

Drug Utilization Review Board

Oklahoma
Health Care
Authority

Wednesday,
November 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 Board Members
FROM: Bethany Holderread, Pharm.D.
SUBJECT: Packet Contents for Board Meeting – November 9, 2016
DATE: November 1, 2016
NOTE: The DUR Board will meet at 4:00 p.m. The meeting will be held at 4345 N Lincoln Blvd.

*Enclosed are the following items related to the November meeting.
Material is arranged in order of the agenda.*

Call to Order

Public Comment Forum

Acknowledgement of Dr. Jim Rhymer for Service to DUR Board

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

Update on Medication Coverage Authorization Unit/Drug Utilization Review of Prenatal Vitamins – Appendix B

Action Item – Proposed Executive Session as recommended by the Office of Legal Services and Authorized by the Open Meetings Act, 25 O.S. § 307(B)(4) – Discussion of Pending and Potential Litigation/Claims

Action Item – Vote to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), and Imlygic® (Talimogene Laherparepvec) – Appendix C

Action Item – Vote to Prior Authorize Relistor® (Methylnaltrexone) Tablets – Appendix D

Action Item – Vote to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szsz), & Amjevita™ (Adalimumab-atto) – Appendix E

Action Item – Vote to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch) – Appendix F

Action Item – Vote to Prior Authorize Ultravate® (Halobetasol Propionate 0.05% Lotion), Sernivo™ (Betamethasone Dipropionate 0.05% Spray), & Flurandrenolide 0.05% Cream and Lotion – Appendix G

Action Item – Annual Review of Orkambi® (Lumacaftor/Ivacaftor) & Kalydeco® (Ivacaftor) – Appendix H

Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) and Eplusa® (Sofosbuvir/Velpatasvir) – Appendix I

30-Day Notice to Prior Authorize Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone) – Appendix J

**Annual Review of Various Antibiotics and 30-Day Notice to Prior Authorize Acticlate® (Doxycycline Hyclate)
– Appendix K**

**Annual Review of Pancreatic Enzyme Products and 30-Day Notice to Prior Authorize Pancreaze®
(Pancrelipase), Pertzze® (Pancrelipase), and Viokace® (Pancrelipase) – Appendix L**

**Annual Review of Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior
Authorize BromSite™ (Bromfenac 0.075% Ophthalmic Solution) – Appendix M**

Annual Review of Keveyis™ (Dichlorphenamide) – Appendix N

FDA and DEA Updates – Appendix O

Future Business

Adjournment

Oklahoma Health Care Authority

Drug Utilization Review Board (DUR Board)

Meeting – November 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. Acknowledgement of Speakers for Public Comment

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

3. Acknowledgement of Dr. Jim Rhymer for Service to DUR Board

Items to be presented by Dr. Muchmore, Chairman:

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

- A. October 12, 2016 DUR Minutes – Vote
B. October 12, 2016 DUR Recommendations Memorandum

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

5. Update on Medication Coverage Authorization Unit/Drug Utilization Review of Prenatal Vitamins – See Appendix B

- A. Medication Coverage Activity for October 2016
B. Pharmacy Help Desk Activity for October 2016
C. Drug Utilization Review of Prenatal Vitamins

Items to be presented by Joseph Young:

6. Action Item – Proposed Executive Session as Recommended by the Office of Legal Services and Authorized by the Open Meetings Act, 25 O.S. § 307(B)(4) – Discussion of Pending and Potential Litigation/Claims

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

7. Action Item – Vote to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), and Imlygic® (Talimogene Laherparepvec) – See Appendix C

- A. Introduction
B. Recommendations

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

8. Action Item – Vote to Prior Authorize Relistor® (Methylnaltrexone) Tablets – See Appendix D

- A. Introduction
B. Cost Comparison: Medications for Opioid Induced Constipation (Chronic Non-Cancer Pain)
C. College of Pharmacy Recommendations

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

9. Action Item – Vote to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szss), & Amjevita™ (Adalimumab-atto) – See Appendix E

- A. Introduction
- B. College of Pharmacy Recommendations

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

10. Action Item – Vote to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch) – See Appendix F

- A. Introduction
- B. College of Pharmacy Recommendations

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

11. Action Item – Vote to Prior Authorize Ultravate® (Halobetasol Propionate Lotion 0.05%), Sernivo™ (Betamethasone Dipropionate 0.05% Spray), & Flurandrenolide 0.05% Cream and Lotion – See Appendix G

- A. Introduction
- B. College of Pharmacy Recommendations

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

12. Action Item – Annual Review of Orkambi® (Lumacaftor/Ivacaftor) & Kalydeco® (Ivacaftor) – See Appendix H

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

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

13. Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir) – See Appendix I

- A. Introduction
- B. Current Prior Authorization Criteria
- C. Utilization of Hepatitis C Medications
- D. Prior Authorization of Hepatitis C Medications
- E. Market News and Updates
- F. Regimen Comparison
- G. Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) Product Summary
- H. Epclusa® (Sofosbuvir/Velpatasvir) Product Summary
- I. College of Pharmacy Recommendations
- J. Utilization Details of Hepatitis C Medications

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

14. 30-Day Notice to Prior Authorize Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone) – See Appendix J

- A. Introduction
- B. Utilization of Oral Iron Chelating Agents
- C. Market News and Updates
- D. Oral Iron Chelating Agents Summary
- E. Estimated Cost Savings
- F. College of Pharmacy Recommendations
- G. Utilization Details of Oral Iron Chelating Agents

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

15. Annual Review of Various Antibiotics and 30-Day Notice to Prior Authorize Acticlate® (Doxycycline Hyclate) – See Appendix K

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

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

16. Annual Review of Pancreatic Enzyme Products and 30-Day Notice to Prior Authorize Pancreaze® (Pancrelipase), Pertzye® (Pancrelipase), and Viokace® (Pancrelipase) – See Appendix L

- A. Introduction
- B. Utilization of Pancreatic Enzyme Products
- C. Market News and Updates
- D. Pancreatic Enzyme Product Summaries
- E. Estimated Cost Savings
- F. College of Pharmacy Recommendations
- G. Utilization Details of Pancreatic Enzyme Products

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

17. Annual Review of Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize BromSite™ (Bromfenac 0.075% Ophthalmic Solution) – See Appendix M

- A. Current Prior Authorization Criteria
- B. Utilization of Ophthalmic NSAIDs
- C. Prior Authorization of Ophthalmic NSAIDs
- D. Market News and Updates
- E. BromSite™ (Bromfenac Ophthalmic Solution) Product Summary
- F. College of Pharmacy Recommendations
- G. Utilization Details of Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Non-presentation: questions only:

18. Annual Review of Keveyis™ (Dichlorphenamide) – See Appendix N

- A. Hyperkalemic and Hypokalemic Periodic Paralysis Background Information
- B. Current Prior Authorization Criteria
- C. Utilization of Keveyis™ (Dichlorphenamide)
- D. Market News and Updates
- E. College of Pharmacy Recommendations

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

19. FDA and DEA Updates – See Appendix O

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

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

- A. Asthma/COPD Medications
- B. Defitelio® (Defibrotide)
- C. Exondys 51™ (Eteplirsen)
- D. Otic Anti-Infectives
- E. Anti-Emetic Medications
- F. Elaprase® (Idursulfase)
- G. Phosphate Binders
- H. Testosterone Products

**Future business subject to change.*

21. Adjournment



Appendix A



**OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES OF MEETING OF OCTOBER 12, 2016**

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

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

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

OTHERS PRESENT:		
M. Patty Laster, Astellas	Denise Hill, Astellas	Todd Edwards, Merck
Dan Gobat, NNI	Eric Campbell, OK Arthritis Center	Andrew Thompson, Celgene
Tim Moran, Circassia	David Large, Supernus	Jason Schwier, Amgen
Corinne Copeland, Eisai	Roger Grotzinger, Bristol-Myers	Audrey Rattan, Alkermes
Matt Phillips, Zylera	Jim Chapman, AbbVie	Marc Parker, Sunovion
Mai Duong, Novartis	Kari Suttee, Novartis	Ron Schnare, Shire
Riaz Sirajuddin MD, Heart Solutions	Brent Hildebrand, Gilead	Jeff Knappen, Allergan
G. Caldwell, Caldwell & Assoc.	Brian Maves, Pfizer	

PRESENT FOR PUBLIC COMMENT:	
Eric Campbell	OK Arthritis Center
Mai Duong	Novartis
Riaz Sirajuddin	Heart Solutions of Oklahoma

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. 12 SPEAKER: ERIC CAMPBELL

2B: AGENDA NO. 12 SPEAKER: MAI DUONG

2C: AGENDA NO. 16 SPEAKER: MAI DUONG

2D: AGENDA NO. 16 SPEAKER: RIAZ SIRAJUDDIN

ACTION: NONE REQUIRED

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: SEPTEMBER 14, 2016 DUR MINUTES – VOTE

