
- If you drink alcoholic beverages, do so in moderation
- See your dentist if you notice any change in your mouth

Consumers using benzocaine products to treat mouth pain should seek medical attention immediately for signs and symptoms of methemoglobinemia. These include pale, gray or blue-colored skin, lips, and nail beds; shortness of breath; fatigue; confusion; headache; lightheadedness; and fast heart rate. Signs and symptoms of methemoglobinemia may appear within minutes to one to two hours after using benzocaine. Symptoms may occur after using benzocaine for the first time, as well as after prior uses.

Health care professionals should warn patients of the possibility of methemoglobinemia and advise them of the signs and symptoms when recommending or prescribing local anesthetic products. Some patients are at greater risk for complications related to methemoglobinemia. This includes those with breathing problems such as asthma, bronchitis, or emphysema; heart disease, and the elderly. Health care professionals using local anesthetics during medical procedures should take steps to minimize the risk for methemoglobinemia. These include monitoring patients for signs and symptoms suggestive of methemoglobinemia; using co-oximetry when possible; and having resuscitation equipment and medications readily available, including methylene blue.

Benzocaine is a local anesthetic contained in some OTC products for the temporary relief of pain due to minor irritation, soreness, or injury of the mouth and throat. Benzocaine products are marketed as gels, sprays, ointments, solutions, and lozenges under brand names such as Anbesol, Orabase, Orajel, Baby Orajel, Hurricaine, and Topex, as well as store brands and generics. Prescription local anesthetics include articaine, bupivacaine, chloroprocaine, lidocaine, mepivacaine, prilocaine, ropivacaine, and tetracaine.

The FDA has been closely monitoring the risk of methemoglobinemia with the use of OTC and prescription local anesthetics and previously communicated about this risk in 2014, 2011, and 2006. The FDA estimates that more than 400 cases of benzocaine-associated methemoglobinemia have been reported to the FDA or published in the medical literature since 1971. There are likely additional cases about which the FDA is unaware.

As part of continued monitoring of this safety risk, the FDA recently evaluated 119 cases of benzocaine-associated methemoglobinemia reported to FDA and identified in the medical literature in the 8½ years between February 2009 and October 2017. The FDA has continued to receive cases even after the 2014 communication. Most of the 119 cases were serious and required treatment. Twenty-two cases occurred in patients younger than 18 years, and 11 of these were in children younger than 2 years. Four patients died among the 119 patients, including one infant. The FDA also conducted a study comparing the relative ability of the two local anesthetics benzocaine and lidocaine to make methemoglobin. The study showed that benzocaine generated much more methemoglobin than lidocaine in a red blood cell model.

The FDA urges patients, consumers, and health care professionals to report side effects involving benzocaine, prescription local anesthetics, or other medicines to the FDA MedWatch program.

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

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

Abciximab (ReoPro) Injection	***Currently in Shortage***
Amino Acids	***Currently in Shortage***
Aminocaproic Acid Injection, USP	***Currently in Shortage***
Amoxapine Tablets	***Currently in Shortage***
Asparaginase Erwinia Chrysanthemi (Erwinaze)	***Currently in Shortage***
Atenolol Tablets	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Azithromycin (Azasite) Ophthalmic Solution 1%	***Currently in Shortage***
Belatacept (Nulojix) Lyophilized Powder for Injection	***Currently in Shortage***
Belladonna and Opium Suppository	***Currently in Shortage***
Bumetanide Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride and Epinephrine Injection, USP	***Currently in Shortage***
Bupivacaine Hydrochloride Injection, USP	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Carbidopa and Levodopa Extended-Release Tablets	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***

Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Cromolyn Sodium Inhalation Solution, USP	***Currently in Shortage***
Deferoxamine Mesylate for Injection, USP	***Currently in Shortage***
Dexrazoxane Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose 50% Injection	***Currently in Shortage***
Diazepam Injection, USP	***Currently in Shortage***
Diltiazem Hydrochloride	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Dobutamine Hydrochloride Injection	***Currently in Shortage***
Dopamine Hydrochloride Injection	***Currently in Shortage***
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution	***Currently in Shortage***
Dorzolamide Hydrochloride Ophthalmic Solution	***Currently in Shortage***
Eflornithine Hydrochloride (Vaniqa) Cream	***Currently in Shortage***
Epinephrine Injection, 0.1 mg/mL	***Currently in Shortage***
Epinephrine Injection, Auto-Injector	***Currently in Shortage***
Erythromycin Lactobionate for Injection, USP	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Etoposide Injection	***Currently in Shortage***
Etoposide Phosphate (Etopophos) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fluorescein Injection	***Currently in Shortage***
Fluorescein Sodium and Benoxinate Hydrochloride Opthalmic Solution	***Currently in Shortage***
Fluorescein Strips	***Currently in Shortage***
Folic Acid Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Guanfacine Hydrochloride Tablets	***Currently in Shortage***
Heparin Sodium and Sodium Chloride 0.9% Injection	***Currently in Shortage***
Hydromorphone Hydrochloride Injection, USP	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Isocarboxazid Tablets	***Currently in Shortage***
Ketamine Injection	***Currently in Shortage***
Ketorolac Tromethamine Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Labetalol Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Lorazepam injection, USP	***Currently in Shortage***
Magnesium Sulfate Injection	***Currently in Shortage***
Methadone Hydrochloride Injection	***Currently in Shortage***
Methotrexate Sodium Injection	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets	***Currently in Shortage***
Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension	***Currently in Shortage***
Metoclopramide Injection, USP	***Currently in Shortage***
Metronidazole Injection, USP	***Currently in Shortage***
Molindone Hydrochloride Tablets	***Currently in Shortage***
Morphine Sulfate Injection, USP	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***

Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Ondansetron Hydrochloride Injection	***Currently in Shortage***
Pantoprazole (Protonix) Powder for Injection	***Currently in Shortage***
Penicillamine (Depen) Titratable Tablets	***Currently in Shortage***
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	***Currently in Shortage***
Penicillin G Procaine Injection	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phenytoin Sodium Injection, USP	***Currently in Shortage***
Phosphate Injection Products	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Potassium Phosphate Injection	***Currently in Shortage***
Procainamide Hydrochloride Injection, USP	***Currently in Shortage***
Progesterone Injection, USP	***Currently in Shortage***
Promethazine (Phenergan) Injection	***Currently in Shortage***
Ranitidine Injection, USP	***Currently in Shortage***
Remifentanil (Ultiva) Lyophilized Powder for Solution Injection	***Currently in Shortage***
Rocuronium Bromide Injection	***Currently in Shortage***
Ropivacaine Hydrochloride injection	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sclerosol Intrapleural Aerosol	***Currently in Shortage***
Sincalide (Kinevac) Lyophilized Powder for Injection	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sodium Phosphate Injection	***Currently in Shortage***
Sterile Talc Powder	***Currently in Shortage***
Sterile Water	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Thioridazine Hydrochloride Tablets	***Currently in Shortage***
Zolpidem Tartrate (Edluar) Sublingual Tablets	***Currently in Shortage***