Oklahoma Health Care Authority

Drug Utilization Review Board

Wednesday,
March 9, 2016
4 p.m.

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

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – March 9, 2016

DATE: February 29, 2016

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

Enclosed are the following items related to the March 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/FDA Safety Alerts – Appendix B

Action Item – Vote to Prior Authorize Spritam® (Levetiracetam) – Appendix C

Action Item – Vote to Prior Authorize Solaraze® (Diclofenac Gel) – Appendix D

Action Item – Vote to Prior Authorize Uceris® (Budesonide Extended-Release Tablets), Uceris® (Budesonide Rectal Foam), and Miscellaneous Mesalamine Products – Appendix E

Action Item – Vote to Prior Authorize Mitigare™ (Colchicine Capsules) and Zurampic® (Lesinurad) – Appendix F

Action Item – Vote to Prior Authorize Pazeo® (Olopatadine Ophthalmic) – Appendix G

Action Item – Annual Review of Multiple Sclerosis Medications – Appendix H

Annual Review of Naloxone Medications and 30-Day Notice to Prior Authorize Evzio® (Naloxone Auto-Injector) – Appendix I

Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Uptravi® (Selexipag) – Appendix J

30-Day Notice to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat) – Appendix K

Annual Review of Vasomotor Symptom Medications and 30-Day Notice to Prior Authorize Elestrin® (Estradiol Gel 0.06%) – Appendix L

Annual Review of Botulinum Toxins – Appendix M

Annual Review of Idiopathic Pulmonary Fibrosis Medications – Appendix N

Annual Review of Sylvant™ (Siltuximab) – Appendix O

FDA and DEA Updates – Appendix P

Future Business (Upcoming Product and Class Reviews)

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board
(DUR Board)
Meeting – March 9, 2016 @ 4:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

1. Call to Order
A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

2. Public Comment Forum
A. Acknowledgment of Speakers and Agenda Items

Items to be presented by Dr. Muchmore, Chairman:

3. Action Item – Approval of DUR Board Meeting Minutes – See Appendix A
A. February 10, 2016 DUR Minutes – Vote
B. February 10, 2016 DUR Recommendations Memorandum

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

4. Update on Medication Coverage Authorization Unit/FDA Safety Alerts – See Appendix B
A. Medication Coverage Activity for February 2016
B. Pharmacy Help Desk Activity for February 2016
C. FDA Safety Alerts

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

5. Action Item – Vote to Prior Authorize Spritam® (Levetiracetam) – See Appendix C
A. Introduction
B. Market News and Updates
C. College of Pharmacy Recommendations

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

6. Action Item – Vote to Prior Authorize Solaraze® (Diclofenac Gel) – See Appendix D
A. Introduction
B. College of Pharmacy Recommendations

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

7. Action Item – Vote to Prior Authorize Uceris® (Budesonide Extended-Release Tablets), Uceris® (Budesonide Rectal Foam), and Miscellaneous Mesalamine Products – See Appendix E
A. Indication(s)
B. College of Pharmacy Recommendations

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

8. Action Item – Vote to Prior Authorize Mitigare™ (Colchicine Capsules) and Zurampic® (Lesinurad) – See Appendix F
A. Introduction
B. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Pazeo® (Olopatadine Ophthalmic) – See Appendix G
A. Introduction
B. College of Pharmacy Recommendations

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

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

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

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

11. Annual Review of Naloxone Medications and 30-Day Notice to Prior Authorize Evzio® (Naloxone Auto-Injector) – See Appendix I

A. Current Prior Authorization Criteria
B. Utilization of Naloxone Medications
C. Naloxone Medication Utilization Analysis
D. Market News and Updates
E. Evzio® (Naloxone Auto-Injector) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Naloxone Medications

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

12. Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Uptravi® (Selexipag) – See Appendix J

A. Current Prior Authorization Criteria
B. Utilization of Pulmonary Arterial Hypertension Medications
C. Prior Authorization of Pulmonary Arterial Hypertension Medications
D. Market News and Updates
E. Uptravi® (Selexipag) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Pulmonary Arterial Hypertension Medications

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

13. 30-Day Notice to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat) – See Appendix K

A. Gaucher Disease (GD) Overview
B. Utilization of GD Medications
C. Cerezyme® (Imiglucerase) Product Summary
D. Elelyso® (Taliglucerase Alfa) Product Summary
E. Vpriv® (Velaglucerase Alfa) Product Summary
F. Cerdelga® (Eliglustat) Product Summary
G. Zavesca® (Miglustat) Product Summary
H. College of Pharmacy Recommendations
I. Utilization Details of GD Medications

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

14. Annual Review of Vasomotor Symptom Medications and 30-Day Notice to Prior Authorize Elestrin® (Estradiol Gel 0.06%) – See Appendix L

A. Current Prior Authorization Criteria
B. Utilization of Vasomotor Symptom Medications
C. Prior Authorization of Vasomotor Symptom Medications
D. Market News and Updates
E. Elestrin® (Estradiol Gel) Product Summary
F. College of Pharmacy Recommendations
G. Utilization Details of Vasomotor Symptom Medications

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

15. Annual Review of Botulinum Toxins – See Appendix M

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

Non-Presentation, Questions Only:

16. Annual Review of Idiopathic Pulmonary Fibrosis Medications – See Appendix N

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

Non-Presentation, Questions Only:

17. Annual Review of Sylvant™ (Siltuximab) – See Appendix O

A. Introduction
B. Current Prior Authorization Criteria
C. Utilization of Sylvant™ (Siltuximab)
D. Prior Authorization of Sylvant™ (Siltuximab)
E. College of Pharmacy Recommendations

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

18. FDA and DEA Updates – See Appendix P

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

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

A. Fiscal Year 2015 Annual Review of SoonerCare Pharmacy Benefit
B. Makena® (Hydroxyprogesterone Caproate)
C. Bowel Preparation Medications
D. Antihypertensive Medications
E. Hemophilia Pharmacy Providers Standards of Care
F. Diabetic Medications
G. Diabetic Supplies
H. Hepatitis C Medications

***Future business subject to change.**

20. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF FEBRUARY 10, 2016

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

COLLEGE OF PHARMACY STAFF:	PRESENT	ABSENT
Terry Cothran, D.Ph.; Pharmacy Director	x	
Melissa Abbott, Pharm.D.; Clinical Pharmacist	x	
Michyla Adams, Pharm.D.; Clinical Pharmacist	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison	x	
Erin Ford, Pharm.D.; Clinical Pharmacist		x
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Tammy Lambert, Ph.D.; Postdoctoral Research Fellow		x
Carol Moore, Pharm.D.; Clinical Pharmacist		x
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Leslie Robinson, D.Ph.; PA Coordinator		x
Ashley Teel, Pharm.D.; Clinical Pharmacist	x	
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist		x
Graduate Students: Christina Bulkley, Pharm.D.		x
David George, Pharm.D.		x
Timothy Pham, Pharm.D.	x	
Visiting Pharmacy Student(s):		

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

OTHERS PRESENT:		
Patrick Mumme, Alexion	Nima Nabavi, Novo Nordisk	Marc Parker, Sunovion
Bryan McGee, Alexion	David Williams, Allergan	Mark DeClerk, Lilly
Clint Degner, Novartis	Julie Brown, Ipsen	Scott Zerby, Lilly
Jim Chapman, AbbVie	Sean Seago, Merck	Brian Maves, Pfizer
Andrew Thompson, Celgene	Gay Thomas, BMS	Ron Schnare, Shire
Toby Thompson, Pfizer	Jim Fowler, AstraZeneca	Janie Huff, Takeda

PRESENT FOR PUBLIC COMMENT:	
Bryan McGee	Alexion

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

1A: ROLL CALL

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

ACTION: NONE REQUIRED

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

2A: AGENDA NO. 8 SPEAKER: BRYAN MCGEE

ACTION: NONE REQUIRED

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

3A: JANUARY 13, 2016 DUR MINUTES – VOTE

3B: JANUARY 13, 2016 DUR RECOMMENDATIONS MEMORANDUM

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: **UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS**

4A: MEDICATION COVERAGE ACTIVITY FOR JANUARY 2016

4B: PHARMACY HELP DESK ACTIVITY FOR JANUARY 2016

4C: ORAL VISCOUS LIDOCAINE CLAIMS ANALYSIS UPDATE

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE DUOPA™ (CARBIDOPA/LEVODOPA ENTERAL SUSPENSION) AND RYTARY™ (CARBIDOPA/LEVODOPA EXTENDED-RELEASE CAPSULES)**

5A: INTRODUCTION

5B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE CORTISPORIN® AND PEDIOTIC® (NEOMYCIN/POLYMYXIN B/HYDROCORTISONE OTIC)**

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented Dr. Holderread

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 7:</u> **VOTE TO PRIOR AUTHORIZE MIGRANAL® (DIHYDROERGOTAMINE NASAL SPRAY)**

7A: INDICATION(S)

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 8:</u> **VOTE TO PRIOR AUTHORIZE STRENSIQ™ (ASFOTASE ALFA)**

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 9:</u> **VOTE TO PRIOR AUTHORIZE VARUBI™ (ROLAPITANT)**

9A: INTRODUCTION

9B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Adams

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

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 10:</u> **VOTE TO PRIOR AUTHORIZE XURIDEN™ (URIDINE TRIACETATE)**

10A: INTRODUCTION

10B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

Dr. Muchmore recommends taking out "i. shown not to improve with iron supplements" of recommendations.

Dr. Preslar moved to approve with changes; seconded by Dr. Garton

ACTION: MOTION CARRIED

<u>AGENDA ITEM NO. 11:</u> **ANNUAL REVIEW OF GOUT MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE MITIGARE™ (COLCHICINE CAPSULES) AND ZURAMPIC® (LESINURAD)**

11A: CURRENT PRIOR AUTHORIZATION CRITERIA

11B: UTILIZATION OF GOUT MEDICATIONS

11C: PRIOR AUTHORIZATION OF GOUT MEDICATIONS

11D: MARKET NEWS AND UPDATES

11E: MITIGARE™ (COLCHICINE CAPSULES) PRODUCT SUMMARY

11F: ZURAMPIC™ (LESINURAD) PRODUCT SUMMARY

11G: COLLEGE OF PHARMACY RECOMMENDATIONS

11H: UTILIZATION DETAILS OF GOUT MEDICATIONS

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

<u>AGENDA ITEM NO. 12:</u> **ANNUAL REVIEW OF SEIZURE MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE SPRITAM® (LEVETIRACETAM)**

12A: CURRENT PRIOR AUTHORIZATION CRITERIA

12B: UTILIZATION OF SEIZURE MEDICATIONS

12C: PRIOR AUTHORIZATION OF SEIZURE MEDICATIONS

12D: MARKET NEWS AND UPDATES

12E: SPRITAM® (LEVETIRACETAM) PRODUCT SUMMARY

12F: VIMPAT® (LACOSAMIDE) PRODUCT SUMMARY

12G: BANZEL® (RUFINAMIDE) PRODUCT SUMMARY
12H: FYCOMPA® (PERAMPANEL) PRODUCT SUMMARY
12I: COLLEGE OF PHARMACY RECOMMENDATIONS
12J: UTILIZATION DETAILS OF SEIZURE MEDICATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: 30-DAY NOTICE TO PRIOR AUTHORIZE SOLARAZE® (DICLOFENAC GEL)
13A: ACTINIC KERATOSIS BACKGROUND INFORMATION
13B: SOLARAZE® (DICLOFENAC 3% GEL) PRODUCT SUMMARY
13C: COLLEGE OF PHARMACY RECOMMENDATIONS
Materials included in agenda packet; presented by Dr. Adams
ACTION: NONE REQUIRED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF ULCERATIVE COLITIS MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE UCERIS® (BUDESONIDE EXTENDED-RELEASE TABLETS), UCERIS® (BUDESONIDE RECTAL FOAM), AND MISCELLANEOUS MESALAMINE PRODUCTS
14A: ULCERATIVE COLITIS (UC) BACKGROUND INFORMATION
14B: CURRENT PRIOR AUTHORIZATION CRITERIA
14C: UTILIZATION OF UC MEDICATIONS
14D: PRIOR AUTHORIZATION OF UC MEDICATIONS
14E: MARKET NEWS AND UPDATES
14F: UCERIS® (BUDESONIDE) EXTENDED-RELEASE TABLETS PRODUCT SUMMARY
14G: UCERIS® (BUDESONIDE) RECTAL FOAM PRODUCT SUMMARY
14H: ASACOL® HD (MESALAMINE) DELAYED-RELEASE TABLETS PRODUCT SUMMARY
14I: PENTASA® (MESALAMINE) CONTROLLED-RELEASE CAPSULES PRODUCT SUMMARY
14J: ROWASA® (MESALAMINE) RECTAL SUSPENSION ENEMA PRODUCT SUMMARY
14K: LIALDA® (MESALAMINE) DELAYED-RELEASE CAPSULES PRODUCT SUMMARY
14L: COLAZAL® (BALSALAZIDE) CAPSULES PRODUCT SUMMARY
14M: DIPENTUM® (OLSALAZINE) CAPSULES PRODUCT SUMMARY
14N: CANASA® (MESALAMINE) SUPPOSITORIES PRODUCT SUMMARY
14O: APRISO® (MESALAMINE) EXTENDED-RELEASE CAPSULES PRODUCT SUMMARY
14P: DELZICOL® (MESALAMINE) DELAYED-RELEASE CAPSULES PRODUCT SUMMARY
14Q: COST COMPARISON
14R: COLLEGE OF PHARMACY RECOMMENDATIONS
14S: UTILIZATION DETAILS OF ULCERATIVE COLITIS MEDICATIONS
Materials included in agenda packet; presented by Dr. Nawaz
ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF OCULAR ALLERGY MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE PAZEO® (OLOPATADINE OPHTHALMIC)
15A: CURRENT PRIOR AUTHORIZATION CRITERIA
15B: UTILIZATION OF OCULAR ALLERGY MEDICATIONS
15C: PRIOR AUTHORIZATION OF OCULAR ALLERGY MEDICATIONS
15D: MARKET NEWS AND UPDATES
15E: PAZEO® (OLOPATADINE OPHTHALMIC) PRODUCT SUMMARY
15F: COLLEGE OF PHARMACY RECOMMENDATIONS
15G: UTILIZATION DETAILS OF OCULAR ALLERGY MEDICATIONS
Materials included in agenda packet; presented by Dr. Holderread
ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: **ANNUAL REVIEW OF GONADOTROPIN RELEASING HORMONES (GNRH)**

16A: INTRODUCTION
16B: FDA APPROVED GNRH OPTIONS FOR TREATMENT OF CENTRAL PRECOCIOUS PUBERTY OR ENDOMETRIOSIS
16C: CURRENT PRIOR AUTHORIZATION CRITERIA
16D: UTILIZATION OF GNRH MEDICATIONS
16E: PRIOR AUTHORIZATION OF GNRH MEDICATIONS
16F: MARKET NEWS AND UPDATES
16G: COLLEGE OF PHARMACY RECOMMENDATIONS
16H: UTILIZATION DETAILS OF GNRH MEDICATIONS

Materials included in agenda packet; presented by Dr. Holderread (Non-presentation; questions only)

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: **ANNUAL REVIEW OF NORTHERA™ (DROXIDOPA)**

17A: INTRODUCTION
17B: CURRENT PRIOR AUTHORIZATION CRITERIA
17C: UTILIZATION OF NORTHERA™ (DROXIDOPA)
17D: PRIOR AUTHORIZATION OF NORTHERA™ (DROXIDOPA)
17E: MARKET NEWS AND UPDATES
17F: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Nawaz (Non-presentation; questions only)

ACTION: NONE REQUIRED

AGENDA ITEM NO. 18: **FDA and DEA Updates**

Materials included in agenda packet; presented by Dr. Cothran

ACTION: NONE REQUIRED

AGENDA ITEM NO. 19: **FUTURE BUSINESS* (UPCOMING PRODUCT AND CLASS REVIEWS)**

19A: MAKENA® (HYDROXYPROGESTERONE CAPROATE)
19B: MULTIPLE SCLEROSIS MEDICATIONS
19C: GROWTH HORMONE
19D: VASOMOTOR SYMPTOM MEDICATIONS
19E: IDIOPATHIC PULMONARY FIBROSIS MEDICATIONS
19F: BOTULINUM TOXINS
19G: PULMONARY ARTERIAL HYPERTENSION MEDICATIONS
19H: CERDELGA™ (ELIGLUSTAT)
19I: HEMOPHILIA MEDICATION PHARMACY PROVIDERS

***Future business subject to change.**

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 20: **ADJOURNMENT**

The meeting was adjourned at 5:02pm

The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: February 11, 2016

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

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

Subject: DUR Board Recommendations From Meeting of February 10, 2016

Recommendation 1: Oral Viscous Lidocaine Claims Analysis Update

NO ACTION REQUIRED.

Assessment of oral viscous lidocaine claims in the pediatric SoonerCare population did not reveal disproportionate prescribing. It is important to note that SoonerCare claims do not encompass over-the-counter (OTC) topical medications for teething pain. Caregivers may continue utilizing OTC topical medications for teething pain if they are uninformed of the potential risks. Based on this claims analysis and the inability to assess OTC lidocaine utilization, the College of Pharmacy recommends including an article in the member newsletter detailing the American Academy of Pediatrics (AAP) recommendations to use a chilled teething ring or gentle rubbing of the gums with a finger for teething pain. Utilization of prescription oral viscous lidocaine claims will be reassessed periodically to ensure prescribing in the pediatric population remains appropriate.

Recommendation 2: Vote to Prior Authorize Duopa™ (Carbidopa/Levodopa Enteral Suspension) and Rytary™ (Carbidopa/Levodopa Extended-Release Capsules)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Duopa™ (carbidopa/levodopa enteral suspension) and Rytary™ (carbidopa/levodopa extended-release capsules) with the following criteria:

Duopa™ (Carbidopa/Levodopa Enteral Suspension) Approval Criteria:

1. An FDA approved diagnosis of advanced Parkinson's disease; and
2. For long-term administration, member or caregivers must be willing and able to administer Duopa® through a percutaneous endoscopic gastrostomy; and
3. Patients must be experiencing three hours or more of "off" time on their current Parkinson's disease drug treatment and they must have demonstrated a clear responsiveness to treatment with levodopa; and
4. Approvals will be for a quantity of one cassette per day.

Rytary™ (Carbidopa/Levodopa Extended-Release Capsules) Approval Criteria

1. An FDA approved diagnosis of Parkinson's disease, post-encephalitic parkinsonism, or parkinsonism that may follow carbon monoxide intoxication or manganese intoxication; and
2. A patient-specific, clinically significant reason why the member cannot use other generic carbidopa/levodopa combinations including Sinemet® CR (carbidopa/levodopa extended-release tablets).

Recommendation 3: Vote to Prior Authorize Cortisporin® and Pediotic® (Neomycin/Polymyxin B/Hydrocortisone Otic)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Otic Anti-Infectives Product Based Prior Authorization (PBPA) category:

1. Place neomycin/polymyxin B/hydrocortisone (Cortisporin®, Pediotic®) into Tier-2. The existing criteria for this category will apply.
2. Place neomycin/colistin/hydrocortisone/thonzonium (Cortisporin® TC, Coly-Mycin® S) into Tier-1. The existing criteria for this category will apply.
3. Initiate an educational mailing regarding these tier changes, which will include the option of utilizing neomycin/colistin/hydrocortisone/thonzonium (Cortisporin® TC, Coly-Mycin® S) for otic conditions as well other Tier-1 otic anti-infectives.

Otic Anti-Infectives		
Tier-1	**Tier-2**	**Special PA**
acetic acid (VoSol®, Acetasol®)	chloroxylenol/benzocaine/HC (Trioxin®)	acetic acid/HC (Acetasol® HC, VoSol® HC)
ciprofloxacin/dexamethasone (Ciprodex®)	ciprofloxacin (Cetraxal®)	
ciprofloxacin/HC (Cipro® HC)	finafloxacin (Xtoro™)	
neomycin/colistin/HC/ thonzonium (Cortisporin® TC, Coly-Mycin® S)	ofloxacin (Floxin® Otic)	
	neomycin/polymyxin B/HC (Cortisporin®, Pediotic®)	

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

Otic Anti-Infectives Tier-2 Approval Criteria:

1. Member must have an adequate 14-day trial of at least two Tier-1 medications; or
2. Approval may be granted if there is a unique FDA approved indication not covered by Tier-1 medications or infection by an organism not known to be covered by any of the Tier-1 medications.

Otic Anti-Infectives Special Prior Authorization (PA) Approval Criteria:

1. Diagnosis of acute otitis externa; and
2. Recent (within six months) trials with all other commonly used topical otic anti-infectives that have failed to resolve infection; or
3. Allergy to all available products and failure of acetic acid alone.

Recommendation 4: Vote to Prior Authorize Migranal® (Dihydroergotamine Mesylate Nasal Spray)

MOTION CARRIED by unanimous approval.

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

1. The addition of a special prior authorization (PA) category:
   a. Placement of sumatriptan (Sumavel® DosePro®), sumatriptan patch (Zecuity®), sumatriptan injection (Imitrex®), and sumatriptan nasal spray (Imitrex®) into the special PA category.
   b. Placement of sumatriptan/naproxen (Treximet®) into the special PA category and require a patient-specific, clinically significant reason why the member cannot use the individual components separately.
   c. Placement of dihydroergotamine nasal spray (Migranal®) and dihydroergotamine injection (D.H.E. 45®) in the special PA category with the criteria noted in red.

Tier-1 products are covered with no prior authorization necessary.
Anti-Migraine Medications Tier-2 Approval Criteria:

1. A trial of all available Tier-1 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 products; or
3. Previous success with a Tier-2 product within the last 60 days.

Anti-Migraine Medications Tier-3 Approval Criteria:

1. A trial of all available Tier-1 and Tier-2 products with inadequate response; or
2. Documented adverse effect to all available Tier-1 and Tier-2 products; or
3. Previous success with a Tier-3 product within the last 60 days.
4. Use of any non-oral formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.

Anti-Migraine Medications Special Prior Authorization Approval Criteria:

1. Use of any non-oral sumatriptan formulation will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation or lower tiered triptan products.

2. Use of Zecuity® will require a patient-specific, clinically significant reason why the member cannot use all available generic formulations of sumatriptan (tablets, nasal spray, and injection) or lower tiered triptan products.
3. Use of Treximet® (sumatriptan/naproxen) will require a patient-specific, clinically significant reason why the member cannot use the individual ingredients separately or lower tiered triptan products.
4. Use of dihydroergotamine injection (D.H.E. 45®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan products.
5. Use of dihydroergotamine nasal spray (Migranal®) will require a patient-specific, clinically significant reason why the member cannot use lower-tiered triptan products and dihydroergotamine injection (D.H.E. 45®).

Anti-Migraine Medications			
Tier-1	**Tier-2**	**Tier-3**	**Special PA**
sumatriptan (Imitrex®) rizatriptan (Maxalt®, Maxalt MLT®)	naratriptan (Amerge®) zolmitriptan (Zomig®, Zomig-ZMT®)	almotriptan (Axert®) eletriptan (Relpax®) frovatriptan (Frova®) zolmitriptan nasal spray (Zomig®)	**dihydroergotamine injection (D.H.E. 45®)** **dihydroergotamine nasal spray (Migranal®)** sumatriptan injection (Imitrex®) sumatriptan nasal spray (Imitrex®) sumatriptan (Sumavel® DosePro®) sumatriptan (Zecuity®)* sumatriptan/Naproxen (Treximet®)

*Requires a clinically significant reason why member cannot use all other available formulations of sumatriptan.

Recommendation 5: Vote to Prior Authorize Strensiq™ (Asfotase Alfa)

MOTION CARRIED; approval was not unanimous.

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

Strensiq™ (Asfotase Alfa) Approval Criteria:

1. An FDA approved indication for the treatment of patients with perinatal/infantile-onset and juvenile-onset hypophosphatasia (HPP); and
2. Confirmed diagnosis by laboratory testing of:
   a. Low age-adjusted ALP activity; and
   b. Elevated pyridoxal 5'-phophate (PLP) levels; and
3. Member's weight (kg) must be provided and have been taken within the last four weeks to ensure accurate weight-based dosing; and
4. The 80mg/0.8mL vial should not be used in pediatric patients weighing less than 40kg.

Recommendation 6: Vote to Prior Authorize Varubi™ (Rolapitant)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Emend® (aprepitant) to differentiate trial requirements in members receiving moderately or highly emetogenic chemotherapy and to include specific criteria for the oral suspension formulation
2. Revising the existing criteria for Diclegis® (doxylamine/pyridoxine) in response to the updated 2015 ACOG practice guidelines for the treatment of nausea and vomiting of pregnancy
3. Revising the existing criteria for Akynzeo® (netupitant/palonosetron) to require a failed trial of aprepitant (Emend®) based on estimated net cost per chemotherapy cycle
4. The prior authorization of Varubi™ (rolapitant) with the criteria noted in red

New proposed criteria specific to each medication is as follows:

Kytril® and Sancuso® (Granisetron), Anzemet® (Dolasetron), and Emend® (Aprepitant) Approval Criteria:

1. An FDA approved diagnosis; and
2. A recent trial of ondansetron (within the past six months) used for at least three days or one cycle that resulted in inadequate response is required for authorization in members receiving moderately emetogenic chemotherapy; and
3. No ondansetron trial is required for authorization of Emend® (aprepitant) in members receiving highly emetogenic chemotherapy; and
4. Approval length will be based on duration of need.
5. For Emend® (aprepitant) oral suspension, an age restriction of six years and younger will apply. Members older than six years of age will require a patient-specific, clinically significant reason why the oral capsule formulation cannot be used.

Diclegis® (Doxylamine/Pyridoxine) Approval Criteria:

1. An FDA approved diagnosis of nausea and vomiting of pregnancy that is not responsive to conservative management; and
2. Trials with at least two non-pharmacological therapies that have failed to relieve nausea and vomiting; and
3. ~~Trials with at least two prescription medications that have failed to relieve nausea and vomiting; and~~
4. A patient-specific, clinically significant reason why member cannot use over-the-counter (OTC) doxylamine and OTC Vitamin B_6 (pyridoxine).