3B: SEPTEMBER 14, 2016 DUR RECOMMENDATIONS MEMORANDUM

3C: CORRESPONDENCE

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 4: VOTE ON 2017 MEETING DATES

4A: 2017 DRUG UTILIZATION REVIEW BOARD MEETING DATES

Materials included in agenda packet; presented by Dr. Muchmore

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 5: UPDATE ON MEDICATION COVERAGE AUTHORIZATION UNIT/LONG-ACTING BETA AGONIST UTILIZATION: PEDIATRIC MEMBERS

5A: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2016

5B: PHARMACY HELP DESK ACTIVITY FOR SEPTEMBER 2016

5C: LONG-ACTING BETA AGONIST UTILIZATION: PEDIATRIC MEMBERS

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE MILLIPRED™ (PREDNISOLONE SODIUM PHOSPHATE ORAL SOLUTION 10MG/5ML)

6A: INTRODUCTION

6B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented Dr. Holderread

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE XIIDRA™ (LIFITEGRAST 5% OPHTHALMIC SOLUTION)

7A: INTRODUCTION

7B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE ALLZITAL® (BUTALBITAL/ACETAMINOPHEN 25MG/325MG) & ESGIC® CAPSULES (BUTALBITAL/ACETAMINOPHEN/CAFFEINE 50MG/325MG/40MG)

8A: INTRODUCTION

8B: COLLEGE OF PHARMACY RECOMMENDATIONS

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 9: ANNUAL REVIEW OF BREAST CANCER MEDICATIONS

9A: INTRODUCTION

9B: UTILIZATION OF BREAST CANCER MEDICATIONS

9C: PRIOR AUTHORIZATION OF BREAST CANCER MEDICATIONS

9D: MARKET NEWS AND UPDATES

9E: RECOMMENDATIONS

9F: UTILIZATION DETAILS OF BREAST CANCER MEDICATIONS

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

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 10: ANNUAL REVIEW OF SKIN CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ODOMZO® (SONIDEGB), ERIVEDGE® (VISMODEGIB), KEYTRUDA® (PEMBROLIZUMAB), OPDIVO® (NIVOLUMAB), YERVOY® (IPILIMUMAB), TAFINLAR® (DABRAFENIB), ZELBORAF® (VEMURAFENIB), COTELLIC® (COBIMETINIB), MEKINIST® (TRAMETINIB), & IMLYGIC® (TALIMOGENE LAHERPAREPVEC)

10A: INTRODUCTION

10B: UTILIZATION OF SKIN CANCER MEDICATIONS

10C: MARKET NEWS AND UPDATES

10D: PRODUCT SUMMARIES

10E: RECOMMENDATIONS

10F: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 11: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE RELISTOR® (METHYLNALTREXONE) TABLETS

- 11A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 11B: UTILIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS**
- 11C: PRIOR AUTHORIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS**
- 11D: MARKET NEWS AND UPDATES**
- 11E: RELISTOR® (METHYLNALTREXONE) TABLETS PRODUCT SUMMARY**
- 11F: COST COMPARISON: MEDICATIONS FOR OPIOID INDUCED CONSTIPATION (CHRONIC NON-CANCER PAIN)**
- 11G: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 11H: UTILIZATION DETAILS OF CONSTIPATION AND DIARRHEA MEDICATIONS**
- 11I: UTILIZATION DETAILS OF XIFAXAN® (RIFAXIMIN)**

Materials included in agenda packet; presented by Dr. Adams

ACTION: NONE REQUIRED

AGENDA ITEM NO. 12: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE XELJANZ® XR (TOFACITINIB EXTENDED-RELEASE), TALTZ® (IXEKIZUMAB), INFLECTRA™ (INFLIXIMAB-DYYB), ERELZI™ (ETANERCEPT-SZZS), & AMJEVITA™ (ADALIMUMAB-ATTO)

- 12A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 12B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS**
- 12C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS**
- 12D: MARKET NEWS AND UPDATES**
- 12E: XELJANZ® XR (TOFACITINIB EXTENDED-RELEASE) PRODUCT SUMMARY**
- 12F: TALTZ® (IXEKIZUMAB) PRODUCT SUMMARY**
- 12G: INFLECTRA™ (INFLIXIMAB-DYYB) PRODUCT SUMMARY**
- 12H: ERELZI™ (ETANERCEPT-SZZS) PRODUCT SUMMARY**
- 12I: AMJEVITA™ (ADALIMUMAB-ATTO) PRODUCT SUMMARY**
- 12J: NONINFECTIOUS INTERMEDIATE UVEITIS, POSTERIOR UVEITIS, & PANUVEITIS SUMMARY**
- 12K: TUMOR NECROSIS FACTOR RECEPTOR ASSOCIATED PERIODIC SYNDROME (TRAPS), HYPERIMMUNOGLOBULIN D SYNDROME (HIDS)/MEVALONATE KINASE DEFICIENCY (MKD), AND FAMILIAL MEDITERRANEAN FEVER (FMF) SUMMARY**
- 12L: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 12M: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS**

Materials included in agenda packet; presented by Dr. Holderread

ACTION: NONE REQUIRED

AGENDA ITEM NO. 13: ANNUAL REVIEW OF BLADDER CONTROL MEDICATIONS

- 13A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 13B: UTILIZATION OF BLADDER CONTROL MEDICATIONS**
- 13C: PRIOR AUTHORIZATION OF BLADDER CONTROL MEDICATIONS**
- 13D: MARKET NEWS AND UPDATES**
- 13E: PRICING TREND(S)**
- 13F: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 13G: UTILIZATION DETAILS OF BLADDER CONTROL MEDICATIONS**

Materials included in agenda packet; presented by Dr. Chandler

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

ACTION: MOTION CARRIED

AGENDA ITEM NO. 14: ANNUAL REVIEW OF LIDODERM® (LIDOCAINE 5% PATCH) AND 30-DAY NOTICE TO PRIOR AUTHORIZE SYNERA® (LIDOCAINE/TETRACAINE TOPICAL PATCH)

- 14A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 14B: UTILIZATION OF LIDODERM® (LIDOCAINE 5% PATCH)**
- 14C: PRIOR AUTHORIZATION OF LIDODERM® (LIDOCAINE 5% PATCH)**
- 14D: SYNERA® (LIDOCAINE/TETRACAINE TOPICAL PATCH) PRODUCT SUMMARY**
- 14E: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler

ACTION: NONE REQUIRED

AGENDA ITEM NO. 15: ANNUAL REVIEW OF TOPICAL CORTICOSTEROIDS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ULTRAVATE® (HALOBETASOL PROPIONATE 0.05% LOTION), SERNIVO™ (BETAMETHASONE DIPROPIONATE 0.05% SPRAY), & FLURANDRENOLIDE 0.05% CREAM AND LOTION

- 15A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 15B: UTILIZATION OF TOPICAL CORTICOSTEROIDS**
- 15C: PRIOR AUTHORIZATION OF TOPICAL CORTICOSTEROIDS**
- 15D: MARKET NEWS AND UPDATES**
- 15E: ULTRAVATE® (HALOBETASOL 0.05% LOTION) PRODUCT SUMMARY**
- 15F: SERNIVO™ (BETAMETHASONE DIPROPIONATE 0.05% TOPICAL SPRAY) PRODUCT SUMMARY**
- 15G: FLURANDRENOLIDE 0.05% CREAM AND LOTION PRODUCT SUMMARY**
- 15H: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 15I: UTILIZATION DETAILS OF TOPICAL CORTICOSTEROIDS**

Materials included in agenda packet; presented by Dr. Nawaz

ACTION: NONE REQUIRED

AGENDA ITEM NO. 16: ANNUAL REVIEW OF CORLANOR® (IVABRADINE) AND ENTRESTO™ (SACUBITRIL/VALSARTAN)

- 16A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 16B: UTILIZATION OF CORLANOR® AND ENTRESTO™**
- 16C: PRIOR AUTHORIZATION OF CORLANOR® AND ENTRESTO™**
- 16D: MARKET NEWS AND UPDATES**
- 16E: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 16F: UTILIZATION DETAILS OF CORLANOR® AND ENTRESTO™**

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

ACTION: NONE REQUIRED

AGENDA ITEM NO. 17: ANNUAL REVIEW OF GROWTH HORMONE

- 17A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 17B: UTILIZATION OF GROWTH HORMONE**
- 17C: PRIOR AUTHORIZATION OF GROWTH HORMONE**
- 17D: MARKET NEWS AND UPDATES**
- 17E: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 17F: UTILIZATION DETAILS OF GROWTH HORMONE**

Materials included in agenda packet; 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: CYSTIC FIBROSIS MEDICATIONS

19B: KEVEYIS™ (DICHLORPHENAMIDE)

19C: VARIOUS SYSTEMIC ANTIBIOTICS

19D: OPHTHALMIC ANTI-INFLAMMATORIES

19E: HEPATITIS C MEDICATIONS

19F: IRON OVERLOAD MEDICATIONS

19G: PANCREATIC ENZYMES

****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 5:30 p.m.



The University of Oklahoma

Health Sciences Center

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

Memorandum

Date: October 13, 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 October 12, 2016

Recommendation 1: 2017 Drug Utilization Review Board Meeting Dates

MOTION CARRIED by unanimous approval.

Meetings are held the second Wednesday of every month at 4:00 PM

January 11, 2017	May 10, 2017	September 13, 2017
February 8, 2017	June 14, 2017	October 11, 2017
March 8, 2017	July 12, 2017	November 8, 2017
April 12, 2017	August 9, 2017	December 13, 2017

Recommendation 2: Long-Acting Beta Agonist Utilization: Pediatric Members

NO ACTION REQUIRED.

SoonerCare claims analysis of pediatric utilization of single-component long-acting Beta₂ Agonist (LABA) medications did not reveal a pressing need for intervention. The results of this analysis are similar to the number of members found in February 2015. Most pediatric members utilizing single-component LABA medications required a unique dosage formulation, had only one paid claim for a single-component LABA, or were being followed by a pulmonary specialist. Based on these findings the College of Pharmacy does not recommend any changes to the current LABA criteria at this time.

Recommendation 3: Vote to Prior Authorize Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Millipred™ (prednisolone sodium phosphate oral solution 10mg/5mL) with criteria similar to Veripred™ 20 (prednisolone sodium phosphate oral solution 20mg/5mL). The recommended criteria can be seen below with additions noted in red.

Veripred™ 20 (Prednisolone Sodium Phosphate Oral Solution 20mg/5mL) and Millipred™ (Prednisolone Sodium Phosphate Oral Solution 10mg/5mL) Approval Criteria:

1. Authorization of Veripred™ 20 or Millipred™ requires a patient-specific, clinically significant reason why the member cannot use a tablet or an alternative strength liquid formulation.

Recommendation 4: Vote to Prior Authorize Xiidra™ (Lifitegrast 5% Ophthalmic Solution)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Xiidra™ (lifitegrast ophthalmic solution) with the following criteria:

Xiidra™ (Lifitegrast Ophthalmic Solution) Approval Criteria:

1. Member must be 17 years of age or older and have an FDA approved diagnosis of dry eye disease (DED); and
2. Prescriber must verify that environmental factors (e.g., humidity, fans) have been addressed; and
3. Member must have trials with at least three over-the-counter (OTC) products for three days in the last 30 days that failed to relieve signs and symptoms of dry eyes; and
4. A patient-specific, clinically significant reason why the member cannot use Restasis® (cyclosporine ophthalmic emulsion), which is available without a prior authorization; and
5. A quantity limit of two vials per day will apply.

Recommendation 5: Vote to Prior Authorize Allzital® (Butalbital/Acetaminophen 25mg/325mg) & Esgic® Capsules (Butalbital/Acetaminophen/Caffeine 50mg/325mg/40mg)

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Butalbital Products category:

1. The prior authorization of Allzital® (butalbital/acetaminophen 25mg/325mg) with criteria similar to the other butalbital containing medications.
 - a. An FDA approved indication for the treatment of tension-type headache; and

- b. Member must be 12 years of age or older; and
- c. Failure within the previous 60 days of the following:
 - i. All available formulations of butalbital/acetaminophen medications that do not require prior authorization (medications available without prior authorization contain butalbital/acetaminophen/caffeine in the standard 50mg/325mg/40mg dose); and
 - ii. Trials of at least two nonsteroidal anti-inflammatory drugs (NSAIDs), unless contraindicated.
- 2. The prior authorization of Esgic® capsules (butalbital/acetaminophen/caffeine 50mg/325mg/40mg) based on state maximum allowable cost (SMAC) with the following criteria:
 - a. A patient-specific, clinically significant reason why the member cannot use Fioricet® tablets (butalbital/acetaminophen/caffeine 50mg/325mg/40mg).

Recommendation 6: Annual Review of Breast Cancer Medications

MOTION CARRIED by unanimous approval.

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

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

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

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

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

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

Ibrance® (Palbociclib) Approval Criteria:

- ~~1. An FDA approved diagnosis of metastatic breast cancer for first-line use only; and~~
- ~~2. Member must be estrogen receptor (ER) positive; and~~
- ~~3. Member must have negative expression of Human Epidermal Receptor Type 2 (HER2); and~~

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

Recommendation 7: Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), & Imlygic® (Talimogene Laherparepvec)

NO ACTION REQUIRED.

Recommendation 8: Annual Review of Constipation and Diarrhea Medications and 30-Day Notice to Prior Authorize Relistor® (Methylnaltrexone) Tablets

NO ACTION REQUIRED.

Recommendation 9: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szys), & Amjevita™ (Adalimumab-atto)

NO ACTION REQUIRED.

Recommendation 10: Annual Review of Bladder Control Medications

MOTION CARRIED by unanimous approval.

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

1. The placement of Oxytrol® (oxybutynin 3.9mg/day patch) into a Special PA Tier of the Bladder Control PBPA category based on estimated acquisition cost (EAC) with the following criteria:
 - a. An FDA approved diagnosis of overactive bladder; and
 - b. A patient-specific, clinically significant reason why all lower tiered medications are not appropriate for the member; and
 - c. A quantity limit of 8 patches every 30 days will apply.

Bladder Control Medications			
Tier-1	Tier-2	Tier-3	Special PA
oxybutynin (Ditropan®)	tolterodine (Detrol®)	darifenacin (Enablex®)	oxybutynin patch (Oxytrol®)
oxybutynin ER (Ditropan XL®)	trospium (Sanctura™)	fesoterodine (Toviaz™)	
		flavoxate (Urispas®)	
		mirabegron (Myrbetriq™)	
		oxybutynin gel (Gelnique™)	
		solifenacin (VESicare®)	
		tolterodine ER (Detrol LA®)	
		trospium ER (Sanctura XR™)	

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

ER = extended release

Urispas® (flavoxate) has been removed from the Bladder Control PBPA category. The FDA approved indications for flavoxate are not consistent with the other products in this category. Flavoxate is FDA approved for symptomatic relief of dysuria, urgency, nocturia, suprapubic pain, frequency and incontinence as may occur in cystitis, prostatitis, urethritis, urethrocystitis/urethrotrigonitis. Additionally, the low state maximum allowable cost (SMAC) would necessitate moving it to Tier-1. Requiring a trial of flavoxate as criteria for approval of a Tier-2 medication would not be appropriate given its unique indications.

Recommendation 11: Annual Review of Lidoderm® (Lidocaine 5% Patch) and 30-Day Notice to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch)

NO ACTION REQUIRED.

Recommendation 12: Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Ultravate® Lotion (Halobetasol Propionate 0.05%), Sernivo™ (Betamethasone Dipropionate Spray 0.05%), & Flurandrenolide 0.05% Cream and Lotion