Akynzeo® (Netupitant/Palonosetron) Approval Criteria:

1. An FDA approved diagnosis for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy; and
2. A previously failed trial of aprepitant (Emend®) that resulted in an inadequate response, or a patient-specific, clinically significant reason why aprepitant cannot be used must be provided; and
3. Approval length based on duration of need.
4. A quantity limit of one capsule per chemotherapy cycle will apply.

Varubi™ (Rolapitant) Approval Criteria:

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

Recommendation 7: Vote to Prior Authorize Xuriden™ (Uridine Triacetate)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Xuriden™ (uridine triacetate) with the following criteria:

Xuriden™ (Uridine Triacetate) Approval Criteria:

1. An FDA approved diagnosis of hereditary orotic aciduria defined by at least one of the following:
   a. Assay of the orotate phosphoribosyltransferase and orotidylic acid decarboxylase enzymes in the patients erythrocytes showing deficiency in both enzymes or deficiency in orotidylic acid decarboxylase alone; or
   b. Evidence of megaloblastic anemia
      i. Normal serum folate and vitamin B12 levels and no evidence of Transcobalamine II deficiency; or
   c. Orotic acid crystals visualized in the urine via microscopy; and
2. Current weight of member must be provided on the prior authorization request; and
   a. Weights should be reassessed every six months to ensure proper dosing and effectiveness; or
   b. Prescriber can indicate urine orotic acid levels are within normal ranges and dosing remains appropriate; and
3. The prescriber must verify that the patient/caregiver is able to properly measure and administer medication; and
4. A quantity limit of four packets per day will apply.

Recommendation 8: Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Mitigare™ (Colchicine Capsules) and Zurampic™ (Lesinurad)

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Seizure Medications and 30-Day Notice to Prior Authorize Spritam® (Levetiracetam)

NO ACTION REQUIRED.

Recommendation 10: 30-Day Notice to Prior Authorize Solaraze® (Diclofenac 3% Gel)

NO ACTION REQUIRED.

Recommendation 11: Annual Review of Ulcerative Colitis Medications and 30-Day Notice to Prior Authorize Uceris® (Budesonide Extended-Release Tablets), Uceris® (Budesonide Rectal Foam), and Miscellaneous Mesalamine Products

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Ocular Allergy Medications and 30-Day Notice to Prior Authorize Pazeo® (Olopatadine Ophthalmic)

NO ACTION REQUIRED.

Recommendation 13: Annual Review of Gonadotropin Releasing Hormone Medications

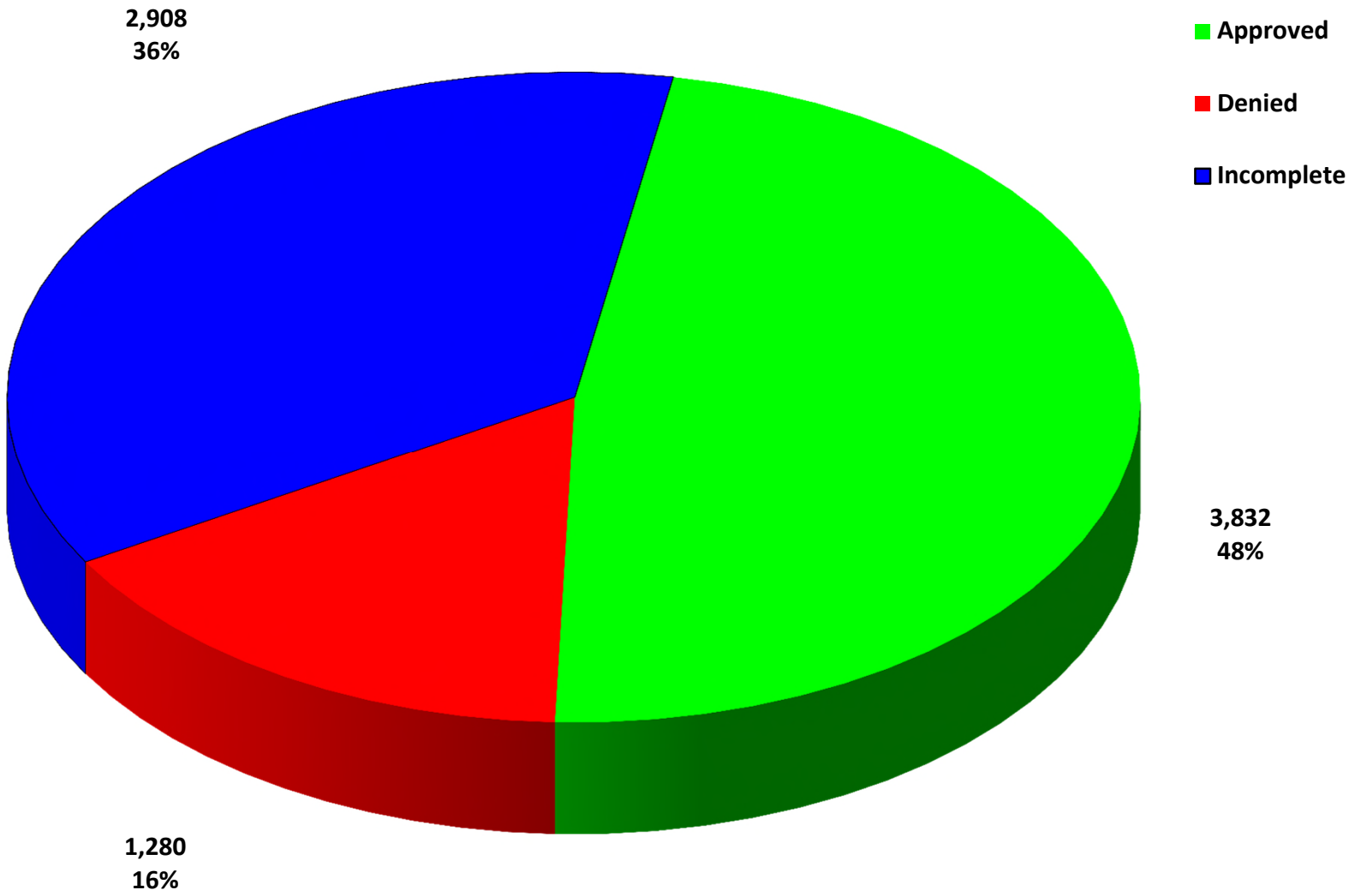
NO ACTION REQUIRED.

Recommendation 14: Annual Review of Northera™ (Droxidopa)

NO ACTION REQUIRED.

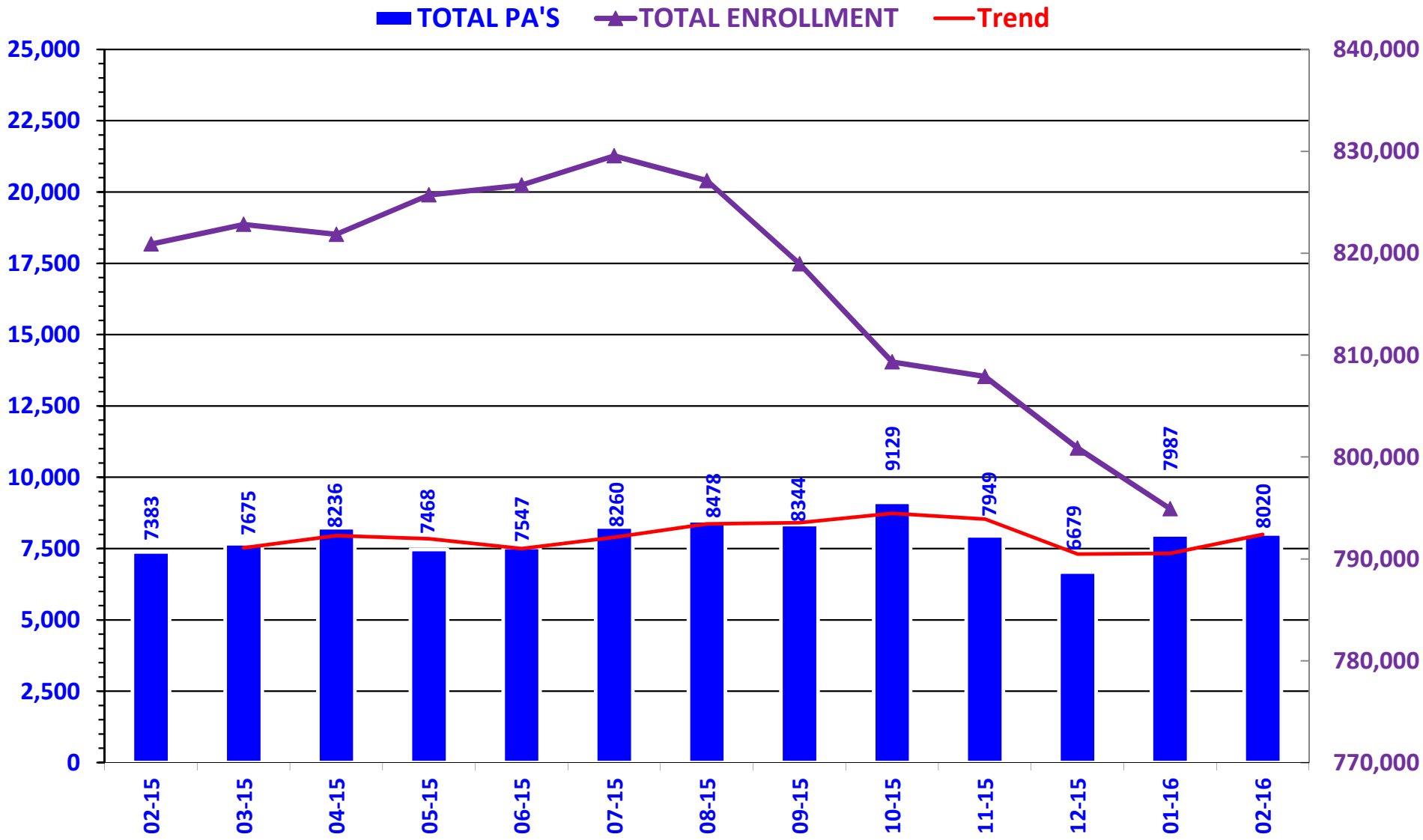
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: FEBRUARY 2016



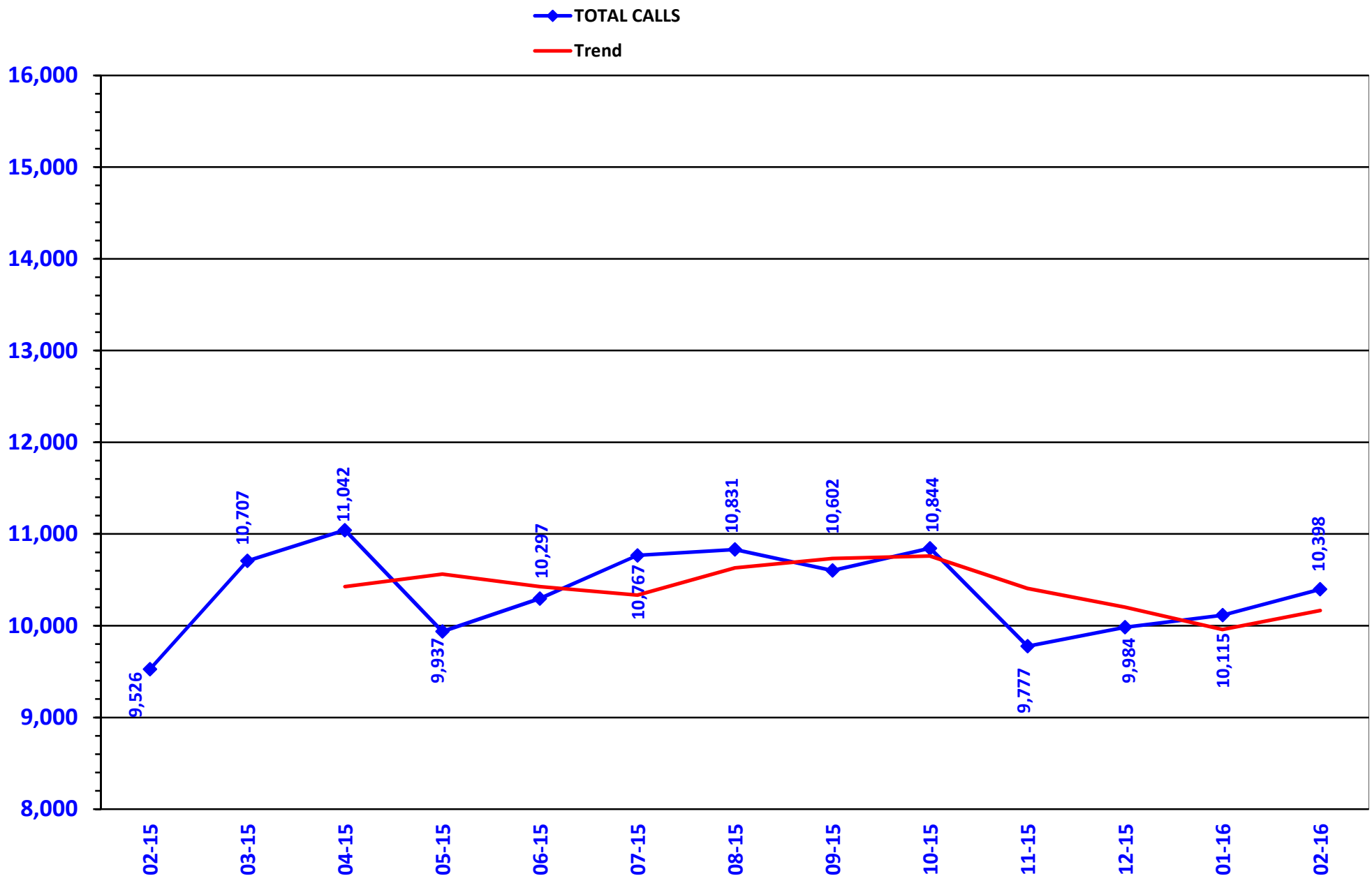
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: FEBRUARY 2015 – FEBRUARY 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT:
FEBRUARY 2015 – FEBRUARY 2016



Prior Authorization Activity

2/1/2016 Through 2/29/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	401	135	88	178	351
Analgesic - NonNarcotic	21	0	5	16	0
Analgesic, Narcotic	418	241	47	130	156
Angiotensin Receptor Antagonist	23	3	7	13	267
Antiasthma	101	26	27	48	345
Antibiotic	23	6	0	17	145
Anticoagulant	11	6	0	5	309
Anticonvulsant	65	29	11	25	328
Antidepressant	85	20	16	49	360
Antidiabetic	167	70	27	70	349
Antifungal	10	3	3	4	43
Antihistamine	163	118	12	33	355
Antimigraine	43	10	12	21	254
Antineoplastic	23	21	0	2	163
Antiulcers	201	37	70	94	115
Anxiolytic	73	51	8	14	306
Atypical Antipsychotics	472	265	31	176	341
Biologics	127	69	17	41	329
Bladder Control	65	28	13	24	347
Blood Thinners	195	126	8	61	297
Botox	33	25	5	3	344
Calcium Channel Blockers	11	3	2	6	251
Cardiovascular	91	43	16	32	305
Cephalosporins	16	6	0	10	7
Chronic Obstructive Pulmonary Disease	56	14	11	31	359
Dermatological	98	11	58	29	79
Diabetic Supplies	565	275	27	263	188
Endocrine & Metabolic Drugs	60	42	5	13	127
Erythropoietin Stimulating Agents	19	12	3	4	103
Fibromyalgia	184	34	88	62	319
Fish Oils	29	6	8	15	313
Gastrointestinal Agents	90	29	23	38	130
Genitourinary Agents	12	3	4	5	48
Growth Hormones	88	63	8	17	146
Hepatitis C	203	98	50	55	7
HFA Rescue Inhalers	42	13	6	23	338
Insomnia	22	3	9	10	176
Insulin	51	13	10	28	359
Linzess, Amitiza, and Relistor	118	7	53	58	168
Miscellaneous Antibiotics	11	0	2	9	0
Multiple Sclerosis	50	24	7	19	179
Muscle Relaxant	62	13	26	23	127
Nasal Allergy	108	26	30	52	295
Neurological Agents	52	34	10	8	354
NSAIDs	163	20	53	90	280
Ocular Allergy	22	5	5	12	251
Ophthalmic Anti-infectives	13	0	6	7	0
Osteoporosis	28	12	6	10	334
Other*	278	58	73	147	245
Otic Antibiotic	13	0	2	11	0
Pediculicide	31	10	6	15	17
Statins	39	13	7	19	359
Stimulant	886	439	83	364	335
Suboxone/Subutex	252	185	15	52	72
Synagis	93	45	26	22	67

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Testosterone	59	16	18	25	320
Topical Antifungal	25	1	7	17	26
Topical Corticosteroids	93	5	30	58	144
Vitamin	58	13	30	15	340
Pharmacotherapy	54	38	0	16	313
Emergency PAs	0	0	0	0	
Total	**6,865**	**2,921**	**1,230**	**2,714**	

Overrides					
Brand	47	32	4	11	320
Cumulative Early Refill	2	2	0	0	180
Diabetic Supplies	3	2	0	1	212
Dosage Change	290	265	3	22	11
High Dose	7	5	0	2	254
Ingredient Duplication	42	35	0	7	22
Lost/Broken Rx	95	87	4	4	13
NDC vs Age	31	31	0	0	254
Nursing Home Issue	79	68	1	10	10
Opioid Quantity	10	7	3	0	156
Other	30	22	2	6	11
Quantity vs. Days Supply	490	333	30	127	253
STBS/STBSM	12	12	0	0	33
Stolen	6	5	1	0	8
Temporary Unlock	2	2	0	0	11
Third Brand Request	24	14	5	5	14
Overrides Total	**1,155**	**911**	**50**	**194**	
Total Regular PAs + Overrides	**8,020**	**3,832**	**1,280**	**2,908**	

Denial Reasons	
Unable to verify required trials.	2,558
Does not meet established criteria.	1,212
Lack required information to process request.	456

Other PA Activity	
Duplicate Requests	567
Letters	6,913
No Process	9
Changes to existing PAs	563
Helpdesk Initiated Prior Authorizations	737
PAs Missing Information	47

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

Overview of FDA Safety Alerts

Oklahoma Health Care Authority
March 2016

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

The following are recent U.S. Food and Drug Administration (FDA) safety alerts included for the Drug Utilization Review (DUR) Board's consideration. SoonerCare specific data may be presented where applicable. The College of Pharmacy will make recommendations as well as take recommendations from the DUR Board.

Date	Drug	Issue
08/28/2015	**DPP-4 Inhibitors (sitagliptin, saxagliptin, linagliptin, & alogliptin)**	**Severe and disabling arthralgia**
Issue Details: The FDA issued safety information regarding dipeptidyl peptidase-4 (DPP-4) inhibitors. Postmarketing data revealed reports of severe and disabling arthralgia in patients taking a DPP-4 for treatment of type-2 diabetes. Onset of symptoms varied from one day to several years. Symptoms resolved with discontinuation of the drug. Some patients experienced recurrence of the pain when started on the same drug or another from the same class. **FDA Recommendations:** Manufacturers of all the medications (individual and combination) in the DPP-4 class are required to update the labeling to include information regarding the risk of joint pain. **Pharmacy Claims Evaluation:** During calendar year 2015, a total of 1,792 SoonerCare members had paid claim(s) for a DPP-4 inhibitor, alone or in fixed combination with metformin, pioglitazone, or empagliflozin. No issues related to DPP-4 adverse effects were reported to the College of Pharmacy.		

Date	Drug	Issue
09/10/2015	**canagliflozin (Invokana®, Invokamet®)**	**Risk of bone fracture and decreased bone mineral density**
Issue Details: The FDA has strengthened the warning regarding the increased risk of bone fractures along with the risk of decreased bone mineral density for patients taking canagliflozin, a sodium/glucose cotransporter 2 (SGLT2) inhibitor, for type-2 diabetes. **FDA Recommendations:** The FDA is requiring that the Warnings and Precautions section of the drug labeling be updated to include information pertaining to the increased risk of bone fracture and decreased bone mineral density for patients using these medications. Prescribers should consider factors that contribute to fracture risk prior to starting patients on canagliflozin, and patients should be instructed to talk to their prescriber about factors that		

may increase their risk for bone fracture.
Pharmacy Claims Evaluation: A review of SoonerCare pharmacy claims data from fiscal year 2015 revealed 115 SoonerCare members with paid claim(s) for a canagliflozin containing medication, primarily canagliflozin alone. A total of 16% of those members were age 61 years and older.

Date	Drug	Issue
09/21/2015	**tramadol (Ultram®)**	**Risk of slowed or difficult breathing in children**

Issue Details: The FDA is investigating the use of tramadol for pain in children aged 17 years and younger because of the risk of slowed or difficult breathing. The risk may be increased in children treated with tramadol after surgery to remove their tonsils. Tramadol is converted in the liver to the active form of the opioid. Some genetic variations can cause tramadol to be converted to the active form of the opioid more quickly and completely than typical. These "ultra-rapid metabolizers" are likely to have larger amounts of the active form in their blood, which can result in breathing difficulty.
FDA Recommendations: The FDA is evaluating all available evidence and will release conclusions and recommendations when the assessment is complete. Tramadol is not FDA-approved for use in children, and the FDA recommends that prescribers consider alternative FDA-approved pain medications for children.
SoonerCare Action: The College of Pharmacy would like to review utilization of tramadol containing medications in the SoonerCare pediatric population in further detail and present the findings to the DUR board. Consideration should be given to implementing an age restriction for members 17 years and younger. Approval of tramadol in this population would require prior authorization. Alternatively, educational interventions including targeted mailings may be an effective measure for reducing prescribing of tramadol in this population.
Pharmacy Claims Evaluation: During calendar year 2015, a total of 2,052 SoonerCare members 17 years of age and younger had paid claim(s) for a tramadol containing medication. The minimum age found with paid claim(s) was 10 years (17 members). A review of diagnosis history of those 17 members revealed the most common diagnoses for use was fracture or sprain.

Date	Drug	Issue
10/22/2015	**ombitasvir/paritaprevir/ritonavir & dasabuvir (Viekira Pak®) and ombitasvir/paritaprevir/ritonavir (Technivie®)**	**Risk of serious liver injury**

Issue Details: The FDA issued a Drug Safety Communication regarding the possibility of liver injury in patients with underlying advanced liver disease. The FDA's review of adverse events reported to the FDA Adverse Events Reporting System (FAERS) database revealed episodes of hepatic decompensation and liver failure in patients with underlying cirrhosis while taking these medications. Some of the cases resulted in liver transplantation or death. Cases were reported mostly in patients taking Viekira Pak® who had evidence of advanced cirrhosis prior

to starting treatment with it. In most of the cases, liver injury occurred within one to four weeks after starting treatment; some of the cases occurred in patients for whom these medicines were already contraindicated.

FDA Recommendations: The FDA is requiring that the labeling of Viekira Pak® and Technivie® include information regarding signs and symptoms of liver injury. Patients should not stop taking these medications unless instructed to do so by their health care provider, as this can lead to drug resistance to other hepatitis C drugs.

SoonerCare Action: The SoonerCare prior authorization criteria for Viekira Pak® and Technivie® have been updated to ensure members with decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C) are not receiving these medications.

Pharmacy Claims Evaluation: During calendar year 2015, a total of 11 SoonerCare members had paid claim(s) for Viekira Pak®. No liver adverse effects related to Viekira Pak® were reported to the College of Pharmacy.

Date	Drug	Issue
11/06/2015	**clopidogrel (Plavix®)**	**Risk of death**

Issue Details: A meta-analysis of long-term clinical trials by the FDA revealed that long-term use of clopidogrel does not increase or decrease the risk of death related to cancer in patients with, or at risk for, heart disease. The Dual Antiplatelet Therapy (DAPT) trial and several other clinical trials were evaluated. Patients with drug-eluting stents who took clopidogrel for 30 months versus 12 months had lower rates of heart attacks and stent thrombosis, but higher rates of death, primarily from cancer or trauma.

FDA Recommendations: The FDA issued a Drug Safety Communication advising patients not to stop taking clopidogrel because doing so may result in an increased risk of heart attacks and blood clots; instead patients are instructed to talk with their health care professional if they have questions or concerns regarding clopidogrel. Health care professionals are advised to consider the benefits and risks of antiplatelet medicines prior to starting treatment.

Pharmacy Claims Evaluation: During calendar year 2015, a total of 2,585 SoonerCare members had paid claim(s) for clopidogrel. No issues related to clopidogrel adverse effects were reported to the College of Pharmacy.

Date	Drug	Issue
01/2016	**lomustine (Gleostine™)**	**Delayed myelosuppression and risk of overdose**

Issue Details: Lomustine is a chemotherapy agent used for breast cancer, Hodgkin's disease, lung cancer, malignant melanoma, and intracranial tumors. Myelosuppression, possibly fatal, can occur four to six weeks after lomustine administration, and can persist for one to two weeks. Myelosuppression is delayed, dose related, and cumulative.

FDA Recommendations: The FDA required the addition of a boxed warning to the lomustine labeling. Package labeling now recommends that blood counts be monitored for at least six weeks after each dose. Lomustine should not be administered more frequently than every six

weeks.
Pharmacy Claims Evaluation: During calendar year 2015, a total of three SoonerCare members had paid pharmacy claim(s) for lomustine. All claims were prescribed by a hematology specialist or a mid-level practitioner who is supervised by a hematology specialist.