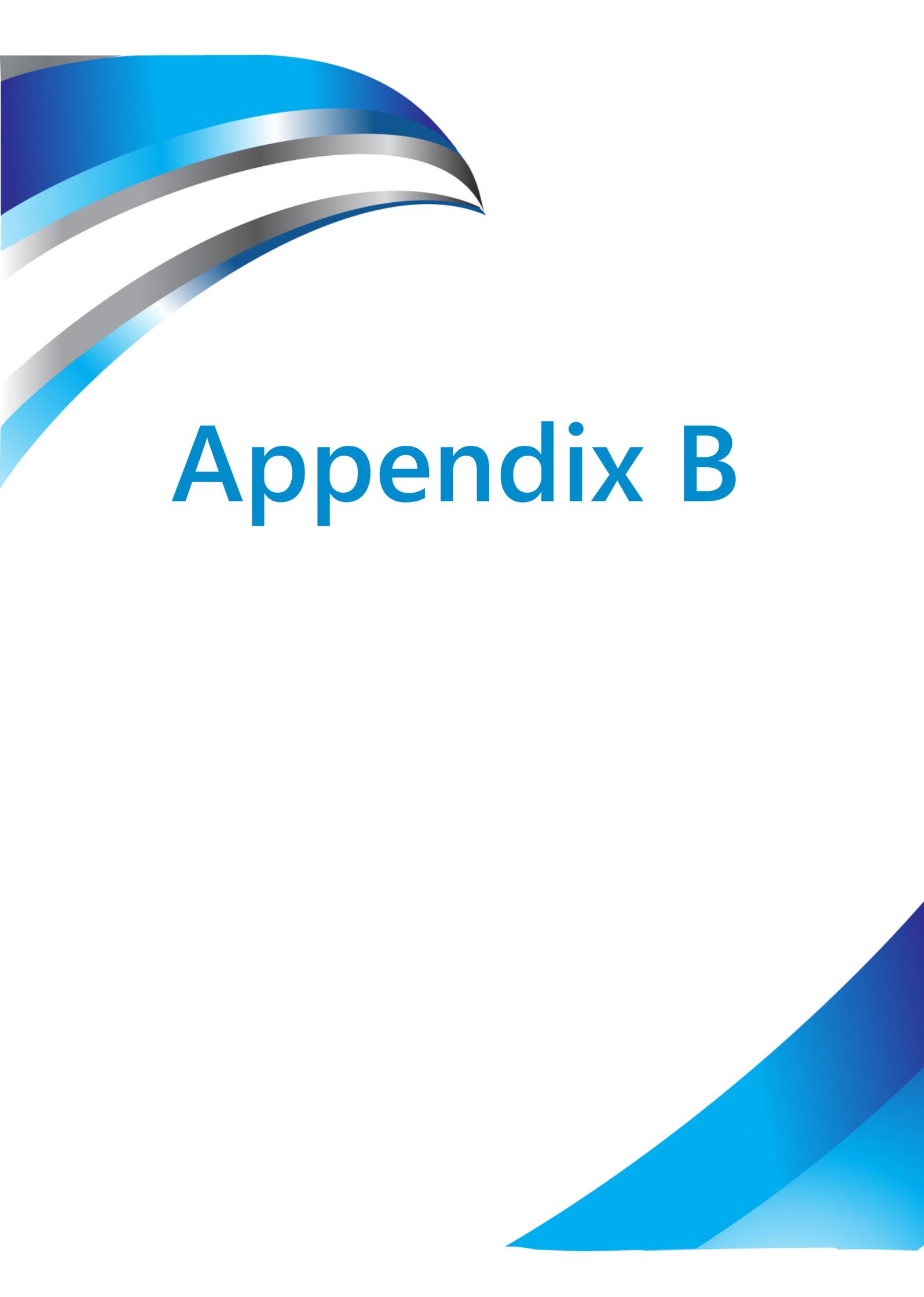
NO ACTION REQUIRED.

Recommendation 13: Annual Review of Corlanor® (Ivabradine) and Entresto™ (Sacubitril/Valsartan)

NO ACTION REQUIRED.

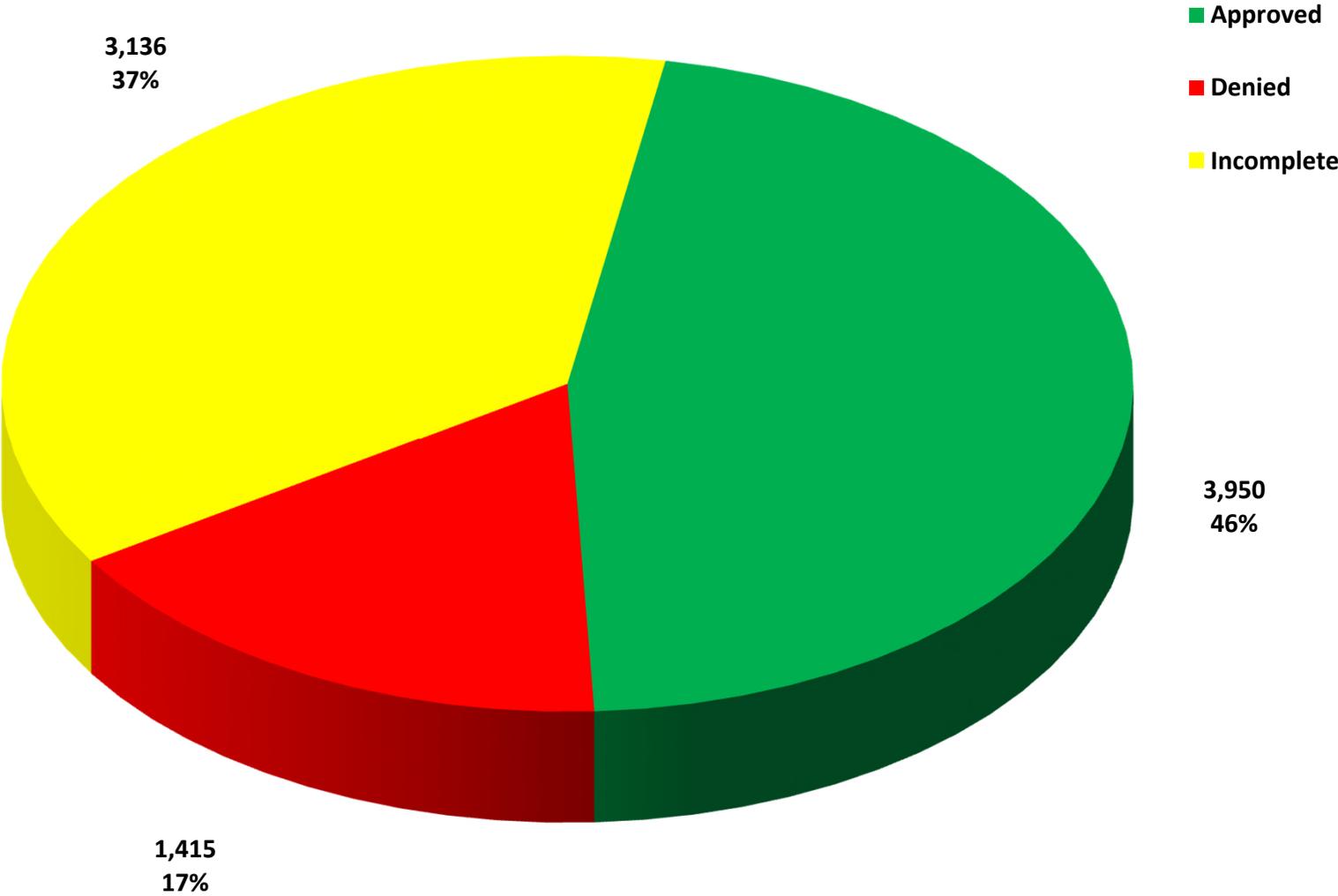
Recommendation 14: Annual Review of Growth Hormone

NO ACTION REQUIRED.



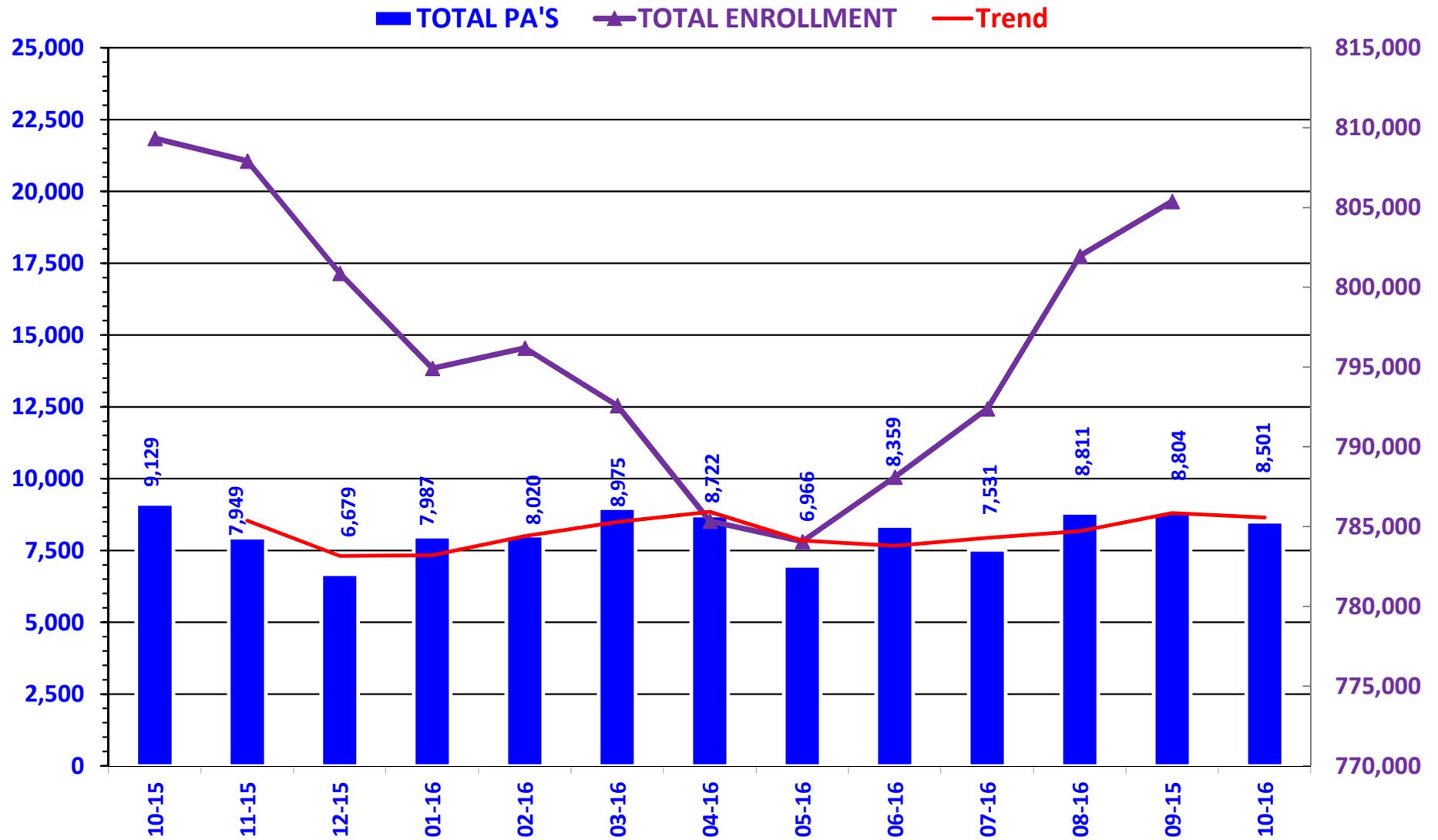
Appendix B

PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER 2016



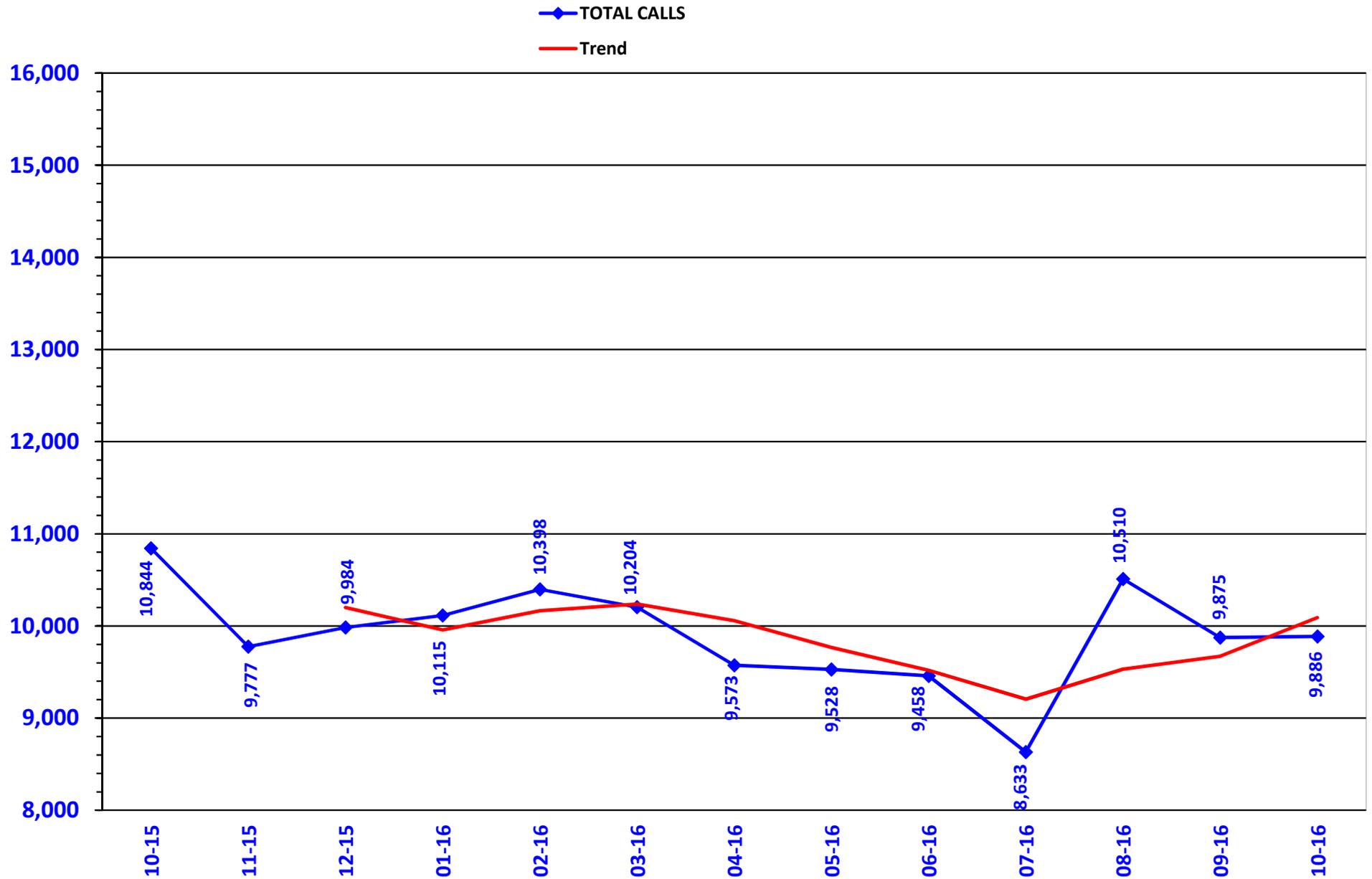
PA totals include approved/denied/incomplete/overrides

PRIOR AUTHORIZATION REPORT: OCTOBER 2015 – OCTOBER 2016



PA totals include approved/denied/incomplete/overrides

CALL VOLUME MONTHLY REPORT: OCTOBER 2015 – OCTOBER 2016



Prior Authorization Activity
10/1/2016 Through 10/31/2016

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	446	164	85	197	350
Analgesic - NonNarcotic	17	0	4	13	0
Analgesic, Narcotic	512	269	44	199	162
Angiotensin Receptor Antagonist	14	4	1	9	357
Antiasthma	107	39	18	50	350
Antibiotic	17	6	3	8	251
Anticonvulsant	116	53	16	47	327
Antidepressant	84	17	23	44	288
Antidiabetic	193	69	35	89	352
Antihistamine	175	143	6	26	355
Antimigraine	30	6	6	18	188
Antineoplastic	10	4	0	6	174
Antiulcers	141	32	58	51	210
Antiviral	58	32	12	14	9
Anxiolytic	66	42	8	16	257
Atypical Antipsychotics	405	220	52	133	332
Biologics	64	34	11	19	313
Bladder Control	38	8	13	17	357
Blood Thinners	196	129	7	60	321
Botox	32	27	3	2	336
Buprenorphine Medications	193	159	10	24	84
Cardiovascular	70	33	10	27	308
Chronic Obstructive Pulmonary Disease	108	13	30	65	355
Constipation/Diarrhea Medications	191	29	77	85	132
Contraceptive	26	20	2	4	300
Dermatological	91	13	54	24	157
Diabetic Supplies	504	281	15	208	198
Endocrine & Metabolic Drugs	74	56	2	16	132
Erythropoietin Stimulating Agents	24	14	2	8	88
Fibromyalgia	216	27	118	71	333
Fish Oils	14	3	6	5	357
Gastrointestinal Agents	129	24	39	66	180
Growth Hormones	93	69	8	16	144
Hepatitis C	77	39	18	20	7
HFA Rescue Inhalers	75	23	15	37	317
Insomnia	35	6	10	19	146
Insulin	62	11	17	34	358
Miscellaneous Antibiotics	18	4	3	11	11
Multiple Sclerosis	57	27	7	23	200
Muscle Relaxant	69	6	26	37	144
Nasal Allergy	84	7	26	51	317
Neurological Agents	63	47	6	10	350
NSAIDs	195	29	56	110	275
Ocular Allergy	32	6	10	16	226
Ophthalmic Anti-infectives	12	2	5	5	6
Osteoporosis	11	2	3	6	358
Other*	295	54	65	176	218
Otic Antibiotic	25	6	2	17	8
Pediculicide	30	12	5	13	15
Respiratory Agents	18	8	1	9	153
Statins	46	15	10	21	357
Stimulant	972	460	95	417	340
Synagis	330	95	123	112	146

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Testosterone	50	16	14	20	339
Topical Antifungal	30	3	5	22	44
Topical Corticosteroids	96	5	36	55	134
Vitamin	50	23	18	9	305
Pharmacotherapy	53	41	0	12	215
Emergency PAs	0	0	0	0	
Total	7,239	2,986	1,354	2,899	

Overrides					
Brand	47	24	9	14	304
Cumulative Early Refill	5	4	1	0	180
Diabetic Supplies	5	3	0	2	204
Dosage Change	334	302	5	27	13
High Dose	9	7	0	2	225
Ingredient Duplication	31	24	0	7	9
Lost/Broken Rx	85	77	2	6	10
NDC vs Age	36	30	3	3	271
Nursing Home Issue	50	47	0	3	11
Opioid Quantity	15	12	2	1	114
Other*	46	40	1	5	11
Quantity vs. Days Supply	545	356	35	154	261
STBS/STBSM	26	21	2	3	44
Stolen	21	19	0	2	20
Temporary Unlock	2	1	1	0	27
Third Brand Request	29	15	3	11	31
Wrong D.S. on Previous Rx	1	1	0	0	18
Overrides Total	1,262	964	61	237	
Total Regular PAs + Overrides	8,501	3,950	1,415	3,136	

Denial Reasons	
Unable to verify required trials.	2,461
Does not meet established criteria.	1,440
Lack required information to process request.	638

Other PA Activity	
Duplicate Requests	571
Letters	8,267
No Process	9
Changes to existing PAs	595
Helpdesk Initiated Prior Authorizations	693
PAs Missing Information	34

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

Update: Drug Utilization Review of Prenatal Vitamins

Oklahoma Health Care Authority
November 2016

Introduction

The College of Pharmacy and the Oklahoma Health Care Authority are engaged in an effort to increase utilization of prenatal vitamins (PV) among pregnant SoonerCare members. Several educational efforts were conducted in the first quarter of 2014 including a prescriber letter, pharmacy fax blast, and articles in the member and provider newsletters; these efforts led to an immediate increase in utilization with a declining effect over time. Follow-up efforts in 2015 saw similar results. More recently a concerning decline can be seen in the percentage of members utilizing PV compared to the number of deliveries (state fiscal year [SFY] 2012: 76.08% vs SFY2016: 58.20%).