Date	Drug	Issue
01/2016	**alosetron (Lotronex®)**	**Risk of serious gastrointestinal adverse reactions**

Issue Details: Alosetron is a selective antagonist of serotonin 5-HT3 receptors indicated for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have not responded to conventional therapy. Serious gastrointestinal adverse reactions have occurred with alosetron use including ischemic colitis and serious complications of constipation that have resulted in hospitalization, blood transfusion, surgery, and death.
FDA Recommendations: The FDA required the addition of a boxed warning to the alosetron labeling. Package labeling now recommends that alosetron be discontinued in patients who develop constipation or symptoms of ischemic colitis and not resumed in patients who develop ischemic colitis.
Pharmacy Claims Evaluation: During calendar year 2015, a total of 3 members had paid claim(s) for alosetron. All members utilizing alosetron were female, and all claims were prescribed by a gastroenterologist or a mid-level practitioner who is supervised by a gastroenterologist or internist. No issues related to alosetron adverse effects were reported to the College of Pharmacy.

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[1] FDA Drug Safety Information: Dipeptidyl peptidase-4 (DPP-4) Inhibitors. Available online at http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm460728.htm. Last revised: 09/10/2015. Last accessed: 02/23/2016.
[2] FDA Drug Safety Communication: FDA revises label of diabetes drug canagliflozin (Invokana, Invokamet) to include updates on bone fracture risk and new information on decreased bone mineral density. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm461449.htm. Last revised: 01/15/2016. Last accessed: 02/23/2016.
[3] FDA Drug Safety Communication: FDA warns of serious liver injury risk with hepatitis C treatments Viekira Pak and Technivie. Available online at: http://www.fda.gov/downloads/drugs/drugsafety/ucm468755.pdf. Last revised: 10/2015. Last accessed. 02/23/2016.
[4] FDA Drug Safety Communication: Tramadol FDA Evaluating Risks of Using in Children Aged 17 and Younger. Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm463499.htm. Last revised 09/29/2015. Last accessed 02/24/2016.
[5] FDA Drug Safety Communication: FDA review finds long-term treatment with blood-thinning medicine Plavix (clopidogrel) does not change risk of death. Available online at: http://www.fda.gov/Drugs/DrugSafety/ucm471286.htm. Last revised: 12/09/2015. Last accessed. 02/24/2016.
[6] FDA: Gleostine (Lomustine) Capsules Safety Labeling Changes Approved By FDA Center for Drug Evaluation and Research (CDER). Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm485677.htm. Last revised: 02/12/2016. Last accessed: 02/24/2016.
[7] FDA: Lotronex (alosetron hydrochloride) Tablets Safety Labeling Changes Approved By FDA Center for Drug Evaluation and Research (CDER). Available online at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm485675.htm. Last revised: 02/12/2016. Last accessed: 02/24/2016.

Appendix C

Vote to Prior Authorize Spritam® (Levetiracetam)

Oklahoma Health Care Authority
March 2016

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

- **Aptiom® (eslicarbazepine)** was first approved by the U.S. Food and Drug Administration (FDA) in 2013 as an adjunctive treatment of partial-onset seizures in adults and received the indication for monotherapy in the treatment of partial-onset seizures in adults in August 2015. Aptiom® is available as oral tablets and is dosed once daily.
- **Spritam® (levetiracetam)** was FDA approved in July 2015 and is indicated as an adjunctive treatment of partial-onset seizures, myoclonic seizures, and primary generalized tonic-clonic (PGTC) seizures in adults and children with epilepsy. Spritam® is the first FDA approved medication to use ZipDose® Technology, which uses three-dimensional printing (3DP) to produce a porous formulation that rapidly disintegrates with a sip of liquid. Spritam® is available as oral, spearmint-flavored tablets that disintegrate in a mean time of 11 seconds in the mouth when taken with a sip of liquid, to produce small particles that may be swallowed. The recommended dosing of Spritam® is based on indication, age group (and weight, if applicable), and renal function, with the maximum recommended dose being 1500mg twice daily. Spritam® is not yet available on the market; likewise, the estimated acquisition cost (EAC) of Spritam® is not yet available.
- **Vimpat® (lacosamide)** was FDA approved in 2008 and is indicated for monotherapy or adjunctive therapy in the treatment of partial-onset seizures in patients 17 years of age and older. Vimpat® is available as oral tablets, oral solution, and intravenous (IV) solution and is dosed twice daily. The EAC of Vimpat® has been steadily increasing over the past few years, resulting in a monthly cost of $845.40 at the maximum recommended maintenance dose of 200mg twice daily.
- **Banzel® (rufinamide)** was FDA approved in 2008 and is indicated for adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut Syndrome in patients one year of age and older. Banzel® is available as oral tablets and oral suspension and is dosed twice daily. The EAC of Banzel® has been steadily increasing over the past few years, resulting in a monthly cost of $4,173.60 at the maximum recommended dose of 3200mg per day. It is not known whether doses lower than 3200mg per day are effective.
- **Fycompa® (perampanel)** was FDA approved in 2012 and is indicated for adjunctive therapy in the treatment of partial-onset seizures with or without secondarily generalized seizures or PGTC seizures in patients with epilepsy 12 years of age and older. Fycompa® is available as oral tablets and is dosed once daily. The EAC of Fycompa® has been steadily increasing over the past few years, resulting in a monthly cost of $713.40 at the maximum recommended dose of 12mg per day.

Market News and Updates[7,8,9]

New FDA Approval:

- **February 2016:** The FDA approved Briviact® (brivaracetam) as an adjunctive treatment for partial-onset seizures in patients age 16 years and older with epilepsy. Brivaracetam is an analogue of levetiracetam and will be available as oral tablets, as an oral solution, and as an injection for intravenous (IV) use.

Recommendations

The College of Pharmacy recommends the following:

1. Revising the existing criteria for Aptiom® (eslicarbazepine) to include its new indication for monotherapy
2. The prior authorization of Spritam® (levetiracetam) with the criteria noted in red
3. The prior authorization of Vimpat® (lacosamide) with the criteria noted in red
4. The prior authorization of Banzel® (rufinamide) with the criteria noted in red
5. The prior authorization of Fycompa® (perampanel) with the criteria noted in red

New proposed criteria specific to each medication is as follows:

Aptiom® (Eslicarbazepine) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures ~~as adjunctive therapy~~; and
2. ~~Member must be on current antiepileptic drug therapy (Aptiom® is only indicated for adjunctive treatment); and~~
3. Member must not currently be taking oxcarbazepine (concurrent use is contraindicated); and
4. A patient-specific, clinically significant reason why member cannot use oxcarbazepine.
5. A quantity limit of 30 tablets per 30 days will apply on the lower strength tablets (200mg and 400mg) and 60 tablets per 30 days on the higher strength tablets (600mg and 800mg).

Spritam® (Levetiracetam) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures, myoclonic seizures, or primary generalized tonic-clonic (PGTC) seizures; and
2. A patient-specific, clinically significant reason why the member cannot use generic formulations of levetiracetam.
3. A quantity limit of 60 tablets per 30 days will apply.

Vimpat® (Lacosamide) Approval Criteria:

1. An FDA approved diagnosis of partial-onset seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Vimpat® and who have a seizure diagnosis will be grandfathered.

Banzel® (Rufinamide) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut Syndrome; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Banzel® and who have a seizure diagnosis will be grandfathered.

Fycompa® (Perampanel) Approval Criteria:

1. An FDA approved indication of adjunctive therapy in the treatment of partial-onset seizures with or without secondarily generalized seizures or primary generalized tonic-clonic (PGTC) seizures; and
2. Initial prescription must be written by a neurologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures.
4. Members currently stable on Fycompa® and who have a seizure diagnosis will be grandfathered.

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[1] Aptiom® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/aptiom-1/. Last revised 9/4/2015. Last accessed 2/11/2016.
[2] Spritam® Prescribing Information, Aprecia Pharmaceuticals Company. Available online at: http://www.spritam.com/pdfs/full-pi.pdf. Last revised 7/2015. Last accessed 1/25/2016.
[3] Micromedex 2.0: Levetiracetam Drug Information. Available online at: http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch. Last revised 12/3/2015. Last accessed 1/25/2016.
[4] Vimpat® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/vimpat-1/. Last revised 6/1/2015. Last accessed 1/28/2016.
[5] Banzel® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/banzel-1/. Last revised 6/25/2015. Last accessed 1/28/2016.
[6] Fycompa® Package Insert, Medlibrary.org. Available online at: http://medlibrary.org/lib/rx/meds/fycompa-1/. Last revised 6/26/2015. Last accessed 1/28/2016.
[7] Medscape Medical News: FDA Clears Brivaracetam (Briviact) for Partial-Onset Seizures. Available online at: http://www.medscape.com/viewarticle/859124. Last revised 2/19/2016. Last accessed 2/19/2016.
[8] FDA News Release: FDA Approves Briviact to Treat Partial-Onset Seizures. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm486827.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery. Last revised 2/19/2016. Last accessed 2/19/2016.
[9] Briviact® Prescribing Information, UCB, Inc. Available online at: http://www.briviact.com/briviact-PI.pdf. Last revised 2/2016. Last accessed 2/19/2016.

Appendix D

Vote to Prior Authorize Solaraze® (Diclofenac 3% Gel)

Oklahoma Health Care Authority
March 2016

Introduction[1]

Solaraze® (diclofenac 3% gel) is a non-steroidal anti-inflammatory drug (NSAID) indicated for the topical treatment of actinic keratosis (AK) in adult patients. AK lesions are caused by damage from the sun's ultraviolet (UV) rays and are considered a precursor of skin cancer. The recommended dosage of Solaraze® is to apply to AK lesions twice daily for 60 to 90 days. Solaraze® is available in 100 gram tubes, with a state maximum allowable cost (SMAC) of $717.00 per 100 gram tube.

Recommendations

The College of Pharmacy recommends the prior authorization of Solaraze® (diclofenac 3% gel) with the following criteria:

Solaraze® (Diclofenac 3% Gel) Approval Criteria:

1. An FDA approved diagnosis of actinic keratosis (AK); and
2. Patient-specific information must be documented on the prior authorization form, including all of the following:
    a. Number of AK lesions being treated; and
    b. Sizes of each lesion being treated; and
    c. Anticipated duration of treatment; and
3. Approval quantity and length will be based on patient-specific information provided, in accordance with Solaraze® prescribing information and FDA approved dosing regimen.

[1] Solaraze® Prescribing Information, Fougera Pharmaceuticals Inc. Available online at: http://www.solaraze.com/pdf/solaraze_pi.pdf. Last revised 12/2012. Last accessed 1/26/2016.

Appendix E

Vote to Prior Authorize Uceris® (Budesonide Extended-Release Tablets), Uceris® (Budesonide Rectal Foam), and Miscellaneous Mesalamine Products

Oklahoma Health Care Authority
March 2016

Indication(s)[1,2,3,4,5,6,7,8,9,10,11]

- **Uceris® (budesonide extended-release tablet)** is a glucocorticosteroid indicated for the induction of remission in patients with active, mild-to-moderate ulcerative colitis (UC).
- **Uceris® (budesonide rectal foam)** is a glucocorticosteroid indicated for the induction of remission in patients with active, mild-to-moderate distal UC extending up to 40cm from the anal verge.
- **Asacol HD® (mesalamine)** delayed-release tablet is an aminosalicylate indicated for the treatment of moderately active UC in adults. Safety and effectiveness of Asacol® HD beyond six weeks have not been established.
- **Pentasa® (mesalamine)** controlled-release capsule is indicated for the induction of remission and for the treatment of patients with mildly to moderately active UC.
- **Rowasa® (mesalamine)** rectal suspension enema is indicated for the treatment of active, mild-to-moderate distal UC, proctosigmoiditis, or proctitis.
- **Lialda® (mesalamine)** delayed-release capsule is a locally acting 5-aminosalicylic acid (5-ASA) indicated for the induction of remission in adults with active, mild-to-moderate UC and for the maintenance of remission of UC.
- **Colazal® (balsalazide)** capsule is indicated for the treatment of mildly to moderately active UC in patients five years of age and older. Safety and effectiveness of Colazal® beyond eight weeks in children (ages 5-17 years) and twelve weeks in adults have not been established.
- **Dipentum® (olsalazine)** capsule is indicated for the maintenance of remission of UC in patients who are intolerant of sulfasalazine.
- **Canasa® (mesalamine)** suppositories are an aminosalicylate indicated for the treatment of mildly to moderately active ulcerative proctitis. Safety and effectiveness of Canasa® beyond six weeks have not been established.
- **Apriso® (mesalamine)** extended-release capsule is indicated for the maintenance of remission of UC in patients 18 years of age and older.
- **Delzicol® (mesalamine)** delayed-release capsule is an aminosalicylate indicated for the treatment of mildly to moderately active UC in patients 12 years of age and older, and maintenance of remission of UC in adults.
- **The following medications do not require prior authorization:** sulfasalazine 500mg tablets, sulfasalazine delayed-release 500mg tablets, Rowasa® (mesalamine) rectal suspension enemas, Lialda® (mesalamine) delayed-release capsules, Colazal® (balsalazide) capsules, Dipentum® (olsalazine) capsules, Pentasa® (mesalamine) 250mg controlled-release capsules, Canasa®(mesalamine) suppositories, Apriso® (mesalamine)

extended-release capsules, Delzicol® (mesalamine) delayed-relase capsules, and hydrocortisone enemas.

Recommendations

The College of Pharmacy recommends the prior authorization of Uceris® extended-release tablets, Uceris® rectal foam, and various mesalamine products with the following criteria:

Uceris® (Budesonide) Extended-Release Tablets Approval Criteria:

1. An FDA approved diagnosis of induction of remission in patients with active, mild-to-moderate ulcerative colitis; and
2. Previous failure of at least two of the following:
    a. Oral aminosalicylates; or
    b. Topical mesalamine; or
    c. Topical steroids; or
    d. A contraindication to all preferred medications; and
3. A patient-specific, clinically significant reason why the member cannot use other oral corticosteroids available without prior authorization; and
4. Approvals will be for the duration of eight weeks in accordance with manufacturer maximum recommended duration of therapy.
5. A quantity limit of 30 tablets per 30 days will apply.

Uceris® (Budesonide) Rectal Foam Approval Criteria:

1. An FDA approved diagnosis of induction of remission in patients with active, mild-to-moderate distal ulcerative colitis extending up to 40cm from the anal verge; and
2. A patient-specific, clinically significant reason why the member cannot use oral aminosalicylates, topical mesalamine, or other topical (rectally administered) corticosteroids available without prior authorization; and
3. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy.
4. A quantity limit of 133.6 grams per 42 days will apply.

Asacol® HD (Mesalamine) Delayed-Release Tablets Approval Criteria:

1. An FDA approved indication of the treatment of moderately active ulcerative colitis; and
2. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that do not require prior authorization; and
3. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 180 tablets per 30 days will apply.

Pentasa® (Mesalamine) 500mg Controlled-Release Capsules Approval Criteria:

1. An FDA approved indication for the induction of remission or for the treatment of patients with mildly to moderately active ulcerative colitis; and
2. A patient-specific, clinically significant reason the member cannot use Pentasa® 250mg controlled-release capsules or other available mesalamine products that do not require prior authorization; and

3. Approvals will be for the duration of eight weeks in accordance with manufacturer recommended duration of therapy; and
4. A quantity limit of 240 capsules per 30 days will apply.

Rowasa® (Mesalamine) Rectal Suspension Enema Approval Criteria:

1. The first three weeks of treatment would not require prior authorization.
2. An FDA approved indication for the treatment of active, mild-to-moderate distal ulcerative colitis, proctosigmoiditis, or proctitis; and
3. A patient-specific, clinically significant reason the member cannot use Canasa® (mesalamine suppositories) which do not require prior authorization; and
4. Provider documentation member is still having active symptoms after three weeks of treatment; and
5. Approvals will be for the duration of six weeks in accordance with manufacturer recommended duration of therapy; and
6. A quantity limit of 30 enemas (1,800mL) per 30 days will apply.

Lialda® (Mesalamine) Delayed-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 60 capsules per 30 days will apply.
2. For quantity limit requests for greater than two capsules per day:
    a. An FDA approved indication for the induction of remission in patients with active, mild-to-moderate ulcerative colitis; and
    b. A patient-specific, clinically significant reason the member cannot use other available mesalamine products that are indicated to induce remission that do not require prior authorization; and
    c. Approvals will be for the duration of eight weeks in accordance with manufacturer recommended duration of therapy; and
    d. A maximum approval of 120 capsules per 30 days will apply.

Colazal® (Balsalazide) Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 270 capsules per 30 days will apply.
2. The first twelve weeks of treatment would not require prior authorization.
3. After twelve weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.
4. An age restriction of five years and older will apply.

Dipentum® (Olsalazine) Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Pentasa® (Mesalamine) 250mg Controlled-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 480 capsules per 30 days will apply.
2. The first eight weeks of treatment would not require prior authorization.
3. After eight weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Canasa® (Mesalamine) Suppositories Quantity Limit Approval Criteria:

1. A quantity limit of 30 suppositories per 30 days will apply.
2. The first six weeks of treatment would not require prior authorization.
3. After six weeks of treatment:
    a. Provider must document a patient-specific, clinically significant reason member needs longer duration of treatment.

Apriso® (Mesalamine) Extended-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 120 capsules per 30 days will apply.

Delzicol® (Mesalamine) Delayed-Release Capsules Quantity Limit Approval Criteria:

1. A quantity limit of 180 capsules per 30 days will apply.

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[1] Uceris® Extended-Release Tablets Prescribing Information, Santarus, Inc. Available online at: http://shared.salix.com/shared/pi/uceris-pi.pdf?id=792328 . Last revised: 01/2013. Last accessed 01/2016.
[2] Uceris® Rectal Foam Prescribing Information, Salix Pharmaceuticals. Available online at: http://www.valeant.com/Portals/25/Pdf/PI/UCERIS-Foam-PI.pdf . Last revised: 11/2015. Last accessed 01/2016.
[3] Asacol® HD (mesalamine) delayed-release tablets Prescribing Information. Warner Chilcott, LLC. Available online at: http://pi.actavis.com/data_stream.asp?product_group=1875&p=pi&language=E. Last revised: 10/2013. Last accessed: 01/2016.
[4] Pentasa® (mesalamine) controlled-release capsules Prescribing Information. Shire US Inc. Available online at: http://pi.shirecontent.com/pi/pdfs/pentasa_usa_eng.pdf. Last revised: 10/2015. Last accessed: 01/2016.
[5] Rowasa® (mesalamine) rectal suspension enema Prescribing Information. Meda Pharmaceuticals. Available online at: http://medapharma.us/products/pi/Rowasa_PI.pdf. Last revised: 06/2013. Last accessed: 01/2016.
[6] Lialda® (mesalamine) delayed-release tablet Prescribing Information. Shire. Available online at: http://pi.shirecontent.com/PI/PDFs/Lialda_USA_ENG.pdf. Last revised: 11/2015. Last accessed: 01/2016.
[7] Colazal® (balsalazide) capsules Prescribing Information. Salix Pharmaceuticals, Inc. Available online at: https://shared.salix.com/shared/pi/colazal-pi.pdf?id=8251081. Last revised: 02/2012. Last accessed: 01/2016.
[8] Dipentum® (olsalazine) capsule Prescribing Information. Meda Pharmaceuticals. Available online at: http://medapharma.us/products/pi/Dipentum_PI.pdf. Last revised: 01/2014. Last accessed: 01/2016.
[9] Canasa® (mesalamine) rectal suppository Prescribing Information. Aptalis Pharma US. Available online at: http://pi.actavis.com/data_stream.asp?product_group=1910&p=pi&language=E. Last revised: 12/2013. Last accessed: 01/2016.
[10] Apriso® (mesalamine) extended-release capsules Prescribing Information. Salix Pharmaceuticals Inc. Available online at: http://www.aprisorx.com/Portals/192/assets/pdf/apriso-pi.pdf. Last revised: 02/2012. Last accessed: 01/2016.
[11] Delzicol® (mesalamine) delayed-release capsules Prescribing Information. Warner Chilcott, LLC. Available online at: http://pi.actavis.com/data_stream.asp?product_group=1877&p=pi&language=E. Last revised: 10/2014. Last accessed: 01/2016.

Appendix F

Vote to Prior Authorize Mitigare™ (Colchicine Capsules) and Zurampic™ (Lesinurad)

Oklahoma Health Care Authority
March 2016

Introduction[1,2]

- **Mitigare™ (colchicine capsules)** is indicated for the prophylaxis of gout flares in adults. It was approved by the FDA in September 2014, followed shortly by the approval of the authorized generic. It is available as a 0.6mg colchicine capsule to be dosed once or twice daily without regard to meals. Mitigare™ is believed to be effective due to its ability to block neutrophil-mediated inflammatory responses induced by monosodium urate crystals in synovial fluid. It also disrupts the polymerization of β-tubulin into microtubules, thereby preventing the activation, degranulation, and migration of neutrophils to sites of inflammation. It also interferes with the inflammasome complex found in neutrophils and monocytes that mediates interleukin-1b (IL-1b) activation.
- **Zurampic™ (Lesinurad)** is an inhibitor of the urate transporter, URAT1 indicated in combination with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a XOI alone. It is not recommended for the treatment of asymptomatic hyperuricemia and it is not recommended to be used as monotherapy. Lesinurad is available as a 200mg oral tablet that should be taken once daily, in the morning, with food and water at the same time as the morning dose of XOI. Patients should be instructed to stay well hydrated when taking lesinurad.

Recommendations

The College of Pharmacy recommends the prior authorization of Mitigare™ (colchicine capsules) and Zurampic™ (Lesinurad) with the following criteria:

Mitigare™ (Colchicine Capsules) and Colcrys® (Colchicine Tablets) Approval Criteria:

1. A quantity of six tablets for a three day supply is available without prior authorization for treatment of acute gouty attacks; and
2. Failure of allopurinol after six months of treatment defined by persistent gouty attacks with serum urate levels greater than 6.0mg/dL; and
3. Patient-specific, clinically significant reason why colchicine/probenecid would not be a viable option for the member.
4. A quantity limit of 60 tablets per 30 days will apply for gout.
5. Members with the diagnosis of Familial Mediterranean Fever verified by genetic testing will be approved for up to 2.4mg per day.

Zurampic™ (Lesinurad) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of gout in patients who have not achieved target serum uric acid (sUA) levels with a xanthine oxidase inhibitor (XOI) alone; and
3. Failure of allopurinol or febuxostat alone defined by serum urate levels greater than 6.0mg/dL; and
4. Prescriber must verify that member has a creatinine clearance greater than 45mL/min prior to initiating treatment and for continued approval; and
5. Prescriber must verify that member will take Zurampic™ concomitantly with a XOI; and
6. Prescriber must document member is not taking more than 325mg of aspirin per day and member is not taking any epoxide hydrolase inhibitors; and
7. Prescriber must document member has no contraindications for use of Zurampic™ including any of the following**:** Tumor lysis syndrome or Lesch-Nyhan syndrome, severe renal impairment (CrCl less than 30mL/min), end stage renal disease, kidney transplant recipients, or patients on dialysis.
8. A quantity limit of one tablet daily will apply.

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[1]Mitigare™ Product Information. Hikma Americas, Inc/West-Ward Pharmaceutical Corp. Available online at: http://www.mitigare.com/wp-content/uploads/2015/10/pi.pdf. Last revised 09/2014. Last accessed 1/28/2016.

[2] Zurampic™ Product Information. AstraZeneca. Available online at: http://www.azpicentral.com/zurampic/zurampic.pdf. Last revised 12/2015. Last accessed 1/21/2016.

Appendix G

Vote to Prior Authorize Pazeo® (Olopatadine Ophthalmic)

Oklahoma Health Care Authority
March 2016

Introduction[1]

Pazeo® (olopatadine ophthalmic) is a mast cell stabilizer indicated for the treatment of ocular itching associated with allergic conjunctivitis. Pazeo® is available as an ophthalmic solution containing 7.76mg of olopatadine hydrochloride per one milliliter of solution (0.7%). The recommended dosage of Pazeo® is to instill one drop in each affected eye once daily.

Recommendations

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

1. The addition of Pazeo® (olopatadine solution) to Tier-3. Current Tier-3 criteria for this category will apply.
    a. Pazeo® (olopatadine solution) is currently rebated to Tier-2, but will be placed in Tier-3 if the manufacturer chooses not to participate in supplemental rebates.
2. Move olopatadine (generic Patanol®) to Tier-2 based on state maximum allowable cost (SMAC). Current Tier-2 criteria for this category will apply.

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

*Tier structure based on supplemental rebate participation and/or state maximum allowable cost (SMAC). Tier-2 medications are subject to move to Tier-3.
OTC = Over-the-counter

Ocular Allergy Tier-2 Approval Criteria:

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

Ocular Allergy Tier-3 Approval Criteria:

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

[1]Pazeo® Prescribing Information. Alcon Laboratories, Inc. Available online at: http://ecatalog.alcon.com/pi/Pazeo_us_en.pdf. Last revised 01/2015. Last accessed 01/29/2016.

Appendix H

Fiscal Year 2015 Annual Review of Multiple Sclerosis Medications

Oklahoma Health Care Authority
March 2016

Current Prior Authorization Criteria

Multiple Sclerosis Interferon Approval Criteria:

1. An FDA approved diagnosis of relapsing-remitting Multiple Sclerosis; and
2. Authorization of Tier-2 medications requires previous failure of the preferred Tier-1 product defined as:
   a. Occurrence of an exacerbation after six months; or
   b. Significant increase in MRI lesions after six months; or
   c. Adverse reactions or intolerable side effects; and
3. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
4. Compliance will be checked for continued approval every six months.

Multiple Sclerosis Interferon Medications*	
Tier-1	**Tier-2**
Interferon β - 1a (Avonex®)	Interferon β - 1a (Rebif®)
Interferon β - 1b (Betaseron®)	Interferon β – 1a (Plegridy™)
	Interferon β - 1b (Extavia®)

*Tier structure based on supplemental rebate participation.