Utilization of Prenatal Vitamins: Fiscal Year 2016

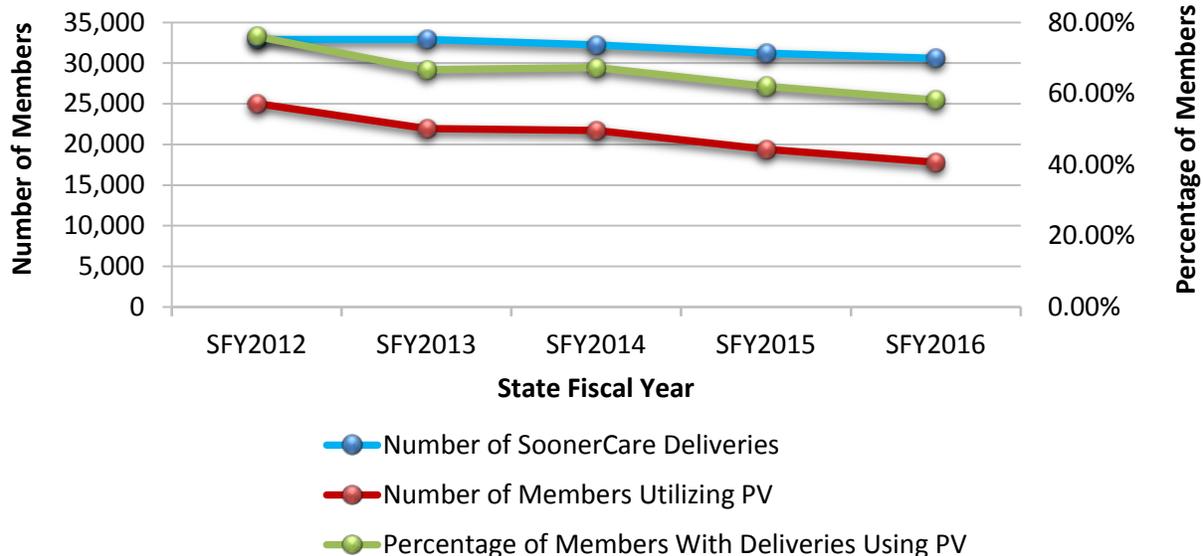
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	19,392	39,037	\$1,271,973.57	\$32.58	\$0.72	1,815,527	1,758,266
2016	17,805	35,889	\$1,805,639.69	\$50.31	\$1.15	1,810,521	1,569,887
% Change	-8.20%	-8.10%	42.00%	54.40%	59.70%	-0.30%	-10.70%
Change	-1,587	-3,148	\$533,666.12	\$17.73	\$0.43	-5,006	-188,379

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Five Year Fiscal Year Utilization Trend of Prenatal Vitamin Utilization



Discussion

While deliveries have declined in the last several fiscal years, utilization of PV has declined at a disproportionate rate. The percentage of members utilizing PV compared to the number of deliveries has decreased by 17.88% from SFY2012 to SFY2016. Increases in the percentage can be seen the first quarter of 2014 and 2015 immediately following educational efforts with a declining result over time.

Another concern revealed by the claims analysis is the number of claims per member. Most members received only two paid claims for PV during a given fiscal year. This number has remained steady over the last five fiscal years, and was not accounted for by an increase in units implying a larger quantity per claim (e.g., three month supply for one claim). The maximum benefit of PV requires continued use throughout pregnancy and ideally starts before the member becomes pregnant.

Utilization of PV is difficult to assess and may be falsely low due to the large number of over-the-counter (OTC) products available that members may be using. Claims for OTC products for SoonerCare members are not obtainable and are therefore not included in this analysis.

Recommendations

Based on the decline in the percentage of members utilizing PV compared to the number of deliveries, further educational efforts are warranted. Efforts in the prenatal class appear to have an initial increase with a waning effect over time. The College of Pharmacy recommends incorporating regular prenatal education, based on previous successful interventions, into its work-flow to maintain increased utilization of PV. Opportunities for new interventions will be sought wherever possible.

Previous successful interventions included a letter sent to more than 3,000 SoonerCare prescribers emphasizing PV utilization. The mailing included a list of PV covered without prior authorization as well as a sample prescription detailing how a physician could write for the desired ingredients in a PV and the pharmacist could substitute to a covered product. Similarly a fax blast was sent to SoonerCare pharmacies which included a list of the PV that do not require prior authorization along with the National Drug Codes (NDCs) so the pharmacy could easily order a product from the list. The pharmacies and prescribers also received directions for accessing the SoonerCare website and locating the updated PV list of non-prior authorized products. Articles regarding the importance of PV have also been included in the SoonerCare member and provider newsletters. Members enrolled in the SoonerCare "Text for Baby" program receive reminders regarding PV as well.



Appendix C



Vote to Prior Authorize Odomzo® (Sonidegib), Erivedge® (Vismodegib), Keytruda® (Pembrolizumab), Opdivo® (Nivolumab), Yervoy® (Ipilimumab), Tafinlar® (Dabrafenib), Zelboraf® (Vemurafenib), Cotellic® (Cobimetinib), Mekinist® (Trametinib), & Imlygic® (Talimogene Laherparepvec)

**Oklahoma Health Care Authority
November 2016**

Introduction^{1,2,3,4,5,6,7,8,9,10,11,12,13,14}

Odomzo® (Sonidegib):

- Sonidegib is a selective Hedgehog pathway inhibitor which binds to and inhibits Smoothed homologue (SMO), the transmembrane protein involved in Hedgehog signal transduction. It is FDA approved for the following:
 - Treatment of adults with locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or those who are not candidates for surgery or radiation therapy

Erivedge® (Vismodegib):

- Vismodegib is a selective Hedgehog pathway inhibitor which binds to and inhibits Smoothed homologue (SMO), the transmembrane protein involved in Hedgehog signal transduction. It is FDA approved for the following:
 - Treatment of metastatic BCC, or locally-advanced BCC that has recurred following surgery or in patients who are not candidates for surgery and not candidates for radiation therapy

Keytruda® (Pembrolizumab):

- Pembrolizumab is a highly selective anti-PD-1 humanized monoclonal antibody which inhibits programmed cell death-1 (PD-1) activity by binding to the PD-1 receptor on T-cells to block PD-1 ligands (PD-L1 and PD-L2) from binding. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling (Hamid 2013). This reverses T-cell suppression and induces antitumor responses (Robert 2014). It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma
 - Treatment of metastatic non-small cell lung cancer (NSCLC) in patients with PD-L1-expressing tumors (as determined by an approved test) who have disease progression on or after platinum-containing chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression (on approved EGFR- or ALK-directed therapy) prior to receiving pembrolizumab
 - Treatment of recurrent or metastatic squamous cell carcinoma of the head and neck in patients with disease progression on or after platinum-containing chemotherapy

Opdivo® (Nivolumab):

- Nivolumab is a fully human immunoglobulin-G4 (IgG4) monoclonal antibody that selectively inhibits programmed cell death-1 (PD-1) activity by binding to the PD-1 receptor to block the ligands PD-L1 and PD-L2 from binding. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling (Hamid 2013). This reverses T-cell suppression and induces antitumor responses (Robert 2014). It is FDA approved for the following:
 - Treatment of classical Hodgkin lymphoma in patients that have relapsed or progressed following autologous hematopoietic stem cell transplant and post-transplant brentuximab vedotin
 - Treatment (as a single-agent) of BRAF V600 wild-type or BRAF V600 mutation-positive unresectable or metastatic melanoma
 - Treatment of unresectable or metastatic melanoma (in combination with ipilimumab)
 - Treatment of metastatic non-small cell lung cancer (NSCLC) that has progressed on or after platinum-based chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression (on approved EGFR- or ALK-directed therapy) prior to receiving nivolumab
 - Treatment of advanced renal cell cancer in patients who have received prior anti-angiogenic therapy