Ampyra® (Dalfampridine) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis; and
2. Kurtzke Expanded Disability Status Scale (EDSS) score between 3 and 7.5; and
3. Initial approvals will be for the duration of 90 days. If the member has responded well to treatment and the prescriber states that the member has shown improvement or the drug was effective, the member may receive authorization for one year; and
4. A quantity limit of 60 tablets for 30 days will apply.
5. Ampyra® may be used with other Multiple Sclerosis therapies.

Aubagio® (Teriflunomide) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. All of the following will be required for initiation of treatment:
   a. Verification that female members are not pregnant and currently using reliable contraception; and
   b. Verification that member has no active infection(s); and
   c. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and

   d. Liver function tests and verification that levels are acceptable to the prescriber; and
   e. Blood pressure measurement and verification that blood pressure is being monitored; and
   f. Verification that members do not have tuberculosis, or completion of standard medical treatment for patients with tuberculosis; and
4. Initial approvals of Aubagio® will be for six months, after which time, all of the following will be required for further approval:
   a. Medication compliance; and
   b. Repeat CBC counts and verification that counts are acceptable to the prescriber; and
   c. Repeat liver function tests and verification that levels are acceptable to the prescriber; and
   d. Verification that female members are not pregnant and will continue using reliable contraception; and
   e. Verification that blood pressure and symptoms of renal failure are being monitored; and
5. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 30 tablets per 30 days will apply.

Copaxone® (Glatiramer Acetate) Approval Criteria:

1. An FDA approved diagnosis of relapsing-remitting Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Approvals for the 40mg strength of Copaxone® will require a patient-specific, clinically significant reason why the member cannot use the 20mg strength; and
4. Compliance will be checked for continued approval every six months.

Gilenya® (Fingolimod) Approval Criteria:

1. An FDA approved diagnosis of relapsing-remitting Multiple Sclerosis with at least one relapse in the previous 12 months, or transitioning from existing Multiple Sclerosis therapy; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. The first dose should be observed in the doctor's office for signs and symptoms of bradycardia for six hours after first dose; and
4. Compliance will be checked for continued approval every six months.

Lemtrada™ (Alemtuzumab) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Member must have had an inadequate response to two or more drugs indicated for the treatment of Multiple Sclerosis; and
3. Lemtrada™ 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 two hours after each infusion; and

4. The prescriber must agree to monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose of Lemtrada™; and
5. The prescriber must agree that baseline and yearly skin examinations will be performed while the member is utilizing Lemtrada™ therapy; and
6. Member, prescriber, pharmacy, and healthcare facility must all enroll in the Lemtrada™ REMS Program and maintain enrollment throughout therapy.

Tecfidera™ (Dimethyl Fumarate) Approval Criteria:

1. An FDA approved diagnosis of relapsing forms of Multiple Sclerosis; and
2. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. Verification from the prescriber that member has no active infection(s); and
4. Complete blood counts (CBC) and verification that levels are acceptable to the prescriber; and
5. Compliance will be checked for continued approval every six months; and
6. A quantity limit of 60 tablets per 30 days will apply.

Tysabri® (Natalizumab) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis or Crohn's disease; and
2. Treatment with at least two different first line therapeutic categories for Multiple Sclerosis or Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second-line alternatives; and
3. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

Utilization of Multiple Sclerosis Medications: Fiscal Year 2015

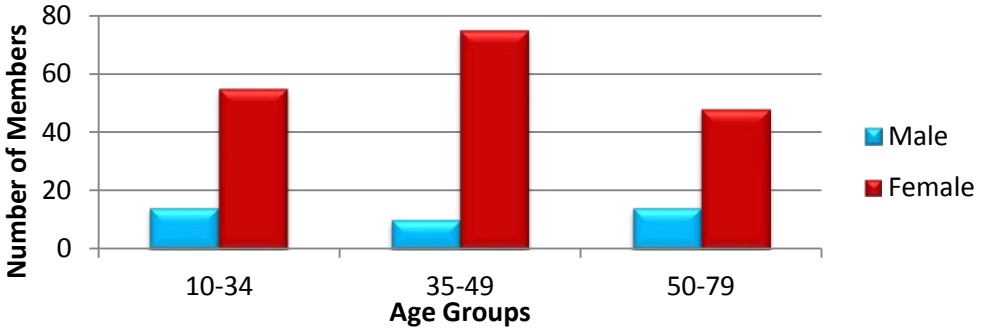
Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	209	1,514	$6,944,096.69	$4,586.59	$156.91	32,195	44,256
2015	216	1,640	$8,187,731.12	$4,992.52	$173.64	43,399	47,154
% Change	**3.30%**	**8.30%**	**17.90%**	**8.90%**	**10.70%**	**34.80%**	**6.50%**
Change	**7**	**126**	**$1,243,634.43**	**$405.93**	**$16.73**	**11,204**	**2,898**

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

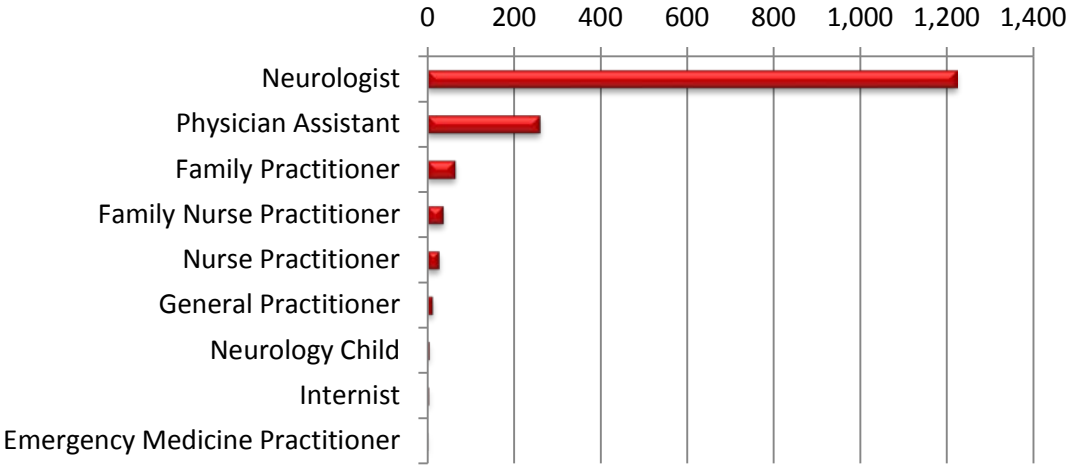
- Medical claim details for Multiple Sclerosis medications during fiscal year 2015 can be found at the end of this report.

Demographics of Members Utilizing Multiple Sclerosis Medications



All members under the age of 21 years were verified to have a diagnosis of Multiple Sclerosis (MS) in their diagnosis history, and their MS therapies were prescribed by a specialist in neurology.

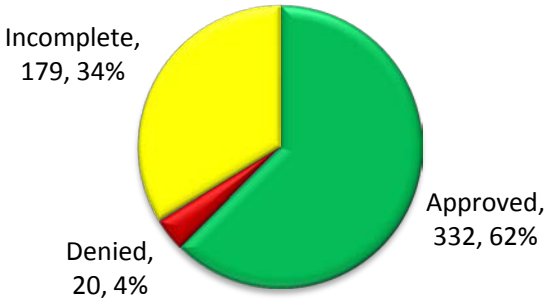
Top Prescriber Specialties of Multiple Sclerosis Medications by Number of Claims



Prior Authorization of Multiple Sclerosis Medications

There were 531 prior authorization requests submitted for 209 unique members for Multiple Sclerosis medications during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated and Recent Patent Expiration(s):

- Copaxone® (glatiramer acetate): There are no unexpired patents for the 20mg/mL strength; however the 40mg/mL strength is patented until August 2030.
- Gilenya® (fingolimod): March 2026
- Ampyra® (dalfampridine): May 2027
- Tecfidera™ (dimethyl fumarate): February 2028
- Aubagio® (teriflunomide): September 2030

Generic Formulation Update(s):

- **October 2015:** The Glatiramer Acetate Clinical Trial to Assess Equivalence With Copaxone (GATE) study demonstrated "equivalence" of a new generic formulation of glatiramer acetate to the branded Copaxone® in patients with relapsing-remitting Multiple Sclerosis (RRMS). The study is the first Phase 3 trial to assess clinical equivalence of a generic formulation of a disease-modifying agent for MS. Study results revealed that the new generic product was associated with a similar reduction in gadolinium-enhancing lesions on MRI as Copaxone® and both products were associated with greater reductions in lesions than placebo.

New FDA Approval(s):

- **December 2013:** The U.S. Food and Drug Administration (FDA) approved a label change for Tysabri® (natalizumab). The label update included the option of using Tysabri® for first-line therapy at the discretion of the prescriber. The American Academy of Neurology (AAN) retired previous guidance stating that Tysabri® was generally recommended for patients who have had an inadequate response to, or were unable to tolerate, other MS therapies. Because of the link between Tysabri® and cases of Progressive Multifocal Leukoencephalopathy (PML), previous guidance recommended that it be reserved for use in select patients with relapsing-remitting disease who have failed other therapies either through continued disease activity, medication intolerance, or who have a particularly aggressive initial disease course. Tysabri® is indicated for use as monotherapy only.
- **October 2015:** The FDA approved the first electronic automatic injector for beta interferon. The auto-injector is manufactured by Bayer and delivers Betaseron®. The older device required the patient to pull the needle out themselves and made a discernable sound during administration; the new device retracts the needle automatically and is completely silent during injection.

Safety Update(s):

- **August 2015:** The FDA is warning that a case of definite PML and a case of probable PML have been in reported in patients taking Gilenya® (fingolimod) for MS. These are the first cases of PML reported in patients taking Gilenya® who had not been previously treated with an immunosuppressant drug for MS or other medical condition(s). Information about these cases is being added to the drug labeling.
- **December 2015:** The FDA approved an update to the Warnings and Precautions section of the product labeling for interferon beta medications. The update included

information regarding the risk of thrombotic microangiopathy (TMA). Cases of TMA, including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, some fatal, have been reported with interferon beta products. Reported cases have occurred several weeks to years after starting interferon beta products. The medication should be discontinued if clinical symptoms and laboratory findings consistent with TMA occur.

Pipeline Update(s):

- **December 2014:** Novartis announced that the Phase 3 study of Gilenya® (fingolimod) in primary progressive MS did not show a significant difference between placebo in a combination of disability measures. In addition to the clinical development program with Gilenya®, Novartis is investigating BAF312 (siponimod), a selective sphingosine 1-phosphate (S1P) and 5 receptor modulator in a large Phase 3 trial in patients with secondary progressive MS.
- **June 2015:** Teva Pharmacueticals and Active Biotech announced the completion of patient enrollment for their Phase 3 trial of laquinimod in patients with RRMS. Laquinimod is an oral, central nervous system immunomodulator that works by preventing brain atrophy and slowing disease progression in MS patients.
- **April 2015:** AbbVie and Biogen announced the submission of their Biologics License Application (BLA) to the FDA for Zinbryta™ (daclizumab high-yield process). Zinbryta™ is an investigational monoclonal antibody that selectively binds to the interleukin-2 (IL-2) receptor subunit (CD25) that is expressed at high levels on T-cells that become abnormally activated in MS. The BLA included results from two trials in which Zinbryta™ 150mg was administered subcutaneously every four weeks in patients with RRMS.
- **August 2015:** Novartis announced that it acquired all remaining rights to ofatumumab, a monoclonal antibody which targets CD20 and is being developed for RRMS and other autoimmune indications. Positive Phase 2 results for ofatumumab demonstrated significant reduction of up to 90% in the number of new brain lesions in patients with MS between weeks 4-12 in the study. Ofatumumab is ready to begin Phase 3 studies.
- **September 2015:** Biogen announced an agreement to exclusively license MT-1303, an experimental oral medicine that targets S1P receptors. Biogen is assessing the potential of MT-1303 in MS, ulcerative colitis, Crohn's disease, and other autoimmune indications. The compound has completed a successful Phase-2 clinical trial in MS and Biogen is evaluating a rapid development program in this indication.
- **October 2015:** Roche announced positive results from three Phase-3 studies of an investigational monoclonal antibody, ocrelizumab, designed to selectively target CD20-positive B cells. CD20-positive B cells are thought to be a contributor to myelin and axonal damage. Ocrelizumab showed superiority to interferon beta-1a in two Phase-3 studies in patients with relapsing forms of MS. Ocrelizumab also showed efficacy in patients with primary progressive MS, and is the first investigational medicine to do so.
- **October 2015:** Studies presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) highlighted the efficacy of rituximab in RR, secondary progressive, and primary progressive MS by showing reduced relapse rates and slowed progression compared to conventionally treated patients. Despite the promising results, none of the studies presented were randomized, prospective, controlled trials; no randomized, controlled trials are currently planned for rituximab in

MS by the manufacturer, Roche. Similarly to ocrelizumab, rituximab targets CD20-positive B-cells to preclude myelin and axonal damage.

- **October 2015:** Minocycline was found to reduce the absolute risk of developing MS by 27.4%, and the relative risk by 44.6%, compared with placebo in adult patients with clinically isolated syndrome. The risk reductions are comparable with the efficacy of other FDA approved therapies. It is not clear how minocycline affects MS, but it has multiple immune-modulating effects, including preventing leukocytes from crossing the blood brain barrier.

Cost Analysis[16]

A recent article published in *Neurology* evaluated the price increases of the disease-modifying therapies for MS. The study found that first-generation disease-modifying therapies initially cost $8,000 to $11,000 per year, but currently cost around $60,000 per year. The authors stated that costs for these medications have increased yearly at rates five to seven times greater than prescription drug inflation, and that newer disease-modifying therapies launch with a cost 25%-60% greater than existing disease-modifying therapies.

SoonerCare is not immune to the cost increases among disease-modifying therapies. The comparison of fiscal years revealed an increase in spending of greater than $1.2 million. Limited generic availability among these agents restricts further cost-management measures. It is important to note that the consumer price index (CPI) penalty of the federal rebate is designed to keep Medicaid net cost relatively flat. The cost increases in the report do not reflect the net cost increases.

Recommendations

The College of Pharmacy recommends updating the criteria for Tysabri® (natalizumab) to reflect current indications and clinical guidelines.

Tysabri® (Natalizumab) Approval Criteria:

1. An FDA approved diagnosis of Multiple Sclerosis (MS) or Crohn's disease; and
2. ~~Treatment with at least two different first line therapeutic categories for MS that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second line alternatives.~~ For a diagnosis of MS the following criteria will apply:
    a. Prescriber must be a neurologist or be an advanced care practitioner with a supervising prescriber that is a neurologist; and
    b. Approvals will not be granted for concurrent use with other disease-modifying therapies; and
3. For a diagnosis of Crohn's disease the following criteria will apply:
    a. Treatment with at least two different first line therapeutic categories for Crohn's disease that have failed to yield an adequate clinical response, or a patient-specific, clinically significant reason why the member cannot use all available first and second line alternatives; and
4. Prescriber, infusion center, and member must enroll in the TOUCH Prescribing Program.

Utilization Details of Multiple Sclerosis Medications: Fiscal Year 2015

Pharmacy Claims: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim
Tier-1 Interferon Beta-1a Products					
AVONEX PREFILLED KIT 30MCG	66	9	$332,351.28	$177.54	$5,035.63
AVONEX PEN KIT 30MCG	41	8	$207,640.90	$180.87	$5,064.41
Subtotal	**107**	**15**	**$539,992.18**	**$178.81**	**$5,046.66**
Tier-1 Interferon Beta-1b Products					
BETASERON INJ 0.3MG	33	6	$171,582.80	$184.90	$5,199.48
Subtotal	**33**	**6**	**$171,582.80**	**$184.90**	**$5,199.48**
Tier-1 Subtotal	**140**	**21**	**$711,574.98**	**$180.24**	**$5,082.68**
Tier-2 Interferon Beta-1a Products[+]					
REBIF INJ 44/0.5	102	14	$558,338.19	$194.54	$5,473.90
REBIF REBIDO INJ 44/0.5	66	13	$361,444.62	$194.95	$5,476.43
REBIF INJ 22/0.5	28	4	$153,416.98	$177.98	$5,479.18
REBIF REBIDO SOL TITRATN	4	4	$21,420.56	$178.50	$5,355.14
REBIF TITRTN INJ PACK	3	3	$15,678.36	$174.20	$5,226.12
Subtotal	**203**	**30**	**$1,110,298.71**	**$191.56**	**$5,469.45**
Tier-2 Peginterferon Beta-1a Products					
PLEGRIDY INJ PEN	11	2	$57,641.70	$187.15	$5,240.15
PLEGRIDY PEN INJ STARTER	3	3	$15,393.49	$178.99	$5,131.16
Subtotal	**14**	**3**	**$73,035.19**	**$185.37**	**$5,216.80**
Tier-2 Subtotal	**217**	**32**	**$1,183,333.90**	**$191.17**	**$5,453.15**
Dalfampridine Products					
AMPYRA TAB 10MG	151	22	$266,531.23	$58.84	$1,765.11
Subtotal	**151**	**22**	**$266,531.23**	**$58.84**	**$1,765.11**
Teriflunomide Products					
AUBAGIO TAB 14MG	45	7	$232,791.21	$184.75	$5,173.14
AUBAGIO TAB 7MG	2	2	$10,725.14	$191.52	$5,362.57
Subtotal	**47**	**9**	**$243,516.35**	**$185.04**	**$5,181.20**
Glatiramer Acetate Products					
COPAXONE KIT 20MG/ML	416	63	$2,132,920.11	$180.39	$5,127.21
COPAXONE INJ 40MG/ML	135	26	$797,976.72	$197.03	$5,910.94
Subtotal	**551**	**79**	**$2,930,896.83**	**$184.64**	**$5,319.23**
Fingolimod Products					
GILENYA CAP 0.5MG	237	29	$1,250,647.40	$187.95	$5,276.99
Subtotal	**237**	**29**	**$1,250,647.40**	**$187.95**	**$5,276.99**
Dimethyl Fumarate Products					
TECFIDERA CAP 240MG	244	43	$1,335,975.70	$182.51	$5,475.31
TECFIDERA MIS STARTER	26	23	$141,820.88	$181.82	$5,454.65
TECFIDERA CAP 120MG	1	1	$5,377.09	$192.04	$5,377.09
Subtotal	**271**	**51**	**$1,483,173.67**	**$182.48**	**$5,472.97**
Natalizumab Products					
TYSABRI INJ 300MG/15ML	26	4	$118,056.76	$229.68	$4,540.64
Subtotal	**26**	**4**	**$118,056.76**	**$229.68**	**$4,540.64**
Total	**1,640**	**216***	**$8,187,731.12**	**$173.64**	**$4,992.52**

*Total number of unduplicated members.

[+]Effective January 1st 2015 Tier-1 product, Rebif®, was moved to Tier-2 based on supplemental rebate participation/net cost.

Medical Claims: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Cost/ Claim
Natalizumab Products					
TYSABRI INJ 300MG/15ML (J2323)	124	17	$554,004.00	7.29	$4,467.77
Total	**124***	**17**	**$554,004.00**	**7.29**	**$4,467.77**

*Total number of unduplicated members.

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[6] U.S. Food and Drug Administration. FDA Drug Safety Communication: FDA Warns About Cases of Rare Brain Infection with MS Drug Gilenya® (fingolimod) in Two Patients with No Prior Exposure to Immunosuppressant Drug. Available online at: http://www.fda.gov/drugs/drugsafety/ucm456919.htm. Last revised 01/2016. Last accessed 02/15/16.

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[11] Novartis. Novartis Acquires All Remaining Rights to GSK's Ofatumumab to Develop Treatments for MS and Other Autoimmune Indications. Available online at: https://www.novartis.com/news/media-releases/novartis-acquires-all-remaining-rights-gsks-ofatumumab-develop-treatments-ms-and. Last revised 08/2015. Last accessed 02/16/2016.

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Appendix I

Calendar Year 2015 Annual Review of Naloxone Medications and 30-Day Notice to Prior Authorize Evzio® (Naloxone Auto-Injector)

Oklahoma Health Care Authority
March 2016

Current Prior Authorization Criteria

Naloxone injection and nasal spray are currently covered without prior authorization.

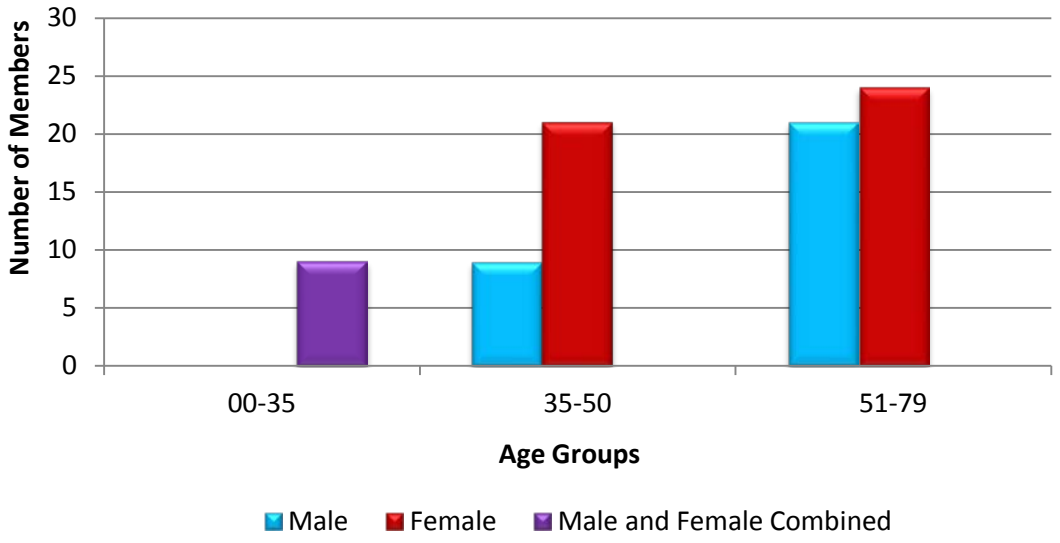
Utilization of Naloxone Medications: Calendar Year 2015

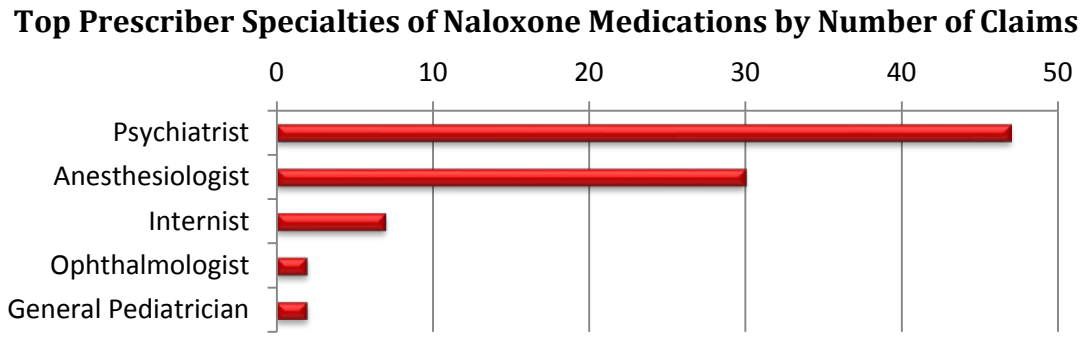
Comparison of Calendar Years

Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	2	2	$69.27	$34.63	$7.70	3	9
2015	84	88	$6,073.19	$69.01	$5.77	3,212	1,053
% Change	**4,100.0%**	**4,300.0%**	**8,667.4%**	**99.30%**	**-25.10%**	**106,966.7%**	**11,600.0%**
Change	**82**	**86**	**$6,003.92**	**$34.38**	**-$1.93**	**3,209**	**1,044**

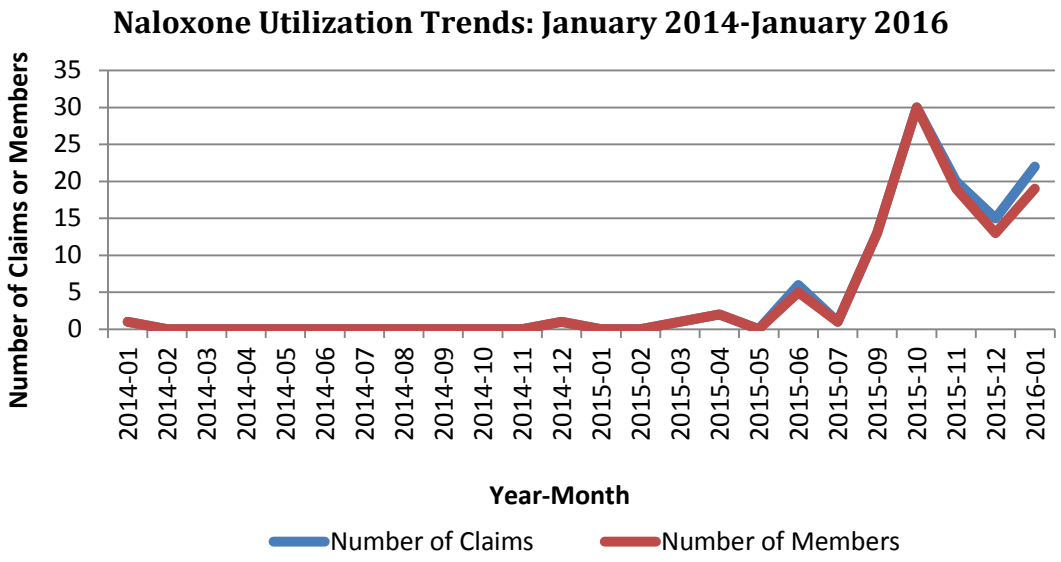
*Total number of unduplicated members.

Demographics of Members Utilizing Naloxone Medications





Naloxone Medication Utilization Analysis



In August 2015, the Oklahoma Health Care Authority (OHCA) sent out an informational fax through the College of Pharmacy to pharmacies regarding injectable formulations of naloxone available for SoonerCare members. The fax highlighted the growing concern for opioid overdose deaths and the importance of naloxone to save lives in the event of an opioid overdose. In addition, the educational intervention highlighted recent legislation interpreted by the Oklahoma State Board of Pharmacy and the U.S. Food and Drug Administration (FDA) to allow pharmacists to dispense naloxone without a prescription, but the pharmacy must have an established protocol or collaborative practice agreement in place to do so. Pharmacies were encouraged to consider making naloxone available for at-risk SoonerCare members. Immediately following the fax a promising increase in both claims and number of members utilizing naloxone can be seen on the above graph. Further interventions are warranted to increase awareness of available naloxone medications.

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

Anticipated Patent Expiration(s):

- Evzio® (naloxone auto-injector): February 2032
- Narcan® (naloxone nasal spray): March 2035

FDA Approval(s):

- **November 2015:** The FDA approved Narcan® (naloxone nasal spray), the first FDA-approved nasal spray version of naloxone hydrochloride. Until this approval, naloxone was only approved in injectable forms. A nasal spray formulation of naloxone may be easier to deliver, and eliminates the risk of a contaminated needle stick. Prior to Narcan® nasal spray, there has been widespread use of unapproved naloxone kits that combine an injectable formulation of naloxone with an atomizer that can deliver naloxone nasally. With the approval of Narcan® nasal spray, there is now access to an FDA-approved product. Narcan® nasal spray does not require assembly and delivers a measured dose. Narcan® nasal spray can be used in adults or children and can be administered by individuals without medical training. The drug is sprayed into one nostril while the patient is lying on his or her back, and can be repeated if necessary.

Guidelines:

- **2014:** The World Health Organization (WHO) published guidelines for the community management of opioid overdose. The guidelines are strongly in favor of naloxone distribution "due to its clear potential for saving lives and apparent low risk of significant adverse effects." The guidelines elaborated further on the availability of naloxone indicating that naloxone distribution and training interventions are currently cost-effective for the treatment of opioid overdose in the community; however should the price increase due to the development of new formulations this may be a less cost-effective intervention. Additionally, the guidance found no difference between the administration of intranasal naloxone and intramuscular naloxone. (WHO 2014)
- **June 2015:** The Centers for Disease Control and Prevention (CDC) released summary results of several surveys conducted to evaluate the programs offering opioid overdose prevention services to laypersons and number of overdose reversals associated with naloxone administration. The summary found a national increase from 2010 of 243% in the number of local sites providing naloxone, 187% increase in the number of laypersons provided naloxone kits, and 160% increase in the number of reversals reported. The CDC included that "providing naloxone kits to laypersons reduces overdose deaths, is safe, and is cost-effective." (CDC 2015)
- **January 2016:** The Center for Medicaid and CHIP Services released an informational bulletin detailing best practices for addressing prescription opioid overdoses, misuse, and addiction. The bulletin outlined strategies for increasing the use of naloxone to reverse drug overdoses and reduce opioid-related overdose deaths. Some suggested strategies outlined in the bulletin included expanding access by making it available without a prescription, and increased naloxone administration training for opioid users, their families and friends, prescribers, and pharmacies.

Evzio® (Naloxone Auto-Injector) Product Summary[6,7]

Indications: Evzio® (naloxone auto-injector) is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and central nervous system depression. Evzio® is intended for immediate administration as emergency therapy in settings where opioids may be present. Evzio® is not a substitute for emergency medical care.

Dosing:

- Evzio® is supplied in a carton containing two pre-filled 0.4mg/0.4mL naloxone hydrochloride auto-injectors and a speaker that provides voice instructions to guide the user through each step of the injection. Each auto-injector contains a single dose of naloxone.
- Evzio® is for intramuscular and subcutaneous use only.
    - Evzio® should be administered according to the printed instructions on the device label or the electronic voice instructions.
    - The initial dose of Evzio® should be administered into the anterolateral aspect of the thigh, through clothing if necessary.
- Upon actuation, Evzio® automatically administers the needle intramuscularly or subcutaneously, delivers 0.4mg naloxone injection, and retracts the needle into its housing. Post-injection, the black base locks in place, a red indicator appears in the viewing window, and electronic visual and audible instructions signal that Evzio® has delivered the intended dose of naloxone and instructs the user to seek emergency medical attention.
- Because treatment of suspected opioid overdose must be performed by someone other than the patient, the prescription recipient should be instructed to inform those around them about the presence of Evzio® and the instructions for use.
- Emergency medical care should be sought after use. Additional doses of Evzio® may be required until emergency medical assistance becomes available.

Mechanism of Action: Naloxone is an opioid antagonist that antagonizes opioid effects by competing for the same receptor sites. Naloxone reverses the effects of opioids including respiratory depression, sedation, and hypotension.

Contraindications: Evzio® is contraindicated in patients known to be hypersensitive to naloxone or to any of the other ingredients.

Warning and Precautions:

- <u>Duration of Effect:</u> The duration of action of most opioids is likely to exceed that of Evzio® resulting in a return of respiratory and central nervous system depression after an initial improvement in symptoms. It is necessary to seek immediate emergency medical assistance after delivering the first dose of Evzio®, the patient should be kept under continued surveillance, and given repeat doses of Evzio® as necessary.
- <u>Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists:</u> Reversal of respiratory depression by partial agonists or mixed agonists/antagonists such as buprenorphine and pentazocine, may be incomplete. Large doses of naloxone are required to antagonize buprenorphine because buprenorphine has a long duration of action due to its slow rate of binding and subsequent slow dissociation from the opioid receptor.
- <u>Precipitation of Severe Opioid Withdrawal:</u> The use of Evzio® in patients who are opioid dependent may precipitate an acute abstinence syndrome characterized by the following: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea/vomiting, nervousness, restlessness/irritability, shivering/ trembling, abdominal cramps, weakness, and increased blood pressure. In neonates, opioid withdrawal may be life-threatening if not recognized and properly treated.

Adverse Reactions: The following adverse reactions have been reported with use of naloxone in the post-operative setting: hypotension, hypertension, ventricular tachycardia and fibrillation, dyspnea, pulmonary edema, and cardiac arrest. Death, coma, and encephalopathy have been reported as consequences of these effects. Abrupt reversal of opioid effects in persons who were physically dependent on opioids has precipitated an acute withdrawal syndrome.

Use in Special Populations:

- Pregnancy: Evzio® is pregnancy category B. There are no adequate or well-controlled studies with Evzio® in pregnant women. Animal studies were conducted with naloxone given during organogenesis in mice and rats at doses up to 8-times the dose of a 50kg human given 10mg/day. These studies demonstrated no embryotoxic or teratogenic effects. Naloxone crosses the placenta, and may precipitate withdrawal in the fetus as well as in the opioid-dependent mother.
- Nursing Mothers: It is not known whether naloxone is present in human milk. Caution should be exercised when Evzio® is administered to a nursing woman.
- Pediatric Use: The safety and effectiveness of Evzio® have been established in pediatric patients for known or suspected opioid overdose. Use of naloxone in pediatric patients is supported by evidence from 15 clinical studies in which neonates and pediatric patients received parenteral naloxone. Absorption of naloxone following subcutaneous or intramuscular administration in pediatric patients may be erratic or delayed. Even when the pediatric patient responds to the naloxone injection they must be monitored for at least 24 hours as a relapse may occur as naloxone is metabolized. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening and should be treated according to protocols developed by neonatology experts.
- Geriatric Use: The systemic exposure of naloxone can be greater in these patients. Clinical studies of naloxone did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects.

Efficacy:

- The safety and bioavailability of Evzio® were evaluated in a randomized, single-blind, crossover study in thirty healthy adult subjects. The primary objective of the study was to compare the pharmacokinetics of 0.4mg naloxone following a single intramuscular or subcutaneous injection administered using either Evzio® or a standard syringe. The secondary objective of the study was to evaluate the safety and tolerability of naloxone injection by Evzio® in comparison to the standard syringe. Subjects received two doses with either Evzio® or the standard syringe on Day 1 and the alternate product on Day 2. Safety and tolerability were evaluated by physical examinations, vital sign assessments, electrocardiograms, and injection site assessments.
    - Evzio® was well tolerated with comparable bioavailability to 0.4mg naloxone HCl delivered via standard syringe. Evzio® provided equivalent naloxone area under the curve (AUC) and 15% greater naloxone C_{max} in comparison to the standard syringe. Median T_{max} was reached at 15 minutes with Evzio® versus 20 minutes with the standard syringe. There were no clinically significant safety findings, and no serious adverse events.

- The usability of Evzio® was evaluated in an open-label study of forty participants. Participants simulated an injection of naloxone using Evzio® on a simulated patient without prior training. The testing environment included variables aimed at inducing stress (e.g., TV playing, observer standing in room, life-like mannequin). Participants were required to follow the on-device written and audio instructions without practice or moderator assistance. The primary endpoint of the study was a successful injection with Evzio® without training. This endpoint was assessed through evaluation of the number and type of use-related errors and the analysis and residual risk associated with Evzio® use.
    - A total of 90% of participants successfully simulated using Evzio® without training.

Cost Comparison:

Medication	Cost/mL	Package Size	Cost/Package
Evzio® (naloxone auto-injector)	**$4,950.00**	**0.8mL (two 0.4mL syringes)**	**$3,960.00**
Narcan® (naloxone nasal spray)	$66.00[+]	8mg (two 4mg blister packages)	$132.00
Naloxone 0.4mg/mL Syringe	$16.30*	1mL	$16.30

*Cost/mL based on state maximum allowable costs (SMAC); all other costs not denoted with an asterisk are based on estimated acquisition cost (EAC).
[+]Cost per blister package. Each carton contains two blister packages each with a single dose of naloxone nasal spray.
Costs listed in the table above do not take into account federal or supplemental rebate participation; therefore, do not reflect net costs.

Recommendations

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

Evzio® (Naloxone Auto-Injector) Approval Criteria:

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

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

Utilization Details of Naloxone Medications: Calendar Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Claims/ Member	Cost/ Claim
NALOXONE INJECTION					
NALOXONE HCL INJECTION 1MG/1ML	84	81	$3,755.85	1.04	$44.71
Subtotal	**84**	**81**	**$3,755.85**	**1.04**	**$44.71**
NALOXONE AUTO-INJECTOR					
EVZIO INJECTION 0.4MG/ML	4	3	$2,317.34	1.33	$579.34
Subtotal	**4**	**3**	**$2,317.34**	**1.33**	**$579.34**
Total	**88**	**84***	**$6,073.19**	**1.05**	**$69.01**

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

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 02/24/2016. Last accessed 02/24/2016.
[2] FDA: FDA moves quickly to approve easy-to-use nasal spray to treat opioid overdose. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm473505.htm. Last revised 11/19/2015. Last accessed 02/24/2016.
[3] World Health Organization. Community Management of Opioid Overdose. Available online at: http://www.who.int. Last revised 2014. Last accessed 02/24/2016.
[4] Centers for Disease Control and Prevention. Opioid Overdose Prevention Programs Providing Naloxone to Laypersons – United States, 2014. Available online at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a2.htm. Last revised 06/2015. Last accessed 02/23/2016.
[5] Center for Medicaid and CHIP Services. CMCS Informational Bulletin: Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction. Available online at: https://www.medicaid.gov/federal-policy-guidance/downloads/CIB-02-02-16.pdf. Last revised 01/2016. Last accessed 02/23/2016.
[6] Evzio® Prescribing Information. Kaléo, Inc. Available online at: http://www.evzio.com/pdfs/Evzio%20PI.PDF. Last revised 04/2014. Last accessed 02/24/2016.
[7] Kaléo, Inc. Evzio® Bioavailability, Safety, and Usability. Available online at: http://www.evzio.com/hcp/about-evzio/safety-and-usability.php. Last revised 02/2016. Last accessed 02/24/2016.

Appendix J

Fiscal Year 2015 Annual Review of Pulmonary Arterial Hypertension Medications and 30-Day Notice to Prior Authorize Uptravi® (Selexipag)

Oklahoma Health Care Authority
March 2016

Current Prior Authorization Criteria

Revatio® (Sildenafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist.
3. A quantity limit of 90 tablets per 30 days will apply.

Revatio® (Sildenafil Suspension) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. An age restriction will apply. The oral suspension formulation may be approvable for ages six years and younger. Members seven years and older must have a patient-specific, clinically significant reason why the member is not able to use the oral tablet formulation.
4. A quantity limit of 224mL per 30 days (two bottles) will apply.

Adcirca® (Tadalafil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. A patient-specific, clinically significant reason why the member cannot use generic sildenafil oral tablets; and
4. A quantity limit of 60 tablets per 30 days will apply.

Adempas® (Riociguat) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension; and
    a. Members with a diagnosis of pulmonary arterial hypertension must have previous failed trials of at least one of each of the following categories:
        i. Revatio® (sildenafil) or Adcirca® (tadalafil); and
        ii. Letairis® (ambrisentan) or Tracleer® (bosentan); and
    b. Members with a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) must currently be on anticoagulation therapy; and
2. Medical supervision by a pulmonary specialist or cardiologist; and
3. Member must not be on any concurrent phosphodiesterase (PDE) inhibitor therapy; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Adempas® REMS program.
5. A quantity limit of 90 tablets per 30 days will apply.

Orenitram™ (Treprostinil) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist or cardiologist; and
4. A quantity limit of 90 tablets per 30 days will apply.

Opsumit® (Macitentan) Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension; and
2. Previous failed trials of at least one of each of the following categories:
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
3. Medical supervision by a pulmonary specialist or cardiologist; and
4. Female members and all healthcare professionals (prescribers and dispensing pharmacies) must be enrolled in the Opsumit® REMS program.
5. A quantity limit of 30 tablets per 30 days will apply.

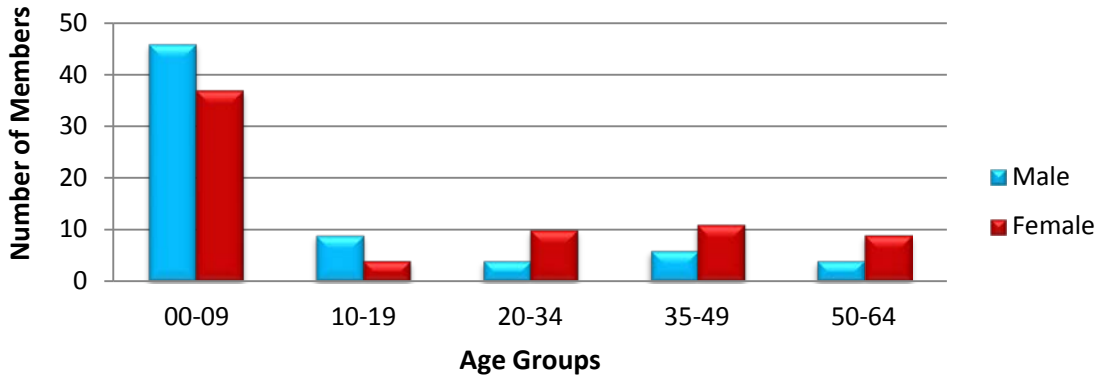
Utilization of Pulmonary Arterial Hypertension Medications: Fiscal Year 2015

Comparison of Fiscal Years

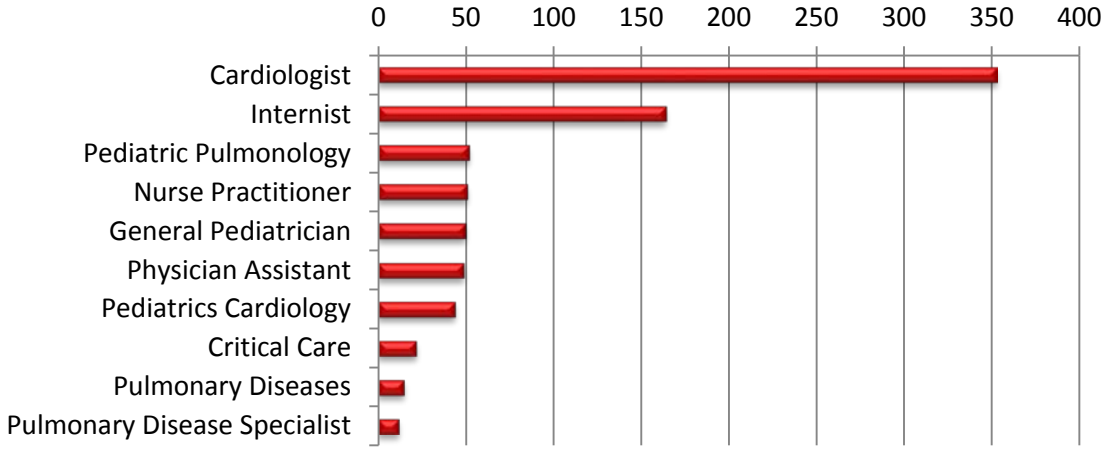
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	132	890	$1,697,570.59	$1,907.38	$63.42	102,933	26,767
2015	140	859	$2,142,517.18	$2,494.20	$81.62	122,428	26,251
% Change	**6.10%**	**-3.50%**	**26.20%**	**30.80%**	**28.70%**	**18.90%**	**-1.90%**
Change	**8**	**-31**	**$444,946.59**	**$586.82**	**$18.20**	**19,495**	**-516**

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

Demographics of Members Utilizing Pulmonary Arterial Hypertension Medications



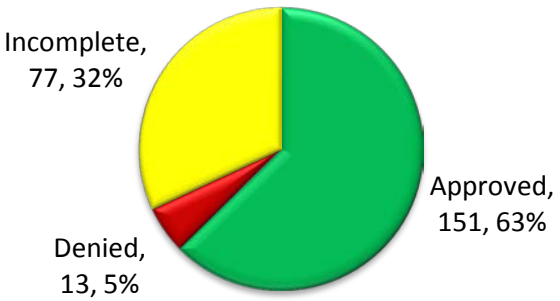
Top Prescriber Specialties of Pulmonary Arterial Hypertension Medications by Number of Claims



Prior Authorization of Pulmonary Arterial Hypertension Medications

There were 241 prior authorization requests submitted for pulmonary arterial hypertension medications during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



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

Anticipated and Recent Patent Expirations:

- Tracleer® (bosentan): November 2015
- Adcirca® (tadalafil): November 2020
- Adempas® (riociguat): April 2023
- Letairis® (ambrisentan): December 2027
- Opsumit® (macitentan): April 2029
- Orenitram™ (treprostinil): January 2031

New FDA Approved Products/Indications:

- **October 2015:** Letairis® (ambrisentan) was approved by the U.S. Food and Drug Administration (FDA) for treatment of pulmonary arterial hypertension (PAH) (World Health Organization {WHO} Group 1) in combination with tadalafil to reduce risks of disease progression and hospitalization for worsening PAH, and to improve tolerability. This is in addition to its indication as monotherapy to improve exercise ability and delay clinical worsening. The AMBITION study published in *The New England Journal of Medicine* in August of 2015 supported the new indication.
- **December 2015:** The FDA approved Uptravi® (selexipag) as an Orphan Drug for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

New Clinical Data:

- **November 2015:** Pediatric Pulmonary Hypertension Guidelines from the American Heart Association and American Thoracic Society were published in *Circulation*. These are the first guidelines published to make recommendations on the diagnosis, evaluation, and treatment of pediatric pulmonary hypertension (PH); however, since there are few studies done in pediatric patients the recommendations are based on an element of evidence based medicine and the consensus of expert opinion. Class I guideline recommendations include the use of inhaled nitric oxide (iNO) in newborns for persistent PH to reduce the need for extracorporeal membrane oxygenation support and evaluation and treatment of pediatric PH outpatients at comprehensive, multidisciplinary clinics at specialized pediatric centers. It is important to note that pediatric PH is distinct from adult PH with the most important distinction being pediatric PH is intrinsically linked to issues of lung growth and development, including many prenatal and postnatal influences. The development of PH in the neonate and young infant is often related to impaired functional and structural adaptation of the pulmonary circulation during transition from fetal to postnatal life.

Uptravi® (Selexipag) Product Summary[7,8,9]

Indications: Uptravi® (selexipag) is a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Dosing:

- Uptravi® is available as oral tablets in the following strengths: 200mcg, 400mcg, 600mcg, 800mcg, 1,000mcg, 1,200mcg, 1,400mcg, and 1,600mcg.
- The recommended starting dose is 200mcg by mouth twice daily.
- The dose should be increased by 200mcg twice daily at weekly intervals to the highest tolerated dose up to 1,600mcg twice daily.
- The maintenance dose is determined by tolerability.
- For patients with moderate hepatic impairment, the starting dose is 200mcg once daily, and the dose should be increased by 200mcg once daily at weekly intervals to the highest tolerated dose up to 1,600mcg once daily.

Mechanism of Action:

- Selexipag is an oral prostacyclin receptor (IP receptor) agonist that is structurally distinct from prostacyclin. Selexipag is hydrolyzed by carboxylesterase-1 to yield its active metabolite, which is approximately 37-fold as potent as selexipag. Selexipag and the active metabolite are selective for the IP receptor versus other prostanoid receptors (e.g., EP1-4, DP, FP, and TP).
- PH is associated with vasoconstriction, thrombosis, and cellular proliferation. Prostacyclin is a potent vasodilator and possesses antithrombotic and antiproliferative properties. Selexipag acting as an IP agonist potentially provides benefit with these three mechanisms of PH.

Contraindications: None.

Safety:

- Pulmonary Veno-Occlusive Disease (PVOD): Should signs of pulmonary edema occur, the possibility of PVOD should be considered. If confirmed, treatment with selexipag should be discontinued.

Adverse Reactions: Adverse reactions in clinical studies occurring more frequently (≥5%) with selexipag compared to placebo are headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, and flushing.

Efficacy: The safety and efficacy of selexipag were based on a long-term, placebo-controlled study involving 1,156 subjects with symptomatic PAH. The primary endpoint was the first occurrence of death, hospitalization for PAH, or evidence of disease progression.

- Compared to placebo, treatment with selexipag resulted in a 40% reduction in the occurrence of the primary endpoint events ($p < 0.0001$). The primary benefit was attributable to a reduction in hospitalization for PAH and a reduction in other disease progression events.
- More deaths occurred in the selexipag arm in comparison to the placebo arm (28 patients [4.9%] vs. 18 patients [3.1%]). It is not known if the excess number of deaths in the selexipag arm was drug-related because there were so few deaths and the imbalance was not observed until 18 months into the study.

Cost Comparison:

Drug	Strength	Cost per Tablet	Cost per Month**
Uptravi® (selexipag) tablet	**200mcg**	**$164.38**	**$9,862.80**
Uptravi® (selexipag) tablet	**400, 600, 800, 1000, 1200, 1400, 1600mcg**	**$255.55**	**$15,333.00**
Uptravi® (selexipag) titration pack	**200mcg and 800mcg**	**$115.00**	**$23,000.00**
Orenitram™ (treprostinil) tablet	0.25mg	$10.30	$618.00[+]
sildenafil tablet	20mg	$0.62*	$55.80
Tracleer® (bosentan) tablet	125mg	$162.78	$9,766.80

Costs listed are based on estimated acquisition cost (EAC) unless otherwise noted.
*Cost based on state maximum allowed cost (SMAC).
[+]Based on 0.25mg twice daily. Dose may be titrated up based on tolerability.
** Costs do not reflect rebated prices or net costs.

Recommendations

The College of Pharmacy recommends the prior authorization of Uptravi® (selexipag) tablets with the following criteria:

Uptravi® (Selexipag) Tablets Approval Criteria:

1. An FDA approved diagnosis of pulmonary arterial hypertension (PAH); and
2. Member must be 18 years of age or older; and
3. Previous failed trials of at least one of each of the following categories (alone or in combination):
    a. Revatio® (sildenafil) or Adcirca® (tadalafil); and
    b. Letairis® (ambrisentan) or Tracleer® (bosentan); and
4. Medical supervision by a pulmonary specialist and/or cardiologist; and
5. A quantity limit of two tablets daily will apply for all strengths with an upper dose limit of 1600mcg twice daily.

Utilization Details of Pulmonary Arterial Hypertension Medications: FY 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
PHOSPHODIESTERASE-5 INHIBITOR (PDE-5)						
SILDENAFIL TAB 20MG	472	99	$24,677.71	$1.77	$52.28	1.15%
ADCIRCA TAB 20MG	151	21	$202,181.74	$42.39	$1,338.95	9.44%
REVATIO SUS 10MG/ML	39	19	$263,667.41	$161.96	$6,760.70	12.31%
REVATIO TAB 20MG	3	1	$7,272.51	$80.81	$2,424.17	0.34%
SUBTOTAL	**665**	**140**	**$497,799.37**	**$71.73**	**$2,644.03**	**23.24%**
ENDOTHELIN RECEPTOR ANTAGONISTS (ERA)						
TRACLEER TAB 62.5MG	74	11	$146,927.07	$66.60	$1,985.50	6.86%
TRACLEER TAB 125MG	24	4	$200,311.99	$278.21	$8,346.33	9.35%
LETAIRIS TAB 10MG	24	4	$179,759.83	$249.67	$7,489.99	8.39%
LETAIRIS TAB 5MG	7	1	$51,427.49	$244.89	$7,346.78	2.40%
OPSUMIT TAB 10MG	1	1	$7,587.07	$252.90	$7,587.07	0.35%
SUBTOTAL	**130**	**21**	**$586,013.45**	**$218.45**	**$6,551.13**	**27.35%**
PROSTACYCLIN VASODILATORS						
REMODULIN INJ	27	4	$661,388.39	$838.26	$24,495.87	30.87%
FLOLAN INJ 1.5MG	12	1	$102,555.91	$276.43	$8,546.33	4.79%
VENTAVIS SOL	9	1	$177,598.65	$657.77	$19,733.18	8.29%
REMODULIN INJ	7	2	$67,382.67	$320.87	$9,626.10	3.15%
VELETRI INJ 1.5MG	3	1	$4,911.28	$59.17	$1,637.09	0.23%
ORENITRAM TAB	2	1	$2,779.34	$46.32	$1,389.67	0.13%
VENTAVIS SOL	2	1	$37,046.02	$617.43	$18,523.01	1.73%
ORENITRAM TAB 1MG	1	1	$1,976.54	$65.88	$1,976.54	0.09%
REMODULIN INJ	1	1	$3,065.56	$102.19	$3,065.56	0.14%
SUBTOTAL	**64**	**13**	**$1,058,704.36**	**$331.59**	**$9,888.15**	**49.42%**
TOTAL	**859**	**140***	**$2,142,517.18**	**$81.62**	**$7,351.40**	**100%**

*Total number of unduplicated members.