Yervoy® (Ipilimumab):

- Ipilimumab is a recombinant human IgG1 immunoglobulin monoclonal antibody which binds to the cytotoxic T-lymphocyte associated antigen 4 (CTLA-4). CTLA-4 is a down-regulator of T-cell activation pathways. Blocking CTLA-4 allows for enhanced T-cell activation and proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma
 - Adjuvant treatment of cutaneous melanoma in patients with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy

Tafinlar® (Dabrafenib):

- Dabrafenib is a selective inhibitor of some mutated forms of BRAF. BRAF V600 mutations result in constitutive activation of the BRAF pathway; through BRAF inhibition, dabrafenib inhibits tumor cell growth. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E mutation (single-agent therapy)
 - Treatment of unresectable or metastatic melanoma in patients with BRAF V600E or BRAF V600K mutations (in combination with trametinib)

Zelboraf® (Vemurafenib):

- Vemurafenib is a selective inhibitor of some mutated forms of BRAF. BRAF V600 mutations result in constitutive activation of the BRAF pathway; through BRAF inhibition, vemurafenib inhibits tumor cell growth. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E mutation (as detected by an approved test)

Cotellic® (Cobimetinib):

- Cobimetinib is a potent and selective inhibitor of the mitogen-activated extracellular kinase (MEK) pathway (Larkin 2014); it reversibly inhibits MEK1 and MEK2, which are upstream regulators of the extracellular signal-related kinase (ERK) pathway. The ERK pathway promotes cellular proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E or V600K mutation (in combination with vemurafenib)

Mekinist® (Trametinib):

- Trametinib is a potent and selective inhibitor of the mitogen-activated extracellular kinase (MEK) pathway (Larkin 2014); it reversibly inhibits MEK1 and MEK2, which are upstream regulators of the extracellular signal-related kinase (ERK) pathway. The ERK pathway promotes cellular proliferation. It is FDA approved for the following:
 - Treatment of unresectable or metastatic melanoma in patients with a BRAF V600E or BRAF V600K mutation (as detected by an approved test), either as a single-agent or in combination with dabrafenib

Imlygic® (Talimogene Laherparepvec):

- Talimogene laherparepvec is a genetically modified attenuated herpes simplex virus 1 (HSV) oncolytic virus which selectively replicates in and lyses tumor cells (Andtbacka 2015). It is FDA approved for the following:
 - Treatment (local) of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery

Recommendations

Odomzo® (Sonidegib) Approval Criteria [Basal Cell Carcinoma Diagnosis]:

1. Either of the following criteria must be met for approval:
 - a. Diagnosis of locally advanced basal cell carcinoma (BCC) that has either:
 - i. Recurred following surgery or radiation therapy; or
 - ii. Surgery or radiation is contraindicated; or
 - b. Diagnosis of metastatic basal cell carcinoma.

Erivedge® (Vismodegib) Approval Criteria [Basal Cell Carcinoma Diagnosis]:

1. Either of the following criteria must be met for approval:
 - a. Diagnosis of locally advanced basal cell carcinoma (BCC) that has either:
 - i. Recurred following surgery or radiation therapy; or
 - ii. Surgery or radiation is contraindicated; or
 - b. Diagnosis of metastatic basal cell carcinoma.

Keytruda® (Pembrolizumab) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. Pembrolizumab must be used as a single-agent; and
 - c. Patient meets one of the following:
 - i. Pembrolizumab is being used as first-line therapy; or

- ii. Pembrolizumab is being used as second-line therapy or subsequent therapy for disease progression if not previously used and patient has ECOG performance status 0 to 2; and
- d. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)].

Keytruda® (Pembrolizumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
 - i. Exception: lymphocyte-predominant Hodgkin lymphoma
 - b. Pembrolizumab must be used as a single-agent; and
 - c. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)].

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

1. All of the following criteria must be met for approval:
 - a. Diagnosis of metastatic NSCLC; and
 - b. The patient has not previously failed other PD-1 inhibitors [i.e. Opdivo® (nivolumab)]; and
 - c. Tumors express PD-L1 (FDA approved test); and
 - d. Patient meets one of the following:
 - i. **New diagnosis as first-line therapy (patient has not received chemotherapy to treat disease) if:**
 1. **Tumor does not express sensitizing EGFR mutations or ALK translocations**
 2. **ECOG performance status 0 to 1**
 - ii. Disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin); or
 1. Patients with EGFR-mutation-positive should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations;* and
 - A. Examples of drugs for EGFR-mutation-positive tumors: osimertinib, erlotinib, afatinib, or gefitinib
 2. Patients with ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab. *This does not apply if tumors do not have these mutations;* and
 - A. Examples of drugs for ALK-mutation-positive tumors: crizotinib, ceritinib, or alectinib
 3. ECOG performance status 0 to 2.

Keytruda® (Pembrolizumab) Approval Criteria [Head and Neck Cancer Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of recurrent or metastatic disease; and
 - b. Squamous cell histology; and
 - c. Patient has received prior platinum containing regimen (cisplatin or carboplatin); and
 - d. ECOG performance status 0 to 1; and
 - e. Dose does not exceed 200mg every three weeks.

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

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

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

1. All of the following criteria must be met for approval:
 - a. Diagnosis of metastatic NSCLC; and
 - b. Tumor histology is one of the following:
 - i. Adenocarcinoma; or
 - ii. Squamous cell; or
 - iii. Large Cell; and
 - c. Nivolumab must be used as a single-agent; and
 - d. Disease progression on or after platinum-containing chemotherapy (cisplatin or carboplatin); and
 - e. ECOG performance status 0 to 2; and
 - f. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)]; and
 - g. Dose as follows:
 - i. Single-agent: 240mg every two weeks.

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

1. All of the following criteria must be met for approval:
 - a. One of the following criteria is met:
 - i. Disease relapsed within six months of initial chemotherapy; or
 - ii. Disease is progressive on initial chemotherapy; and

- b. Nivolumab must be used as a single-agent or in combination with ipilimumab; and
- c. ECOG performance status 0 to 2
- d. The patient has not previously failed other PD-1 inhibitors (i.e. Keytruda® (pembrolizumab)).

Opdivo® (Nivolumab) Approval Criteria [Hodgkin Lymphoma Diagnosis]:

- 1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or refractory classical Hodgkin lymphoma; and
 - i. Exception: lymphocyte-predominant Hodgkin lymphoma
 - b. Nivolumab must be used as a single-agent; and
 - c. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)].

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

- 1. All of the following criteria must be met for approval:
 - a. Diagnosis of relapsed or surgically unresectable stage IV disease; and
 - b. Tumor histology: predominantly clear cell; and
 - c. Failed prior therapy with one of the following medications:
 - i. Sunitinib; or
 - ii. Sorafenib; or
 - iii. Pazopanib; or
 - iv. Axitinib; and
 - d. Nivolumab must be used as a single-agent; and
 - e. ECOG performance status 0 to 2; and
 - f. The patient has not previously failed other PD-1 inhibitors [i.e. Keytruda® (pembrolizumab)]
 - g. Dose as follows:
 - i. Single-agent: 240mg every two weeks.

Yervoy® (Ipilimumab) Approval Criteria [Unresectable or Metastatic Melanoma Diagnosis]:

- 1. All of the following criteria must be met for approval:
 - a. ECOG performance status 0 to 2; and
 - b. Ipilimumab is used in combination with nivolumab as:
 - i. First-line therapy; or
 - ii. Second-line or subsequent therapy for disease progression if nivolumab was not previously used; and
 - c. Ipilimumab is used as a single-agent for one of the following:
 - i. First-line therapy as a single course of four treatments; or
 - ii. Second-line or subsequent lines of therapy as a single course of four treatments; or
 - iii. Retreatment, consisting of a 4-dose limit, for an individual who had no significant systemic toxicity during prior ipilimumab therapy, and whose disease progressed after being stable for greater than six months following completion of a prior course of ipilimumab, and for whom no intervening therapy has been administered; and

- d. Maximum dose of 3mg/kg will apply.

Yervoy® (Ipilimumab) Approval Criteria [Adjuvant Treatment of Melanoma]:

1. All of the following criteria must be met for approval:
 - a. Patient has complete resection of melanoma with lymphadenectomy; and
 - b. Patient has Stage III disease with regional nodes of greater than 1 mm and no in-transit metastasis; and
 - c. Ipilimumab must be used as a single-agent; and
 - d. Maximum doses of 10mg/kg will apply.