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

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last updated: 01/2016. Last accessed: 02/2016.

[2] FDA Approves New Orphan Drug to Treat Pulmonary Arterial Hypertension. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm478599.htm . Last updated: 12/2015. Last accessed: 02/2016.

[3] U.S. Food and Drug Administration Approves New Treatment Combination of Gilead's Letairis® with Tadalafil for Pulmonary Arterial Hypertension (WHO Group 1). Available at: https://www.gilead.com/news/press-releases/2015/10/us-food-and-drug-administration-approves-new-treatment-combination-of-gileads-letairis-with-tadalafil-for-pulmonary-arterial-hypertension-who-group-1. Last updated: 10/2015. Last accessed: 02/2016.

[4] "Initial Use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension." *New England Journal of Medicine*. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1413687. Last updated: 08/2015. Last accessed: 02/2016.

[5] "Pediatric Pulmonary Hypertension Guidelines From the American Heart Association and American Thoracic Society". Available at: http://circ.ahajournals.org/content/early/2015/10/29/CIR.0000000000000329.full.pdf+html. Last updated: 11/2015. Last accessed: 02/2016.

[6] New Guidelines Focus on Pediatric Pulmonary Hypertension. Available at: http://www.medpagetoday.com/Cardiology/Hypertension/54482. Last updated: 11/2015. Last accessed: 02/2016.

[7] Uptravi® Tablets Prescribing Information, Actelion Pharmaceutical US, Inc. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207947s000lbl.pdf . Last updated: 12/2015. Last accessed: 02/2016.

[8] Uptravi® (selexipag) - New Orphan Drug Approval. Optum Rx. Available at: https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals%20Uptravi%202015%201222.pdf. Last accessed: 02/2016.

[9] Bardal, Stan K., Jason E. Waechter, and Douglas S. Martin. "Applied Pharmacology." *Google Books*. Chapter 24: Pulmonary System. Available at: https://books.google.com/books?id=nYPy70d1E50C&pg=PA401&lpg=PA401&dq=prostacyclin+MOA+in+pulmonary+hypertension&source=bl&ots=W4tZ1BMD16&sig=Z6qhB5gHfPGtKWIzXYsco7aRjkQ&hl=en&sa=X&ved=0ahUKEwjxpo7Nm5HLAhXim4MKHWt8As0Q6AEIRzAG#v=onepage&q=prostacyclin%20MOA%20in%20pulmonary%20hypertension&f=false. Last updated: 2011. Last accessed: 02/2016.

Appendix K

30-Day Notice to Prior Authorize Cerezyme® (Imiglucerase), Elelyso® (Taliglucerase Alfa), Vpriv® (Velaglucerase Alfa), Cerdelga® (Eliglustat), and Zavesca® (Miglustat)

Oklahoma Health Care Authority
March 2016

Gaucher Disease Overview[1,2,3,4,5,6,7]

Gaucher disease (GD) is an autosomal recessive disease that affects many of the body's organs. It is one of the most common lysosomal storage disorders and occurs in approximately 1 in 75,000 live births worldwide. In the mid-1990s, there were approximately 20,000 individuals with GD in the United States.[1] GD is sub-divided into three subtypes according to the presence or absence of neurological involvement. The most prevalent is Type 1 GD (GD1) and occurs with greater frequency in the Ashkenazi-Jewish population. It usually does not affect the central nervous system. Type 2 and 3 are less common and occur in all ethnic populations. Types 2 and 3 are characterized by neurological involvement.

GD results from a deficiency of a lysosomal enzyme glucocerebrosidase (also known as glucosylceramidase or acid beta-glucosidase [GBA]) in the body. The enzyme deficiency causes lipid-laden macrophages to accumulate in the spleen, liver, bone marrow, bone, and other tissues/organs.

The disease course is quite variable and the presenting features may occur at any age with varying severity. GD can cause anemia, fatigue, easy bruising, nosebleeds, osteoporosis, bone pain and easily broken bones, and swollen stomach due to enlarged liver or spleen. Features seen only in Type 2 and Type 3 GD include developmental delay, strabismus, nonimmune hydrops, and congenital ichthyosis.

There is no cure for GD; however, there are a number of treatments available to help control symptoms, prevent irreversible damage, and improve quality of life in patients with Types 1 and 3. There are currently no treatment options available for Type 2, which is the most fatal form of the disease and typically causes death before 2 years of age. Current pharmacologic treatment includes enzyme replacement therapy (ERT) or substrate-reduction therapy (SRT). There are three ERTs, Cerezyme® (imiglucerase), Elelyso® (taliglucerase alfa), and Vpriv® (velaglucerase alfa), available for treatment of Type 1 and the non-neurological manifestations of Type 3. There are two SRTs, Cerdelga® (eliglustat) and Zavesca® (miglustat), available for the treatment of GD1. Cerdelga® (eliglustat) is the only first-line oral therapy for certain adult patients with GD1. Zavesca® (miglustat) is only indicated for patients who cannot be treated with ERT.

Utilization of GD Medications: Fiscal Year 2015

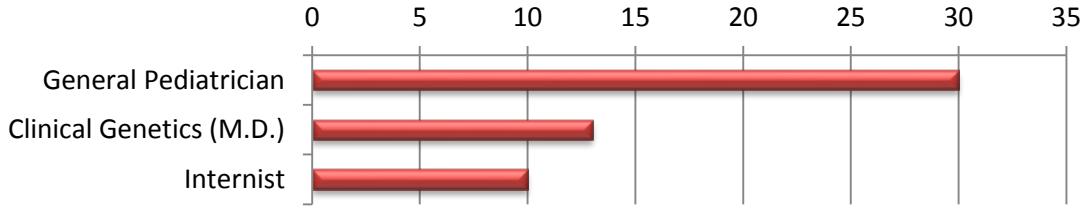
Cerezyme® (Imiglucerase) and Zavesca® (Miglustat) Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	4	34	$738,284.21	$21,714.24	$770.65	710	958
2015	5	53	$965,982.16	$18,226.08	$638.03	1,926	1,514
% Change	**25.00%**	**55.90%**	**30.80%**	**-16.10%**	**-17.20%**	**171.30%**	**58.00%**
Change	**1**	**19**	**$227,697.95**	**-$3,488.16**	**-$132.62**	**1,216**	**556**

*Total number of unduplicated members.

- There were no pharmacy claims for Cerdelga® (eliglustat), Elelyso® (taliglucerase alfa), and Vpriv® (velaglucerase alfa) during fiscal year 2014 or 2015.
- There were no medical claims for Elelyso® (taliglucerase alfa) or Cerezyme® (imiglucerase) during fiscal year 2015. Details of medical claims for Vpriv® (velaglucerase alfa) during fiscal year 2015 can be found at the end of the report.

Top Prescriber Specialties of Cerezyme® (Imiglucerase) and Zavesca® (Miglustat) by Number of Claims



Cerezyme® (Imiglucerase) Product Summary[8]

FDA Approved: May 1994. There are no unexpired patents for Cerezyme® (imiglucerase); however, there are currently no generic products available.

Indications: Cerezyme® (imiglucerase) is an analogue of the human enzyme β-glucocerebrosidase. It is indicated for long-term ERT for pediatric and adult patients with a confirmed diagnosis of GD1 that results in one or more of the following conditions:

a. Anemia
b. Thrombocytopenia
c. Bone disease
d. Hepatomegaly or splenomegaly

Dosing: Cerezyme® (imiglucerase) dosage should be individualized to each patient. The initial dosage range for which the most data is available is 2.5 units/kg of body weight three times a

week to 60 units/kg every two weeks. Imiglucerase is administered by intravenous infusion over 1-2 hours.

Estimated Acquisition Cost: The estimated acquisition cost (EAC) of Cerezyme® (imiglucerase) 400 unit vial is $1,674.82, resulting in a monthly cost of $35,171.64 for a 70kg patient at a dose of 60 units/kg every two weeks.

Elelyso® (Taliglucerase Alfa) Product Summary[9]

FDA Approved: May 2012

Indications: Elelyso® (taliglucerase alfa) is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for the treatment of patients 4 years of age and older with a confirmed diagnosis of GD1.

Dosing:

- The recommended dosage for treatment-naïve patients is 60 units/kg of body weight every other week. It is administered as an intravenous infusion over 1-2 hours.
- For patients switching from a stable dosage of imiglucersase to taliglucerase alfa, it is recommended that treatment begin with taliglucerase alfa at the same units/kg dosage as imiglucerase.

Estimated Acquisition Cost: The EAC of Elelyso® (taliglucerase alfa) 200 unit vial is $823.10, resulting in a monthly cost of $34,570.20 for a 70kg patient at a dose of 60 units/kg every two weeks.

Vpriv® (Velaglucerase Alfa) Product Summary[10]

FDA Approved: February 2010

Indications: Vpriv® (velaglucerase alfa) is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for long-term ERT for adult and pediatric patients with GD1 4 years of age or older.

Dosing:

- The recommended starting dose in treatment-naïve patients is 60 units/kg administered as a 60-minute intravenous infusion every other week.
- Patients currently being treated with stable imiglucerase dosages can switch to Vpriv® (velaglucerase alfa) at their previous imiglucerase dose two weeks after the last imiglucerase dose.

Estimated Acquisition Cost: The EAC of Vpriv® (velaglucerase alfa) 400 unit vial is $1,454.11, resulting in a monthly cost of $30,536.31 for a 70kg patient at a dose of 60 units/kg every two weeks.

Cerdelga® (Eliglustat) Product Summary[11]

FDA Approved: August 2014

Indications: Cerdelga® (eliglustat) is a glucosylceramide synthase inhibitor indicated for the long-term treatment of adult patients with GD1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.

Dosing:

- Cerdelga® (eliglustat) is available as an 84mg oral capsule.
- The recommended dosing regimen is based upon patient CYP2D6 metabolizer status.
    - The dose for CYP2D6 EMs or IMs is 84mg orally twice daily.
    - The dose for CYP2D6 PMs is 84mg orally once daily.
- Cerdelga® (eliglustat) is not indicated in patients who are CYP2D6 ultra-rapid metabolizers, since they may not achieve adequate concentrations of eliglustat to achieve a therapeutic effect.

Estimated Acquisition Cost: The EAC of Cerdelga® (eliglustat) 84mg capsules is $448.80, resulting in a monthly cost of $13,464.00 for PM at the recommended dose of 84mg daily and $26,928.00 for EMs or IMs at the recommended dose of 84mg twice daily.

Zavesca® (Miglustat) Product Summary[12]

FDA Approved: July 2003

Indications: Zavesca® (miglustat) is a glucosylceramide synthase inhibitor indicated as monotherapy for the treatment of adult patients with mild/moderate GD1 for whom ERT is not a therapeutic option.

Dosing: The recommended dose is 100mg administered orally three times a day. A dosage reduction to 100mg once or twice daily may be necessary in some patients due to adverse effects, such as tremor or diarrhea.

Estimated Acquisition Cost: The EAC of Zavesca® (miglustat) 100mg capsules is $314.69, resulting in a monthly cost of $28,322.10 at the recommended dose of 100mg three times daily.

Recommendations

The College of Pharmacy recommends the prior authorization of Cerezyme® (imiglucerase), Elelyso® (taliglucerase alfa), Vpriv® (velaglucerase alfa), Cerdelga® (eliglustat), and Zavesca® (miglustat) with the following criteria:

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

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

Cerdelga® (Eliglustat) Approval Criteria:

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

Zavesca® (Miglustat) Approval Criteria:

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

Utilization Details of GD Medications: Fiscal Year 2015

Medical Claims: Fiscal Year 2015

Product Utilized	J-code	Total Claims	Total Members	Total Cost	Cost/ Claim
VPRIV INJ 400 UNIT	J3385	22	2	$236,831.04	$10,765.05
Total		**22**	**2***	**$236,831.04**	**$10,765.05**

*Total number of unduplicated members.

Pharmacy Claims: Fiscal Year 2015

Product Utilized	Total Claims	Total Members	Total Cost	Cost/ Day	Cost/ Claim	% Cost
CEREZYME INJ 400UNIT	38	3	$964,835.41	$906.80	$25,390.41	99.88%
ZAVESCA CAP 100MG	15	2	$1,146.75	$2.55	$76.45	0.12%
Total	**53**	**5***	**$965,982.16**	**$638.03**	**$18,226.08**	**100%**

*Total number of unduplicated members.

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[3] Gaucher's disease. Available online at: http://www.mayoclinic.org/diseases-conditions/gauchers-disease/basics/definition/con-20031396. Last revised 7/2015. Last accessed 2/2016.

[4] National Gaucher Foundation, Inc. Available online at: http://www.gaucherdisease.org/. Last accessed 2/2016.

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[6] UpToDate: Gaucher disease: Treatment. Available online at: http://www.uptodate.com/contents/gaucher-disease-treatment?source=search_result&search=gaucher+disease+treatment&selectedTitle=1%7E55. Last revised 7/2015. Last accessed 2/2016.

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[8] Cerezyme® Prescribing Information. Genzyme. Available online at: https://www.cerezyme.com/healthcare.aspx. Last revised 5/2011. Last accessed 2/2016.

[9] Elelyso™ Prescribing Information. Pfizer. Available online at: http://labeling.pfizer.com/ShowLabeling.aspx?id=798. Last revised 11/2015.Last accessed 2/2016.

[10] Vpriv® Prescribing Information. Shire. Available online at: http://pi.shirecontent.com/PI/PDFs/Vpriv_USA_ENG.pdf. Last revised 4/2015. Last accessed 2/2016.

[11] Cerdelga™ Prescribing Information. Genzyme. Available online at: http://www.cerdelga.com/pdf/cerdelga_prescribing_information.pdf. Last revised 8/2014. Last accessed 2/2016.

[12] Zavesca® Prescribing Information. Actelion. Available online at: https://www.zavesca.com/pdf/ZAVESCA-Full-Prescribing-Information.pdf. Last revised 7/2015. Last accessed 2/2016.

Appendix L

Fiscal Year 2015 Annual Review of Vasomotor Symptom Medications and 30-day Notice to Prior Authorize Elestrin® (Estradiol Gel 0.06%)

Oklahoma Health Care Authority
March 2016

Current Prior Authorization Criteria

Duavee® (Conjugated Estrogens/Bazedoxifene) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe vasomotor symptoms associated with menopause or for prevention of postmenopausal osteoporosis; and
2. Member must be a female with an intact uterus; and
3. For a diagnosis of moderate-to-severe vasomotor symptoms associated with menopause:
    a. Member must have at least seven moderate-to-severe hot flushes per day or at least 50 per week prior to treatment; and
4. For a diagnosis of prevention of postmenopausal osteoporosis:
    a. A trial of Fosamax® (alendronate), Actonel® (risedronate), Boniva® (ibandronate) or Reclast® (zoledronic acid) compliantly used for at least six months concomitantly with calcium + vitamin D, that failed to prevent fracture or improve BMD scores; or
    b. Contraindication to, hypersensitivity to, or intolerable adverse effects with all bisphosphonates indicated for prevention of postmenopausal osteoporosis; and
5. Member must not have any of the contraindications for use of Duavee®; and
6. Members greater than 65 years of age will generally not be approved without supporting information.
7. Approvals will be for the duration of six months to ensure the need for continued therapy is reassessed periodically and the medication is being used for the shortest duration possible.
8. A quantity limit of 30 tablets per 30 days will apply.

Brisdelle® (Paroxetine Mesylate 7.5mg) Approval Criteria:

1. An FDA approved diagnosis of moderate-to-severe vasomotor symptoms associated with menopause; and
2. Approvals for Brisdelle® will not be granted for psychiatric indications; and
3. Member must not have any of the contraindications for use of Brisdelle®; and
4. Two previous trials with either a selective serotonin reuptake inhibitor (SSRI) or a selective serotonin norepinephrine reuptake inhibitor (SNRI) or both, or a patient-specific, clinically significant reasoning why a SSRI or SNRI is not appropriate for the member; and
5. Authorization requires a patient-specific, clinically significant reason why paroxetine 10mg is not appropriate for the member; and
6. A quantity limit of 30 capsules per 30 days will apply.

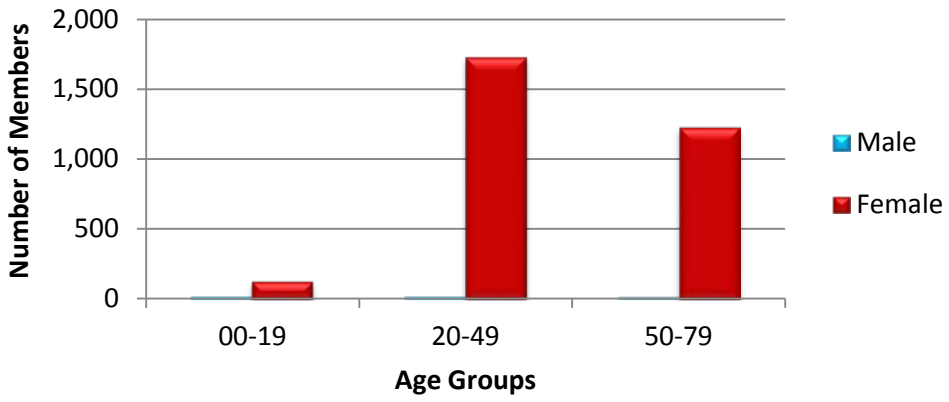
Utilization of Vasomotor Symptom Medications: Fiscal Year 2015

Comparison of Fiscal Years

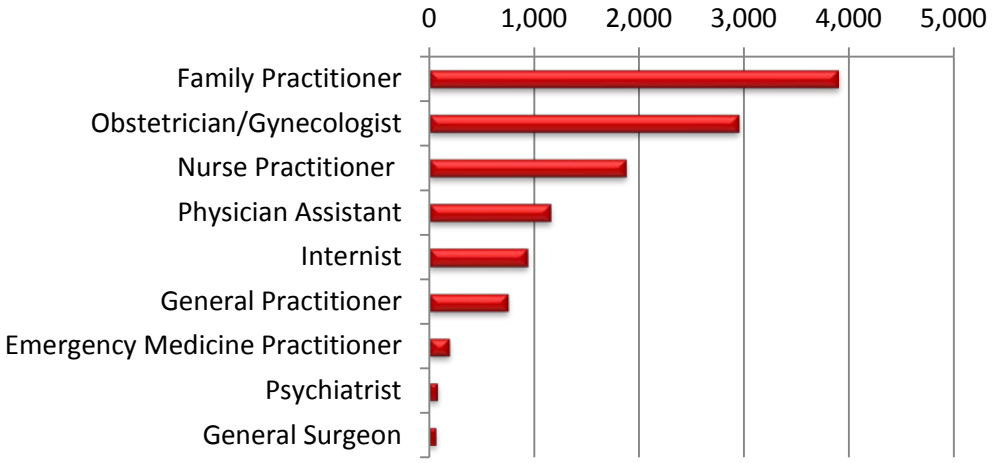
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	3,888	15,013	$1,070,372.84	$71.30	$1.78	539,919	602,557
2015	3,107	12,364	$989,485.79	$80.03	$1.97	449,165	502,620
% Change	-20.10%	-17.60%	-7.60%	12.20%	10.70%	-16.80%	-16.60%
Change	-781	-2,649	-$80,887.05	$8.73	$0.19	-90,754	-99,937

*Total number of unduplicated members.

Demographics of Members Utilizing Vasomotor Symptom Medications



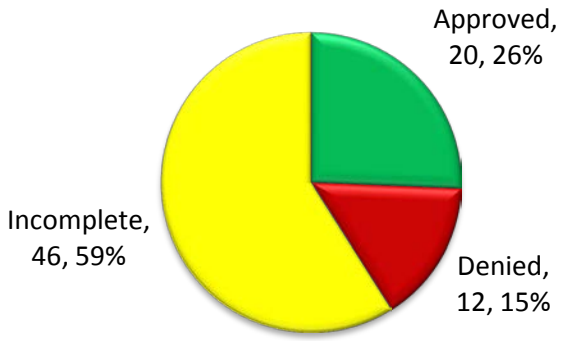
Top Prescriber Specialties of Vasomotor Symptom Medications by Number of Claims



Prior Authorization of Vasomotor Symptom Medications

There were 78 prior authorization requests submitted for vasomotor symptom medications during fiscal year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[1,2,3]

Recent Patent Expirations:

- Cenestin® (synthetic conjugated estrogen): July 2015
- Femring® (estradiol acetate): December 2015

Anticipated Patent Expirations:

- Angeliq® (drospirenone and estradiol): October 2031
- Brisdelle® (paroxetine): April 2029
- Duavee® (conjugated estrogens/bazedoxifene): March 2027
- Elestrin® Gel (estradiol gel): June 2022
- Enjuvia® (synthetic conjugated estrogen): March 2021
- Evamist® (estradiol transdermal spray): July 2022
- Minivelle® (estradiol transdermal system): July 2030

The North American Menopause Society (NAMS) Position Statement:

In 2015, NAMS released a position statement on the continued use of systemic hormones after the age of 65 years. The official position of NAMS is that there shouldn't be any hard and fast rules for hormone use after the age of 65 years. The statement points out that research continues to document the occurrence of hot flashes lasting into the mid-60's for many women. NAMS recommends using the lowest dose of hormones for the time appropriate to meet the woman's needs. Further, NAMS states that under some circumstances hormone therapy can be appropriate for women older than 65 years. In those instances, as with all age groups, the benefits of treatment should outweigh the risks. NAMS supports judicious use of hormone therapy, wherein the patient fully understands all the risks and the prescriber monitors the patient closely for any problems. The position statement points out a gap between current guidelines and real-world clinical practice, as well as a low utilization of non-hormonal therapies. According to NAMS, these are indicators that menopause is not being treated as an important health care issue and is largely undertreated. NAMS supports the use

of individualized hormone therapy where discontinuation of therapy is not based only on a woman's age. Further, they encourage all women bothered by menopause symptoms to seek help and consider all their options with the guidance of their clinician.

Endocrine Society Clinical Practice Guidelines:
The Endocrine Society deemed management of menopause a priority area in need of practice guidelines and appointed a task force to formulate evidence-based recommendations. For menopausal women younger than 60 years of age and less than 10 years past menopause with bothersome vasomotor symptoms who do not have contraindications or excessive cardiovascular or breast cancer risks and are willing to take hormone therapy, the Endocrine Society suggests estrogen therapy for those without a uterus and estrogen plus progestogen for those with a uterus. Nonoral or transdermal estrogen formulations are recommended for those with moderate risk of cardiovascular disease (CVD) and increased risk of venous thromboembolism. For women with a high risk of CVD and high or intermediate risk of breast cancer, nonhormonal therapies are recommended. Custom-compounded hormones are not recommended. The Endocrine Society supports a shared decision-making approach for menopausal hormone therapy (MHT) that tailors treatment to each woman's individual situation, risks, and treatment goals. Further, the decision to continue MHT should be revisited at least annually targeting the shortest total duration. For women seeking treatment who choose not to take MHT or for whom it is contraindicated, SSRIs, SNRIs, gabapentin, or pregablin are recommended. The guidance emphasizes safety in identifying which late perimenopausal and recently postmenopausal women are candidates for various therapeutic agents. Considerations include the risks and benefits of each available therapy, the expected duration of treatment, the intensity of monitoring during therapy, and most importantly, individualizing the course of therapy to reflect the specific characteristics of the patient who is making decisions regarding symptom management.

Elestrin® (Estradiol Gel) Product Summary[4]

Indications: Elestrin® (estradiol gel) is indicated for the treatment of moderate-to-severe vasomotor symptoms due to menopause.

Dosing:

- Elestrin® is designed with the unique and patented Advanced Transdermal Delivery (ATD™) system. This system increases the absorption rate of low-dose estrogen into the skin.
- Elestrin® 0.06% is available in a metered dose pump which delivers 0.52mg of estradiol in 0.87g of gel per pump actuation.
- Patients should be started with the lowest effective dose, which is one pump per day (0.87g per day, which contains 0.52mg of estradiol). Subsequent dosage adjustments may be made based upon the individual patient response.
- The gel is applied onto clean, dry skin in a thin layer. The recommended area of application is the upper arm to shoulder (approximately 320 cm^2).

- Patients should be advised to wash hands with soap and water immediately following application. Patients should avoid contact with others for at least two hours after applying the gel.

Mechanism of Action: Elestrin® acts through binding to nuclear receptors in estrogen-responsive tissues. To date, two estrogen receptors have been identified. These vary in proportion from tissue to tissue. Circulating estrogens modulate the pituitary secretion of the gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), through a negative feedback mechanism. Estrogens act to reduce the elevated levels of these hormones seen in postmenopausal women.

Contraindications: Elestrin® should not be used in women with any of the following conditions:

- Undiagnosed abnormal genital bleeding
- Known, suspected, or history of breast cancer
- Known or suspected estrogen-dependent neoplasia
- Active deep vein thrombosis (DVT), pulmonary embolism (PE), or history of these conditions
- Active arterial thromboembolic disease (e.g., stroke and myocardial infarction [MI]) or a history of these conditions
- Known anaphylactic reaction or angioedema to Elestrin®
- Known liver impairment or disease
- Known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders
- Known or suspected pregnancy

Warning and Precautions:

- <u>Cardiovascular Disorders:</u> An increased risk of stroke and DVT has been reported with estrogen-alone therapy. An increased risk of PE, DVT, stroke, and MI has been reported with estrogen plus progestin therapy. Should any of these occur or be suspected, estrogen with or without progestin therapy should be discontinued immediately. Risk factors for arterial vascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) or venous thromboembolism (VTE) (e.g., personal history or family history of VTE, obesity, and systemic lupus erythematosus) should be managed appropriately.
- <u>Malignant Neoplasms:</u> An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in a woman with a uterus. The reported endometrial cancer risk among unopposed estrogen users is about two to twelve times greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with use of estrogens for less than one year. The greatest risk appears associated with prolonged use which has an increased risk of 15- to 24-fold for five to ten years or more. This risk has been shown to persist for at least eight to fifteen years after estrogen therapy is discontinued. Clinical surveillance of all women using estrogen-alone or estrogen plus progestin therapy is important. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out

malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal vaginal bleeding. The use of estrogen-alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. All women should receive yearly breast examinations by a healthcare provider and perform monthly self-examinations. In addition, mammography examinations should be scheduled based on patient age, risk factors, and prior mammogram results. In some epidemiological studies, the use of estrogen plus progestin and estrogen-only products, in particular for five or more years, has been associated with an increased risk of ovarian cancer. However, the duration of exposure associated with increased risk is not consistent across all epidemiologic studies, and some report no association.

- Probable Dementia: In the Women's Health Initiative Memory Study (WHIMS) estrogen-alone ancillary study of WHI, a population of 2,947 hysterectomized women 65 to 79 years of age was randomized to daily conjugated estrogen (CE) alone or placebo. After an average follow-up of 5.2 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE-alone versus placebo was 1.49 (95% CI, 0.83-2.66). The absolute risk of probable dementia for CE-alone versus placebo was 37 versus 25 cases per 10,000 women-years.
- Gallbladder Disease: A 2- to 4-fold increase in the risk of gallbladder disease requiring surgery in post-menopausal women receiving estrogens has been reported.
- Hypercalcemia: Estrogen administration may lead to severe hypercalcemia in women with breast cancer and bone metastases. If hypercalcemia occurs, use of the drug should be stopped and appropriate measures taken to reduce the serum calcium level.
- Visual Abnormalities: Retinal vascular thrombosis has been reported in patients receiving estrogens. Medication should be discontined pending examination if there is sudden partial or complete loss of vision, or a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, estrogens should be permanently discontinued.
- Addition of a Progestin When a Woman Has Not Had a Hysterectomy: Studies of the addition of a progestin for ten or more days of a cycle of estrogen administration, or daily with estrogen in a continuous regimen, have reported a lowered incidence of endometrial hyperplasia than would be induced by estrogen treatment alone. Endometrial hyperplasia may be a precursor to endometrial cancer. There are, however, possible risks that may be associated with the use of progestins with estrogens compared to estrogen-alone regimens. These include an increased risk of breast cancer.
- Elevated Blood Pressure: In a small number of case reports, substantial increases in blood pressure have been attributed to idiosyncratic reactions to estrogens. In a large, randomized, placebo-controlled clinical trial, a generalized effect of estrogens on blood pressure was not seen.
- Hypertriglyceridemia: In women with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Consideration should be given to discontinuation of treatment if pancreatitis occurs.

- Hepatic Impairment and/or Past History of Cholestatic Jaundice: Estrogens may be poorly metabolized in women with impaired liver function. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, caution should be exercised, and in the case of recurrence, medication should be discontinued.
- Hypothyroidism: Estrogen administration leads to increased thyroid-binding globulin (TBG) levels. Women with normal thyroid function can compensate for the increased TBG by making more thyroid hormone, thus maintaining free T_4 and T_3 serum concentrations in the normal range. Women dependent on thyroid hormone replacement therapy who are also receiving estrogens may require increased doses of their thyroid replacement therapy. These women should have their thyroid function monitored to maintain their free thyroid hormone levels in an acceptable range.
- Fluid Retention: Estrogens may cause some degree of fluid retention. Women with conditions that might be influenced by this factor, such as a cardiac or renal dysfunction, warrant careful observation when estrogen-alone is prescribed.
- Hypocalcemia: Estrogen therapy should be used with caution in women with hypoparathyroidism as estrogen-induced hypocalcemia may occur.
- Exacerbation of Endometriosis: A few cases of malignant transformation of residual endometrial implants have been reported in women treated post-hysterectomy with estrogen-alone therapy. For women known to have residual endometriosis posthysterectomy, the addition of progestin should be considered.
- Hereditary Angioedema: Exogenous estrogens may exacerbate symptoms of angioedema in women with hereditary angioedema.
- Exacerbation of Other Conditions: Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions.
- Photosensitivity or Photoallergy: Increased sensitivity to direct exposure to the sun on areas of Elestrin® application has not been evaluated.
- Sunscreen Application: Estradiol absorption was increased when sunscreen was applied ten minutes before Elestrin® application. Sunscreen should not be applied to the same site until at least 25 minutes after the application of Elestrin®. Concomitant application of sunscreen and Elestrin® to the same application site for seven or more days may increase estradiol absorption and should be avoided.
- Miscellaneous: Alcohol based gels are potentially flammable. Fire, flame, or smoking should be avoided until the gel has dried.

Adverse Reactions: The adverse reactions that occurred at a rate greater than 5% in clinical studies in any of the treatment groups include the following:

- Reproductive system and breast disorders
- Breast tenderness
- Metrorrhagia
- Respiratory, thoracic, and mediastinal disorders
- Nasopharyngitis
- Upper respiratory tract infection

Drug Interactions:

- No drug interaction studies have been conducted for Elestrin®.
- *In vitro* and *in vivo* studies have shown that estrogens are metabolized partially by cytochrome P450 3A4 (CYP3A4). Therefore, inducers or inhibitors of CYP3A4 may affect estrogen drug metabolism.

Use in Special Populations:

- Pregnancy: Elestrin® should not be used during pregnancy. There appears to be little or no increased risk of birth defects in children born to women who have used estrogens and progestins as an oral contraceptive inadvertently during early pregnancy.
- Nursing Mothers: Elestrin® should not be used during lactation. Estrogen administration to nursing women has been shown to decrease the quantity and quality of the breast milk. Detectable amounts of estrogens have been identified in the breast milk of women receiving estrogen therapy.
- Pediatric Use: Elestrin® is not indicated in children. Clinical studies have not been conducted in the pediatric population.
- Geriatric Use: There have not been sufficient numbers of geriatric women involved in clinical studies utilizing Elestrin® to determine whether those over 65 years of age differ from younger subjects in their response to Elestrin®.
- Renal Impairment: The effect of renal impairment on the pharmacokinetics of Elestrin® has not been studied.
- Hepatic Impairment: The effect of hepatic impairment on the pharmacokinetics of Elestrin® has not been studied.

Efficacy: A randomized, double-blind, placebo-controlled trial evaluated the efficacy of 12-week treatment with three different daily doses of Elestrin® for the treatment of vasomotor symptoms in 484 postmenopausal women between 28 and 74 years of age (mean 54 years) who had at least 60 moderate-to-severe hot flushes per week at baseline. At baseline, mean hot flushes was 13 per day. Subjects applied placebo, Elestrin® 1.7 grams (1.04mg estradiol), or 2.6 grams (1.56mg estradiol) once daily to the upper arm. The study was amended to identify the lowest effective dose of Elestrin® and limit the number of subjects exposed to the 2.6 gram dose. After the study amendment, Elestrin® 0.87 grams (0.52mg estradiol) was added and the 2.6 gram dose was discontinued from further enrollment. Reduction in both the frequency and severity of moderate-to-severe hot flushes was statistically significant for the Elestrin® 1.7 gram per day dose compared to placebo at week four. Statistically significant reductions in both the frequency and severity of moderate-to-severe hot flushes when compared to placebo were delayed for the Elestrin® 0.87 gram per day dose to week five. Both the 0.87 gram per day and 1.7 gram per day doses were statistically significant compared to placebo at week twelve.

Cost Comparison:

Medication	Cost Per Gram, Packet, or Tablet	Cost for 30 Days of Therapy
Elestrin® (Estradiol Gel 0.06%)	**$3.92***	**$203.84***
Divigel® (Estradiol Gel 0.1%)	$3.06*	$91.80*
Estradiol tablets	$0.17+	$5.10+

Dosing based on maintenance and maximum recommended dosing according to package labeling.
Costs do not reflect supplemental rebated prices or net costs.
*EAC = Estimated Acquisition Cost
+SMAC = State Maximum Allowable Cost

Recommendations

The College of Pharmacy recommends sending an educational mailing to prescribers of members who are 65 years of age or older receiving hormone therapy. The purpose of the mailing would be to ensure appropriate use of hormone therapy for vasomotor symptoms in members over the age of 65 years. The letter will address the need for regular monitoring of these members, and to ensure members are receiving the lowest effective dose of hormone therapy for the shortest duration of time.

Additionally, the College of Pharmacy recommends the prior authorization of Elestrin® (estradiol gel) with the following criteria:

Elestrin® (Estradiol Gel 0.06%) Approval Criteria:

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

Utilization Details of Vasomotor Symptom Medications: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER
ORAL ESTROGEN PRODUCTS						
ESTRADIOL TAB 1MG	2,073	664	$11,027.00	$0.13	$5.32	1.02
ESTRADIOL TAB 2MG	1,725	527	$10,873.10	$0.15	$6.30	1.09
PREMARIN TAB 0.625MG	1,600	430	$231,578.30	$3.63	$144.74	1.01
PREMARIN TAB 1.25MG	1,247	310	$204,334.67	$3.80	$163.86	1.04
PREMARIN TAB 0.3MG	701	181	$99,305.92	$3.60	$141.66	1
ESTRADIOL TAB 0.5MG	650	247	$3,231.51	$0.11	$4.97	1.01
PREMARIN TAB 0.9MG	274	69	$40,955.09	$3.66	$149.47	1.01
MENEST TAB 0.625MG	229	40	$13,923.49	$1.80	$60.80	1.11
PREMARIN TAB 0.45MG	158	46	$24,361.44	$3.64	$154.19	0.99
MENEST TAB 1.25MG	131	25	$10,914.48	$2.41	$83.32	1.06
ESTROPIPATE TAB 0.75MG	82	23	$1,608.46	$0.41	$19.62	1.11
ESTROPIPATE TAB 1.5MG	72	17	$2,184.14	$0.58	$30.34	1.1
MENEST TAB 0.3MG	68	11	$2,490.83	$1.22	$36.63	1
ENJUVIA TAB 1.25MG	58	14	$6,793.45	$2.63	$117.13	1.03
MENEST TAB 2.5MG	32	7	$4,703.35	$4.13	$146.98	1
ESTROPIPATE TAB 3MG	12	2	$369.24	$1.03	$30.77	1
ENJUVIA TAB 0.3MG	11	3	$1,219.24	$3.69	$110.84	1.45
CENESTIN TAB 0.45MG	5	1	$541.02	$3.86	$108.20	1
ENJUVIA TAB 0.45MG	3	1	$454.68	$2.53	$151.56	1
ENJUVIA TAB 0.9MG	3	1	$214.74	$2.39	$71.58	1
CENESTIN TAB 0.9MG	1	1	$119.03	$3.97	$119.03	1
CENESTIN TAB 0.3MG	1	1	$115.34	$3.84	$115.34	1
CENESTIN TAB 0.625MG	1	1	$345.66	$3.84	$345.66	1
SUBTOTAL	**9,137**	**2622**	**$671,664.18**	**$1.77**	**$73.51**	**1.04**
TOPICAL ESTROGEN PRODUCTS						
ESTRADIOL DIS 0.1MG	252	83	$15,412.61	$2.16	$61.16	3.04
VIVELLE-DOT DIS 0.1MG	223	49	$18,737.93	$2.96	$84.03	4.55
ESTRADIOL DIS 0.05MG	171	50	$10,069.77	$2.08	$58.89	3.42
MINIVELLE DIS 0.1MG	130	26	$10,585.32	$2.88	$81.43	5
ESTRADIOL DIS 0.1MG	89	43	$6,414.17	$2.55	$72.07	2.07
ESTRADIOL DIS 0.025MG	77	24	$4,501.82	$2.07	$58.47	3.21
ESTRADIOL DIS 0.0375MG	64	17	$4,153.63	$2.31	$64.90	3.76
VIVELLE-DOT DIS 0.075MG	55	11	$5,087.18	$3.28	$92.49	5
VIVELLE-DOT DIS 0.05MG	43	10	$3,652.90	$2.99	$84.95	4.3
MINIVELLE DIS 0.05MG	32	12	$2,663.98	$2.97	$83.25	2.67
VIVELLE-DOT DIS 0.025MG	31	9	$2,743.77	$2.42	$88.51	3.44
ESTRADIOL DIS 0.05MG	29	16	$2,122.33	$2.60	$73.18	1.81
ESTRADIOL DIS 0.0375MG	26	11	$1,181.76	$1.56	$45.45	2.36
ESTRADIOL DIS 0.075MG	25	11	$1,712.60	$2.41	$68.50	2.27
CLIMARA DIS 0.025MG	25	5	$1,610.41	$2.29	$64.42	5
ALORA DIS 0.1MG	24	9	$1,848.31	$2.67	$77.01	2.67
VIVELLE-DOT DIS 0.0375MG	22	8	$1,771.84	$2.48	$80.54	2.75
MINIVELLE DIS 0.0375MG	21	9	$1,921.17	$3.20	$91.48	2.33
EVAMIST SPR 1.53MG	20	7	$2,012.09	$2.01	$100.60	2.86
DIVIGEL GEL 1MG/GM	19	10	$2,018.61	$3.28	$106.24	1.9
MINIVELLE DIS 0.075MG	18	2	$1,754.89	$3.48	$97.49	9

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER
ALORA DIS 0.075MG	16	3	$1,189.17	$2.63	$74.32	5.33
ESTRADIOL DIS 0.025MG	15	8	$985.72	$2.10	$65.71	1.88
DIVIGEL GEL 0.25MG	15	6	$1,346.32	$3.09	$89.75	2.5
CLIMARA DIS 0.1MG	10	2	$822.21	$2.92	$82.22	5
ALORA DIS 0.05MG	10	6	$763.71	$2.63	$76.37	1.67
DIVIGEL GEL 0.5MG	10	3	$1,163.91	$3.88	$116.39	3.33
ESTRADIOL DIS 0.075MG	10	5	$672.68	$2.40	$67.27	2
ALORA DIS 0.025MG	10	4	$658.41	$2.22	$65.84	2.5
ESTRADIOL DIS 0.06MG	10	3	$531.41	$1.90	$53.14	3.33
MENOSTAR DIS 14MCG	6	1	$703.08	$4.19	$117.18	6
CLIMARA DIS 0.05MG	4	2	$277.44	$2.48	$69.36	2
ELESTRIN GEL 0.06%	2	2	$313.07	$5.22	$156.54	1
SUBTOTAL	**1,514**	**467**	**$111,404.22**	**$2.54**	**$73.58**	**4.21**
INJECTABLE ESTROGEN PRODUCTS						
DEPO-ESTRADI INJ 5MG/ML	334	163	$18,091.87	$0.58	$54.17	2.05
ESTRAD VAL INJ 20MG/ML	9	6	$1,046.64	$1.24	$116.29	1.5
ESTRAD VAL INJ 40MG/ML	5	3	$977.60	$1.60	$195.52	1.67
DELESTROGEN INJ 10MG/ML	3	2	$379.88	$1.19	$126.63	1.5
DELESTROGEN INJ 20MG/ML	2	1	$235.20	$3.92	$117.60	2
ESTRAD VAL INJ 10MG/ML	1	1	$83.81	$2.79	$83.81	1
DELESTROGEN INJ 40MG/ML	1	1	$331.71	$11.06	$331.71	1
SUBTOTAL	**355**	**177**	**$21,146.71**	**$0.64**	**$59.57**	**2.03**
ESTROGEN POWDER PRODUCTS						
ESTRIOL POW MICRONIZ	76	20	$6,845.49	$2.78	$90.07	3.8
ESTRADIOL POW	32	9	$1,598.07	$1.51	$49.94	3.56
ESTRADIOL POW MICRONIZ	14	5	$541.34	$1.29	$38.67	2.8
ESTRONE POW	1	1	$41.30	$1.38	$41.30	1
SUBTOTAL	**123**	**35**	**$9,026.20**	**$2.27**	**$73.38**	**4.1**
VAGINAL ESTROGEN PRODUCTS						
FEMRING MIS 0.1MG/24	9	4	$2,564.80	$3.31	$284.98	2.25
FEMRING MIS 0.05/24H	8	4	$2,232.77	$3.38	$279.10	2
SUBTOTAL	**17**	**8**	**$4,797.57**	**$3.35**	**$282.21**	**2.13**
ORAL ESTROGEN/PROGESTIN PRODUCTS						
PREMPRO TAB .625-2.5	327	71	$48,605.54	$4.49	$148.64	4.61
PREMPRO TAB 0.3-1.5	253	59	$37,245.39	$4.46	$147.21	4.29
PREMPRO TAB 0.45-1.5	109	28	$16,281.98	$4.50	$149.38	3.89
ESTRA/NORETH TAB 0.5-0.1	105	24	$13,854.22	$3.59	$131.94	4.38
PREMPRO TAB 0.625-5	88	20	$13,109.12	$4.50	$148.97	4.4
ESTRA/NORETH TAB 1-0.5MG	73	16	$9,579.36	$3.53	$131.22	4.56
MIMVEY TAB 1-0.5MG	39	12	$5,916.45	$3.46	$151.70	3.25
JINTELI TAB 1MG-5MCG	38	8	$3,810.63	$2.13	$100.28	4.75
ANGELIQ TAB 0.25-0.5	36	7	$4,337.21	$4.08	$120.48	5.14
ANGELIQ TAB 0.5-1MG	18	5	$2,682.62	$4.08	$149.03	3.6
FEMHRT TAB 0.5-2.5	15	8	$2,224.90	$3.78	$148.33	1.88
ACTIVELLA TAB 0.5-0.1	11	1	$1,793.81	$5.79	$163.07	11
PREMPHASE TAB	9	3	$1,874.29	$4.40	$208.25	3
LOPREEZA TAB 0.5-0.1	5	2	$504.45	$3.60	$100.89	2.5

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	CLAIMS/ MEMBER
PREFEST TAB	1	1	$108.80	$3.63	$108.80	1
LOPREEZA TAB 1-0.5MG	1	1	$107.83	$3.85	$107.83	1
SUBTOTAL	**1,128**	**265**	**$162,036.60**	**$4.15**	**$143.65**	**4.66**
TOPICAL ESTROGEN/PROGESTIN PRODUCTS						
COMBIPATCH DIS .05/.25	37	6	$3,793.19	$3.60	$102.52	6.17
COMBIPATCH DIS .05/.14	35	14	$3,402.82	$2.94	$97.22	2.5
CLIMARA PRO DIS WEEKLY	18	10	$2,214.30	$4.32	$123.02	1.8
SUBTOTAL	**90**	**30**	**$9,410.31**	**$3.46**	**$104.56**	**3.1**
PAROXETINE PRODUCTS						
BRISDELLE	0	0	$0.00	$0.00	$0.00	0
SUBTOTAL	**0**	**0**	**$0.00**	**$0.00**	**$0.00**	**0**
ESTROGEN/SERM PRODUCTS						
DUAVEE	0	0	$0.00	$0.00	$0.00	0
SUBTOTAL	**0**	**0**	**$0.00**	**$0.00**	**$0.00**	**0**
TOTAL	**12,364**	**3,604***	**$989,485.79**	**$1.97**	**$80.03**	**3.43**

*Total number of unduplicated members.
Costs do not reflect rebated prices or net costs.
Cost per claim may correspond to a member receiving several months of therapy in one claim.

[1] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 12/28/2015. Last accessed 2/23/2016.
[2] NAMS Supports Judicious Use of Systemic Hormone Therapy Even After Age 65. Available online at: http://www.menopause.org/docs/default-source/2015/nams-statement-on-continuing-ht-after-age-65.pdf. Last revised 6/2015. Last accessed 2/24/2016.
[3] Treatment of Symptoms of Menopause: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, November 2015; 100(11):3975-4011. Available online at: http://press.endocrine.org/doi/pdf/10.1210/jc.2015-2236. Last revised 10/2015. Last accessed 2/24/2016.
[4] Elestrin® Product Information. Meda Pharmaceuticals®. Available online at http://www.elestrin.com/pdf/Elestrin_Full_Prescribing_Information.pdf. Last revised 2/1/2014. Last accessed 2/24/2016.

Appendix M

Fiscal Year 2015 Annual Review of Botulinum Toxins

Oklahoma Health Care Authority
March 2016

Current Prior Authorization Criteria

Botulinum Toxins Approval Criteria:

1. Cosmetic indications will not be covered.
2. A diagnosis of chronic migraine (tension headaches are not a covered diagnosis), non-neurogenic overactive bladder, and neurogenic overactive bladder will require manual review (see specific criteria below).
3. The following indications listed below have been determined to be appropriate and are covered:

Covered Indications
▪ Spasticity associated with: o Cerebral Palsy o Paralysis o Generalized weakness/incomplete paralysis o Larynx o Anal fissure o Esophagus (achalasia and cardiospasms) o Eye and eye movement disorders ▪ Cervical Dystonia

Botulinum toxins are billed through the medical claims system and require a manual prior authorization for any covered diagnosis to ensure appropriate reimbursement for the billing provider. Prior authorization requests for botulinum toxins are first reviewed by a clinical pharmacist and if necessary, the prior authorization request is sent to Oklahoma Health Care Authority (OHCA) for a second review from an OHCA physician. Botulinum toxin claims are denied if submitted through the pharmacy point of sale system. There are four covered products in this class: Botox® (onabotulinumtoxinA), Dysport® (abobotulinumtoxinA), Xeomin® (incobotulinumtoxinA), and Myobloc® (rimabotulinumtoxinB).

Botox® is the only botulinum toxin product indicated for the prevention of migraine headaches and for the treatment of non-neurogenic overactive bladder and neurogenic overactive bladder. Approval criteria for Botox® for the prevention of chronic migraine headaches, non-neurogenic overactive bladder, and neurogenic overactive bladder were developed internally by medical staff at OHCA in collaboration with two SoonerCare contracted neurologists. Due to the modest effect, high cost, and potential for severe adverse reactions, Botox® should be reserved for patients who have failed all available recommended therapies.

Approval Criteria for Botox® for Prevention of Migraine Headaches *(other botulinum toxins will not be approved for this diagnosis)*:

1. Non-migraine medical conditions known to cause headache have been ruled out and/or have been treated. This includes but is not limited to:
    a. Increased intracranial pressure (e.g., tumor, pseudotumor cerebri, and central venous thrombosis); or
    b. Decreased intracranial pressure (e.g. post-lumbar puncture headache and dural tear after trauma); and
2. Migraine headache exacerbation secondary to other medication conditions or therapies have been ruled out and/or treated. This includes but is not limited to:
    a. Hormone replacement therapy or hormone-based contraceptives; and
    b. Chronic insomnia; and
    c. Obstructive sleep apnea; and
3. Member has no contraindications to Botox® injections; and
4. FDA indications are met:
    a. Member is 18 years of age or older; and
    b. Member has documented chronic migraine headaches
        i. Frequency of 15 or more days per month; and
        ii. Duration of four hours per day or longer; and
5. The member has failed medical migraine preventative therapy including at least three agents in three or more categories, but not limited to:
    a. Select antihypertensive therapy such as beta-blocker therapy; or
    b. Select anticonvulsant therapy; or
    c. Select antidepressant therapy (e.g. TCA or SNRI); and
6. Member is not frequently taking medications which are known to cause medication overuse headaches (MOH or rebound headaches) in the absence of intractable conditions known to cause chronic pain. MOH are a frequent cause of chronic headaches. A list of prescription or non-prescription medications known to cause MOH includes, but is not limited to:
    a. Decongestants (alone or in combination products); and
    b. Combination analgesics containing caffeine and/or butalbital (>5 days/month); and
    c. Narcotics; and
    d. Analgesic medications including acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs); and
    e. Ergotamine-containing medications (>8 days/month); and
    f. Triptans (>8 days/month); and
7. Member is not taking any medications that are likely to be the cause of the headaches; and
8. Member must have been evaluated within the last six months by a neurologist for chronic migraine headaches and Botox® recommended as treatment (not necessarily prescribed or administered by a neurologist); and
9. Members who smoke or use tobacco products will not be approved.

Approval Criteria for Botox® for Non-Neurogenic Overactive Bladder *(other botulinum toxins will not be approved for this diagnosis)*:

1. Member must have severe disease (≥ 5 urinary incontinence episodes per day on medication) and specific pathology determined via urodynamic studies; and
2. Member must have participated in behavioral therapy for at least 12 weeks that did not yield adequate clinical results; and
3. Member must have had compliant use of at least three anti-muscarinic or beta-3 adrenoceptor agonist medications for at least 12 weeks each, alone or in combination with behavioral therapy, that did not yield adequate clinical results. One of those trials must have been an extended-release formulation; and
4. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
5. Botox® must be administered by an urologist.

Approval Criteria for Botox® for Neurogenic Overactive Bladder (*other botulinum toxins will not be approved for this diagnosis)*:

1. Diagnosis of neurogenic bladder including underlying pathological dysfunction subtype confirmed by:
    a. Urodynamic studies to determine pathology and serve to provide objective evidence of bladder and external sphincter function; and
    b. A diary of fluid intake, incontinence, voiding, and catheterization times and amounts to provide a record of actual occurrences; and
2. Member must have a clinically significant reason why anticholinergic medications are no longer an option for the member; and
3. Member must be 18 years of age or older and have adequate hand function and sufficient cognitive ability to know when the bladder needs emptying and to self-catheterize, or have a caregiver able to catheterize the member when necessary; and
4. Botox® must be administered by an urologist.

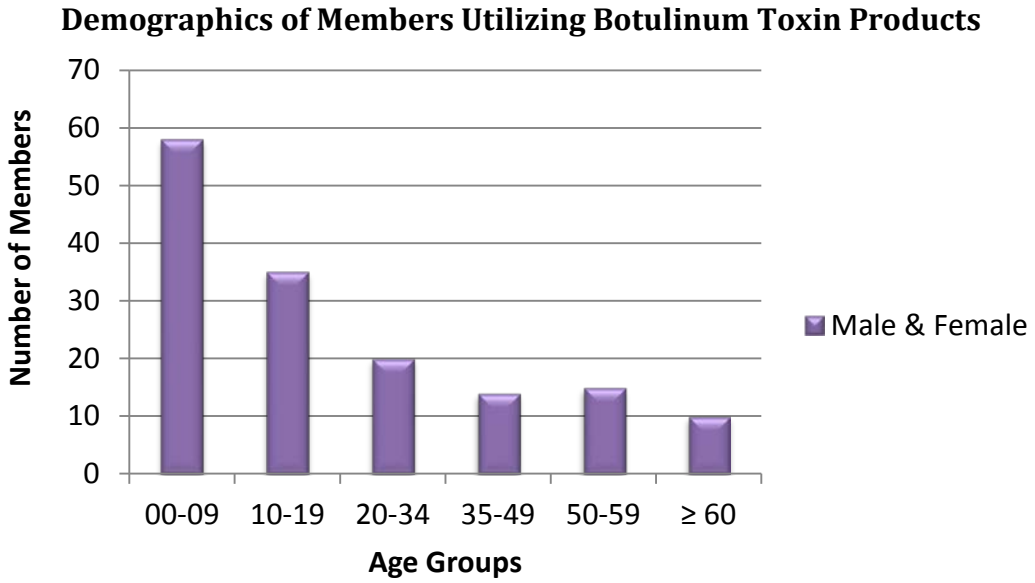
Utilization of Botulinum Toxin Products: Fiscal Year 2015

Please note, utilization details included in this report are derived from medical claims data.

Comparison of Fiscal Years

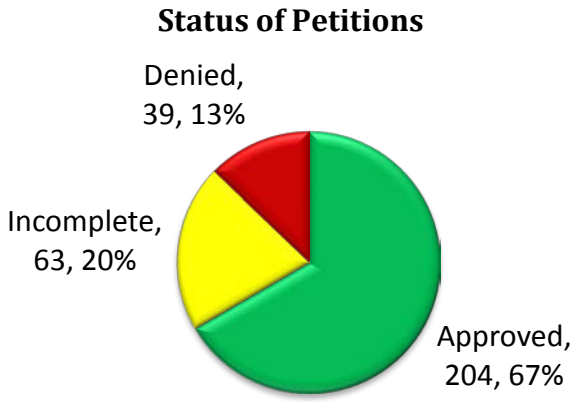
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Claims/ Member
2014	153	295	$368,017.00	$1,247.52	1.93
2015	152	301	$398,583.43	$1,324.20	1.98
% Change	**-0.65%**	**2.03%**	**8.31%**	**6.15%**	**2.71%**
Change	**-1**	**6**	**$30,566.43**	**$76.68**	**0.05**

*Total number of unduplicated members.



Prior Authorization of Botulinum Toxins

There were 306 prior authorization requests submitted for the botulinum toxins category during fiscal year 2015. The following chart shows the status of the submitted petitions.



Market News and Updates[1,2,3]

New FDA Approved Indications:

- **April 2015:** The FDA approved an expansion of the Botox® (onabotulinumtoxinA) label for the treatment of adults with upper limb spasticity. The expanded label now includes the addition of two thumb muscles (flexor pollicis longus, a muscle in the forearm that flexes the thumb, and adductor pollicis, a muscle in the hand that functions to adduct the thumb), and also increases the maximum dose from 360 to 400 units for the treatment of upper limb spasticity. The FDA also approved an increase to the maximum Botox® cumulative dose within three months from 360 to 400 units in adults treated for one or more indications. Botox® was FDA approved for the treatment of upper limb spasticity in 2010. The approval criteria for botulinum toxins and covered diagnosis

codes have been updated to reflect the expanded indication for the treatment of upper limb spasticity to include the addition of two thumb muscles.

- **December 2015:** The FDA approved Xeomin® (incobotulinumtoxinA) for the treatment of upper limb spasticity in adult patients. Xeomin® was first FDA approved in 2010 for the treatment of cervical dystonia and blepharospasm in adult patients.
- **January 2016:** The FDA approved Botox® (onabotulinumtoxinA) for the treatment of lower limb spasticity in adult patients to decrease the severity of increased muscle stiffness in ankle and toe muscles. The FDA approval was based on a large, international developmental program that included a phase three, multi-center, double-blind, randomized, placebo-controlled clinical trial that evaluated the safety and efficacy of Botox® compared to placebo in more than 400 patients with lower limb spasticity following stroke. Botox® is the first and only botulinum toxin product to be approved by the FDA to treat multiple muscle groups of the upper (elbow, wrist, fingers, and thumb) and lower limbs that may be impacted by spasticity. The approval criteria for botulinum toxins and covered diagnosis codes have been updated to include the new indication for the treatment of lower limb spasticity.

Recommendations

The College of Pharmacy does not recommend any changes to the Botulinum Toxins category at this time.

Utilization Details of Botulinum Toxin Products: Fiscal Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	PERCENT COST
ONABOTULINUMTOXINA PRODUCTS						
BOTOX®	287	148	$388,955.83	$1,355.25	1.9	97.58%
INCOBOTULINUMTOXINA PRODUCTS						
XEOMIN®	10	4	$3,981.35	$398.14	2.5	1.00%
RIMABOTULINUMTOXINB PRODUCTS						
MYOBLOC®	4	1	$5,646.25	$1,411.56	4.0	1.42%
TOTAL	**301**	**152***	**$398,583.43**	**$1,324.20**	**1.98**	**100.00%**

*Total number of unduplicated members.
Dysport® had no utilization in fiscal year 2015.

[1] Actavis Press Release: Actavis Announces FDA Approval of Expanded Label for Botox® (OnabotulinumtoxinA) for the Treatment of Upper Limb Spasticity in Adults. Available online at: http://www.actavis.com/news/news/thomson-reuters/actavis-announces-fda-approval-of-expanded-label-f. Last revised 4/20/2015. Last accessed 2/16/2016.
[2] Business Wire: Merz North America Announces FDA Approval of Xeomin® (IncobotulinumtoxinA) for Treatment of Adult Upper Limb Spasticity. Available online at: http://www.businesswire.com/news/home/20151223005633/en/Merz-North-America-Announces-FDA-Approval-XEOMIN%C2%AE. Last revised 12/23/2015. Last accessed 2/16/2016.
[3] Allergan Press Release: U.S. FDA Approves Botox® (OnabotulinumtoxinA) for the Treatment of Lower Limb Spasticity in Adults. Available online at: http://www.allergan.com/news/news/thomson-reuters/u-s-fda-approves-botox-onabotulinumtoxina-for-the. Last revised 1/22/2016. Last accessed 2/16/2016.

Appendix N

Calendar Year 2015 Annual Review of Idiopathic Pulmonary Fibrosis Medications

Oklahoma Health Care Authority
March 2016

Introduction[1,2,3]

Idiopathic pulmonary fibrosis (IPF) is a chronic, incurable lung condition that is characterized by varying degrees of fibrosis, collagen deposits, and distortion of the pulmonary architecture. Clinical manifestations of IPF include progressive symptoms of dyspnea, cough, and worsening pulmonary function. Over time, fibrosis of the lungs increases until the lungs can no longer provide enough oxygen to the body's organs and tissues. Prognosis of IPF is poor, with a median survival of approximately three years after diagnosis.

It is estimated that IPF affects approximately 100,000 individuals in the United States, with 30,000-40,000 new cases being diagnosed each year.[4] IPF is usually diagnosed in adults over the age of 50 years and is more common in men than in women.

Pharmacologic treatments for IPF are limited. The FDA granted approval through a process of fast track, orphan product, breakthrough designation, and priority review to two new products for the treatment of IPF, Ofev® (nintedanib) and Esbriet® (pirfenidone), in October 2014. Ofev® and Esbriet® slow the rate of progressive lung function decline, but do not cure IPF or lead to improvement of lung function.

Prior to the FDA approval of Ofev® and Esbriet®, no medications were approved for the treatment of IPF. Traditional approaches to treat IPF have included prednisone, azathioprine, and N-acetylcysteine, either alone or in combination; however, this approach does not seem to be effective and there is not adequate evidence to support the use of these medications. Treatment has predominantly been limited to supportive care (e.g., oxygen therapy, pulmonary rehabilitation), with lung transplantation an option for selected patients.

Current Prior Authorization Criteria

Ofev® (Nintedanib) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by a pulmonologist or pulmonary specialist; and
4. A quantity limit of 60 capsules per 30 days will apply.

Esbriet® (Pirfenidone) Approval Criteria:

1. An FDA approved diagnosis of idiopathic pulmonary fibrosis (IPF); and
2. Member must be 18 years of age or older; and
3. Medication must be prescribed by a pulmonologist or pulmonary specialist; and
4. A quantity limit of 270 capsules per 30 days will apply.

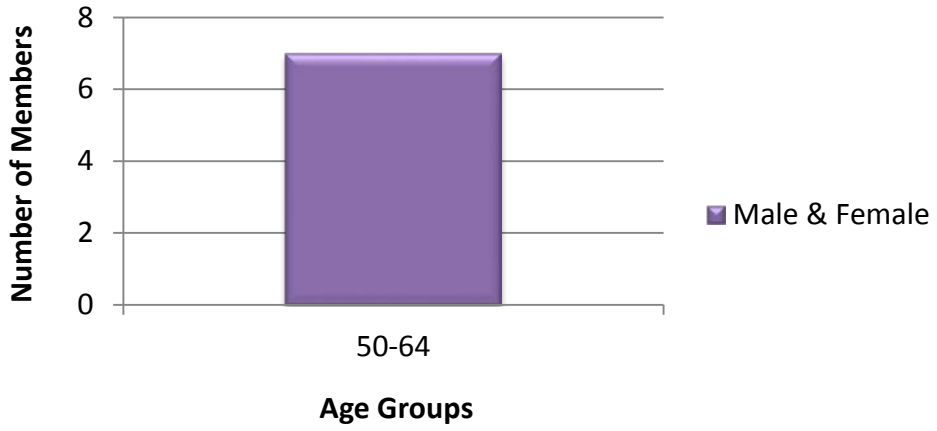
Utilization of IPF Medications: Calendar Year 2015

Comparison of Calendar Years

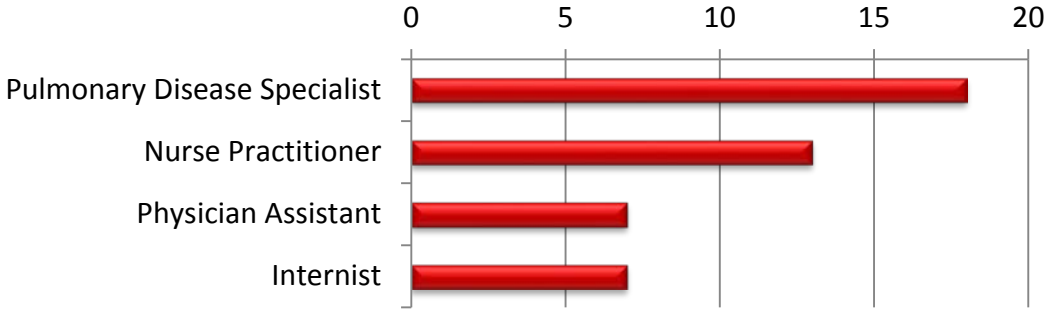
Calendar Year	*Total Members	Total Claims	Total Cost	Cost/ Claim	Cost/ Day	Total Units	Total Days
2014	1	2	$16,895.42	$8,447.71	$281.59	120	60
2015	7	45	$376,386.69	$8,364.15	$278.80	6,480	1,350
% Change	**600.00%**	**2150.00%**	**2127.70%**	**-1.00%**	**-1.00%**	**5300.00%**	**2150.00%**
Change	**6**	**43**	**$359,491.27**	**-$83.56**	**-$2.79**	**6,360**	**1,290**

*Total number of unduplicated members.
Please note, both Ofev® and Esbriet® were FDA approved in October 2014, resulting in minimal use in calendar year 2014.

Demographics of Members Utilizing IPF Medications



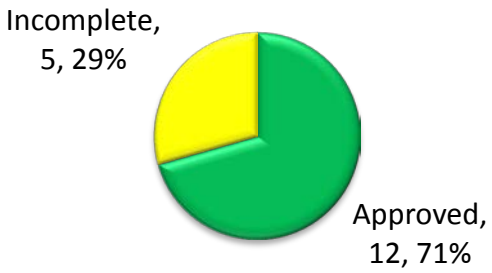
Top Prescriber Specialties of IPF Medications by Number of Claims



Prior Authorization of IPF Medications

There were 17 prior authorization requests submitted for IPF medications during calendar year 2015. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates[5,6]

Anticipated Patent Expirations:

- Ofev® (nintedanib): April 2024
- Esbriet® (pirfenidone): August 2033

Updated Treatment Guidelines:

- **July 2015:** The American Thoracic Society (ATS), in collaboration with European Respiratory Society (ERS), the Japanese Respiratory Society (JRS), and the Latin American Thoracic Association (ALAT), published an update of the 2011 clinical practice guidelines regarding the treatment of idiopathic pulmonary fibrosis. Significant changes to the treatment recommendations include:
  - Strong recommendation against the use of the following agents for the treatment of IPF: warfarin (specifically for anticoagulation in patients with IPF who do not have a known alternative indication for its use); imatinib (tyrosine kinase inhibitor with one target); combination prednisone, azathioprine, and *N*-acetylcysteine; ambrisentan (selective endothelin receptor antagonist)
  - Conditional recommendation against the use of the following agents for the treatment of IPF: sildenafil (phosphodiesterase-5 inhibitor); macitentan or bosentan (dual endothelin receptor antagonists)
  - Conditional recommendation for the use of the following agents for the treatment of IPF: nintedanib (tyrosine kinase inhibitor with multiple targets); pirfenidone (oral antifibrotic drug with pleiotropic effects)
    - Nintedanib and pirfenidone trials do not allow suggestions about the optimal duration of therapy, and it is unknown how long the treatment effect endures with ongoing therapy.
    - Future trials should focus on patients with IPF with severe impairment in pulmonary function tests (PFTs), rather than mild-to-moderate impairment, as well as patients with coexisting airflow obstruction less than the FEV_1/FVC (forced expiratory volume in 1 second/forced vital capacity) of 0.8, or those with comorbid emphysema. More information on proper duration of treatment is needed.

Recommendations

The College of Pharmacy does not recommend any changes to the IPF Medications category at this time.

Utilization Details of IPF Medications: Calendar Year 2015

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
NINTEDANIB PRODUCTS						
OFEV CAP 150MG	27	3	$228,095.17	$281.60	$8,447.97	60.60%
PIRFENIDONE PRODUCTS						
ESBRIET CAP 267MG	18	4	$148,291.52	$274.61	$8,238.42	39.40%
TOTAL	**45**	**7***	**$376,386.69**	**$278.80**	**$8,364.15**	**100.00%**

*Total number of unduplicated members.

[1] National Institutes of Health. National Heart, Lung, and Blood Institute: Idiopathic Pulmonary Fibrosis. Available online at: http://www.nhlbi.nih.gov/health/health-topics/topics/ipf/. Last revised 9/20/2011. Last accessed 2/19/2016.
[2] Medscape. Idiopathic Pulmonary Fibrosis. Available online at: http://emedicine.medscape.com/article/301226-overview. Last revised 8/12/2015. Last accessed 2/19/2016.
[3] UpToDate. Pathogenesis of Idiopathic Pulmonary Fibrosis. Available online at: http://www.uptodate.com/contents/pathogenesis-of-idiopathic-pulmonary-fibrosis. Last revised 11/12/2015. Last accessed 2/19/2016.
[4] National Library of Medicine. Genetics Home Reference: Idiopathic Pulmonary Fibrosis. Available online at: http://ghr.nlm.nih.gov/condition/idiopathic-pulmonary-fibrosis. Last revised 10/2010. Last accessed 2/18/2016.
[5] FDA: Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Last revised 2/17/2016. Last accessed 2/18/2016.
[6] American Thoracic Society: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis. Available online at: https://www.thoracic.org/statements/resources/interstitial-lung-disease/IPF-Full-length.pdf. Last revised 7/15/2015. Last accessed 2/23/2016.

Appendix O

Calendar Year 2015 Annual Review of Sylvant™ (Siltuximab)

Oklahoma Health Care Authority
March 2016

Introduction[1]

- Sylvant™ (siltuximab) is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with Multicentric Castleman's disease (MCD) who are Human Immunodeficiency Virus (HIV) negative and Human Herpesvirus-8 (HHV-8) negative.
- Limitations of Use: Siltuximab was not studied in patients with MCD who are HIV positive or HHV-8 positive because siltuximab did not bind to virally produced IL-6 in a nonclinical study.

Current Prior Authorization Criteria

Sylvant™ (Siltuximab) Approval Criteria:

1. An FDA approved diagnosis of Multicentric Castleman's Disease (also known as giant lymph node hyperplasia); and
2. Member must be Human Immunodeficiency Virus (HIV) and Human Herpesvirus-8 (HHV-8) negative; and
3. Member must be 18 years of age or older; and
4. The following FDA approved dosing restrictions will apply:
    a. 11 mg/kg via intravenous (IV) infusion every three weeks until treatment failure (defined as disease progression based on increase in symptoms, radiologic progression, or deterioration in performance status); and
5. Sylvant™ must be administered in a clinical setting able to provide resuscitation equipment, medications, and trained personnel; and
6. The prescriber must verify that a complete blood count (CBC) will be done prior to each dose for the first twelve months and for an additional three doses thereafter; and
7. Approvals will be for the duration of six months.

Utilization of Sylvant™ (Siltuximab): Calendar Year 2015

There have been no medical or pharmacy claims of Sylvant™ (siltuximab) during calendar year 2015.

Prior Authorization of Sylvant™ (Siltuximab)

There were no prior authorization requests submitted for Sylvant™ (siltuximab) during calendar year 2015.

Recommendations

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

[1] Sylvant™ Prescribing Information. Janssen Biotech Inc. Available online at: http://www.sylvant.com/shared/product/sylvant/sylvant-prescribing-information.pdf. Last revised 05/2015. Last accessed 02/2016.

Appendix P

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

FDA NEWS RELEASE

For Immediate Release: February 19th, 2016

FDA approves Briviact to treat partial onset seizures

The U.S. Food and Drug Administration approved Briviact (brivaracetam) as an add-on treatment to other medications to treat partial onset seizures in patients age 16 years and older with epilepsy.

Epilepsy is a brain disorder that causes people to have recurring seizures. A seizure is an episode, usually of relatively short duration, of abnormal brain activity. Seizures can cause a variety of symptoms, including uncontrolled movements or spasms, abnormal thinking and behavior, and abnormal sensations. Muscle spasms can be violent, and loss of consciousness can occur. Seizures occur when clusters of nerve cells (neurons) in the brain undergo uncontrolled activation. A partial onset seizure begins in a limited area of the brain.

Epilepsy has many possible causes including, among others, stroke, infection, tumors, traumatic brain injury, and abnormal brain development. In many cases, the specific cause is unknown. Epilepsy is one of the most common conditions affecting the brain. Approximately 5.1 million people in the United States have a history of epilepsy and approximately 2.9 million people in the United States have active epilepsy.

Briviact's effectiveness was studied in three clinical trials involving 1,550 participants. Briviact, taken along with other medications, was shown to be effective in reducing the frequency of seizures.

The most common side effects reported by people taking Briviact in clinical trials included drowsiness, dizziness, fatigue, nausea and vomiting.

Briviact must be dispensed with a Medication Guide for patients, which provides important information about the medication's use and risks. As is true for all drugs that treat epilepsy, the most serious risks include thoughts about suicide, attempts to commit suicide, feelings of agitation, new or worsening depression, aggression, and panic attacks. Rarely, patients may exhibit an allergic reaction associated with swelling of the lips, eyelids, or tongue with or without difficulty breathing.

Briviact is marketed by UCB, Inc. of Smyrna, Georgia.

Safety Announcements

FDA alerts compounding pharmacies of a nationwide voluntary recall of Syrspend SF and Syrspend SF Grape suspending agents from Fagron Inc., due to microbial contamination with yeast

[2-10-2016] The U.S. Food and Drug Administration is alerting compounding pharmacies of the voluntary recall of certain lots of SyrSpend SF and SyrSpend SF Grape suspending agents used in compounding of various oral liquid drug products, due to the presence of yeast (Candida galli).

The SyrSpend SF lots are:

- 15I21-U01-026920
- 15J26-U05-027457
- 15J26-U05-027473
- 15I21-U01-027370
- 15J19-U05-027406

The SyrSpend SF Grape lots are:

- 15G29-U03-025975
- 15A05-U03-022765
- 15A05-U06-023277

If an immunocompromised patient or a child with an immature immune system ingests the contaminated product, there is a potential the patient will get an infection for which systemic antimicrobial therapy would be necessary.

FDA recommends that compounders not use the referenced lots of contaminated Syrspend SF and Syrspend SF Grape in compounding drug products for patients. Compounding pharmacieswho have received the referenced lots of Syrspend SF and Syrspend SF Grape flavor should immediately discontinue use, quarantine the products,and return the products to Fagron, Inc.

FDA is not aware of adverse events reports with patients who may have used the suspending agents. FDA asks compounding pharmacies to report any adverse reactions to the FDA's MedWatch program:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm
- Download and complete the form, then submit it via fax at 1-800-FDA-0178

Current Drug Shortages Index (as of March 1st, 2016):

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

Acetohydroxamic Acid (Lithostat) Tablets	***Currently in Shortage***
Ammonium Chloride Injection	***Currently in Shortage***
Anagrelide Hydrochloride Capsules	***Currently in Shortage***
Atropine Sulfate Injection	***Currently in Shortage***
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	***Currently in Shortage***
Calcium Chloride Injection, USP	***Currently in Shortage***
Calcium Gluconate Injection	***Currently in Shortage***
Cefazolin Injection	***Currently in Shortage***
Cefepime Injection	***Currently in Shortage***
Cefotaxime Sodium (Claforan) Injection	***Currently in Shortage***
Cefotetan Disodium Injection	***Currently in Shortage***
Chloramphenicol Sodium Succinate Injection	***Currently in Shortage***
Chloroquine Phosphate Tablets	***Currently in Shortage***
Desmopressin Acetate Injection	***Currently in Shortage***
Dexamethasone Sodium Phosphate Injection	***Currently in Shortage***
Dextrose 5% Injection Bags	***Currently in Shortage***
Dextrose Injection USP, 70%	***Currently in Shortage***
Disopyramide Phosphate (Norpace) Capsules	***Currently in Shortage***
Doxorubicin (Adriamycin) Injection	***Currently in Shortage***
Epinephrine Injection	***Currently in Shortage***
Eptifibatide (Integrilin) Injection	***Currently in Shortage***
Ethiodized Oil (Lipiodol) Injection	***Currently in Shortage***
Fentanyl Citrate (Sublimaze) Injection	***Currently in Shortage***
Fomepizole Injection	***Currently in Shortage***
Gemifloxacin Mesylate (Factive) Tablets	***Currently in Shortage***
Imipenem and Cilastatin for Injection, USP	***Currently in Shortage***
Indigotindisulfonate Sodium (Indigo Carmine) Injection	***Currently in Shortage***
L-Cysteine Hydrochloride Injection	***Currently in Shortage***
Leucovorin Calcium Lyophilized Powder for Injection	***Currently in Shortage***
Leuprolide Acetate Injection	***Currently in Shortage***
Lidocaine Hydrochloride (Xylocaine) Injection	***Currently in Shortage***
LifeCare PCA™ Sterile Empty Vial and Injector	***Currently in Shortage***
Liotrix (Thyrolar) Tablets	***Currently in Shortage***
Mecasermin [rDNA origin] (Increlex) Injection	***Currently in Shortage***
Meropenem for Injection, USP	***Currently in Shortage***
Methyldopate Hydrochloride Injection	***Currently in Shortage***
Metoprolol Injection	***Currently in Shortage***
Morphine Sulfate Injection, USP, CII, (Preservative-Free)(For PCA Use Only)	***Currently in Shortage***
Multi-Vitamin Infusion (Adult and Pediatric)	***Currently in Shortage***

Mupirocin Calcium Nasal Ointment	***Currently in Shortage***
Nimodipine (Nymalize) Oral Solution	***Currently in Shortage***
Peritoneal Dialysis Solutions	***Currently in Shortage***
Phentolamine Mesylate Injection	***Currently in Shortage***
Piperacillin and Tazobactam (Zosyn) Injection	***Currently in Shortage***
Potassium Acetate Injection, USP	***Currently in Shortage***
Potassium Chloride Injection	***Currently in Shortage***
Reserpine Tablets	***Currently in Shortage***
Sacrosidase (Sucraid) Oral Solution	***Currently in Shortage***
Sodium Acetate Injection, USP	***Currently in Shortage***
Sodium Bicarbonate Injection, USP	***Currently in Shortage***
Sodium Chloride 0.9% Injection Bags	***Currently in Shortage***
Sodium Chloride 23.4% Injection	***Currently in Shortage***
Sufentanil Citrate (Sufenta) Injection	***Currently in Shortage***
Sumatriptan (Imitrex) Nasal Spray	***Currently in Shortage***
Technetium Tc99m Succimer Injection (DMSA)	***Currently in Shortage***
Tigecycline (Tygacil) Injection	***Currently in Shortage***
Tiopronin (Thiola)	***Currently in Shortage***
Tobramycin Injection	***Currently in Shortage***
Tretinoin Capsules	***Currently in Shortage***
Triamcinolone Hexacetonide Injectable Suspension (Aristospan)	***Currently in Shortage***
Trimipramine Maleate (SURMONTIL) Capsules	***Currently in Shortage***
Vancomycin Hydrochloride for Injection, USP	***Currently in Shortage***