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

1. All of the following criteria must be met for approval:
 - a. One of the following criteria is met:
 - i. Disease relapsed within six months of initial chemotherapy; or
 - ii. Disease is progressive on initial chemotherapy; and
 - b. Used in combination with nivolumab; and
 - c. ECOG performance status 0 to 2.

Tafinlar® (Dabrafenib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF melanoma
 - c. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®); and
 - d. One of the following is met:
 - i. Used as first-line therapy; or
 - ii. Used as second-line therapy or subsequent therapy and patient has an ECOG performance status of 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF NSCLC
 - b. Dabrafenib must be used as a single-agent or in combination with trametinib (Mekinist®)
 - c. Diagnosis of refractory or metastatic disease.

Zelboraf® (Vemurafenib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Not indicated for wild-type BRAF melanoma
 - c. Vemurafenib must be used as a single-agent or in combination with cobimetinib; and

- d. One of the following is met:
 - i. Used as first-line therapy; or
 - ii. Used as second-line therapy or subsequent therapy and patient has an ECOG performance status of 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Vemurafenib is not indicated for wild-type BRAF NSCLC
 - b. Vemurafenib must be used as a single-agent
 - c. Diagnosis of refractory or metastatic disease.

Zelboraf® (Vemurafenib) Approval Criteria [Hairy-Cell Leukemia Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Vemurafenib must be used as a single-agent; and
 - b. Vemurafenib is being used to treat disease progression following failure of purine analog therapy (i.e. pentostatin, cladribine).

Cotellic® (Cobimetinib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Cobimetinib is not indicated for wild-type BRAF melanoma
 - c. One of the following is met:
 - i. Used as first-line therapy in combination with vemurafenib; or
 - ii. Used as second-line therapy or subsequent therapy with vemurafenib and patient has an ECOG performance status of 0 to 2.

Mekinist® (Trametinib) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Diagnosis of unresectable or metastatic melanoma; and
 - b. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Trametinib is not indicated for wild-type BRAF melanoma.
 - c. One of the following is met:
 - i. Used as first-line therapy in combination with dabrafenib; or
 - ii. Used as second-line therapy or subsequent therapy with dabrafenib and patient has an ECOG performance status of 0 to 2; or
 - iii. Used as second-line therapy or subsequent therapy as a single-agent if:
 1. Patient was intolerant to prior BRAF inhibitor therapy (dabrafenib, vemurafenib); and
 2. No evidence of disease progression on prior BRAF inhibitor therapy (dabrafenib, vemurafenib); and
 3. ECOG performance status is 0 to 2.

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

1. All of the following criteria must be met for approval:
 - a. BRAF V600E or V600K mutation detected by an FDA-approved test; and
 - i. Trametinib is not indicated for wild-type BRAF NSCLC
 - b. Trametinib must be used in combination with dabrafenib.
 - c. Diagnosis of refractory or metastatic disease.

Imlygic® (Talinogene Laherparepvec) Approval Criteria [Melanoma Diagnosis]:

1. All of the following criteria must be met for approval:
 - a. Patient has unresectable cutaneous, subcutaneous, or nodal lesions that are recurrent after initial surgery; and
 - i. Talinogene laherparepvec is not indicated with visceral metastases.
 - b. The patient is not immunocompromised or pregnant.

¹ NCCN. *NCCN Clinical Practice Guidelines in Oncology (Basal Cell Skin Cancer)*. Retrieved September 20, 2016, from https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf.

² National Cancer Institute. *SEER Cancer Statistics*. Retrieved September 8, 2016, from <http://www.cancer.gov/about-cancer/what-is-cancer/statistics>.

³ NCCN. *NCCN Clinical Practice Guidelines in Oncology (Melanoma)*. Retrieved September 15, 2016, from https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf.

⁴ Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. *Nature* 2002; 417(6892):949–954.

⁵ Hodi FS, O’Day SJ, McDermott DF, et al. Improved survival with Ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010; 363(8):711–723.

⁶ McArthur GA, Chapman PB, Robert C, et al. Safety and efficacy of vemurafenib in BRAFV600E and BRAFV600K mutation-positive melanoma (BRIM-3): extended follow-up of a phase 3, randomised, open-label study. *Lancet Oncol* 2014; 15(3):323–332.

⁷ Hamid O, Robert C, Daud A, et al. Safety and tumor responses with LAMBROLIZUMAB (Anti-PD-1) in melanoma. *N Engl J Med* 2013; 369(2):134–144.

⁸ Hauschild A, Grob J-J, Demidov LV, et al. Dabrafenib in BRAF-mutated metastatic melanoma: a multicenter, open-label, phase 3 randomised controlled trial. *Lancet* 2012; 380(9839):358–365.

⁹ Flaherty KT, Robert C, Hersey P, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. *N Engl J Med* 2012; 367(2):107–114.

¹⁰ Larkin J, Ascierto PA, Dréno B, et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med* 2014; 371(20):1867–1876.

¹¹ Topalian SL, Sznol M, McDermott DF, et al. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving Nivolumab. *J Clin Oncol* 2014; 32(10):1020–1030.

¹² Guy GP, Machlin S, Ekwueme DU, Yabroff KR. Prevalence and costs of skin cancer treatment in the US, 2002–2006 and 2007–2011. *Am J Prev Med*. In press 2014.

¹³ Robert C, Thomas L, Bondarenko I, et al. Ipilimumab plus Dacarbazine for previously untreated metastatic melanoma. *N Engl J Med* 2011; 364(26):2517–2526.

¹⁴ Andtbacka RHI, Kaufman HL, Collichio F, et al. Talinogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma. *J Clin Oncol* 2015; doi: 10.1200/JCO.2014.58.3377.



Appendix D



Vote to Prior Authorize Relistor® (Methylnaltrexone) Tablets

Oklahoma Health Care Authority

November 2016

Introduction^{1,2}

- **Relistor® (methylnaltrexone) tablets** were approved by the U.S. Food and Drug Administration (FDA) in July 2016 and are indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain. Methylnaltrexone is a selective antagonist of opioid binding at the mu-opioid receptor. As a quaternary amine, the ability of methylnaltrexone to cross the blood-brain barrier is restricted. This allows methylnaltrexone to function as a peripherally-acting mu-opioid receptor antagonist (PAMORA) in tissues such as the gastrointestinal tract, thereby decreasing the constipating effects of opioids without impacting opioid-mediated analgesic effects on the central nervous system.
- **Relistor® (methylnaltrexone) injection** was first FDA approved in 2008 and is indicated for the treatment of OIC in adults with advanced terminal illness who are receiving palliative care, when response to laxative therapy has not been sufficient, and for the treatment of OIC in adults with chronic non-cancer pain.

Cost Comparison: Medications for OIC (Chronic Non-Cancer Pain)

Medication	Dosing Regimen	Cost/Unit*	Cost/Month
Relistor® (methylnaltrexone) 150mg tablets	450mg PO Q day	\$16.67	\$1,500.30
Amitiza® (lubiprostone) 24mcg capsules	24mcg PO BID	\$5.32	\$319.20
Movantik® (naloxegol) 25mg tablets	25mg PO Q day	\$9.27	\$278.10
Relistor® (methylnaltrexone) 12mg/0.6mL vials or syringes	12mg subQ Q day	\$163.07	\$4,892.10

BID = Twice Daily; Q day = Once daily; PO = By mouth; subQ = Subcutaneous

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

Recommendations

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

Relistor® (Methylnaltrexone) Tablets Approval Criteria:

1. An FDA approved diagnosis of opioid-induced constipation (OIC) in members 18 years of age or older with chronic, non-cancer pain who are currently on chronic opioid therapy; and
2. Member must not have known or suspected gastrointestinal obstruction; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Documented and updated colon screening for members greater than 50 years of age; and
5. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and
 - a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
6. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone) or Movantik® (naloxegol) must be provided; and
7. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
8. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 90 tablets for a 30 day supply will apply.

Additionally the College of Pharmacy recommends updating the criteria for Relistor® injection with the changes noted in red:

Relistor® (Methylnaltrexone) Injection Approval Criteria (Chronic Non-Cancer Pain Diagnosis):

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of opioid-induced constipation (OIC) in patients with chronic pain unrelated to cancer; and
3. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
4. Member must have current use of opioid medications; and
5. Documented and updated colon screening for members greater than 50 years of age; and
6. Documentation of hydration attempts and trials of at least three different types of products that failed to relieve constipation. Trials must be within the past 90 days. Products may be over-the-counter (OTC) or prescription (does not include fiber or stool softeners); and

- a. One of the three trials must be polyethylene glycol 3350 (PEG-3350); and
 - b. Members with an oncology-related diagnosis are exempt from the trial requirements; and
7. Mechanical gastrointestinal obstruction has been ruled out; and
8. A patient-specific, clinically significant reason why member cannot use Amitiza[®] (lubiprostone) or Movantik[®] (naloxegol) must be provided; and
9. A patient-specific, clinically significant reason why member cannot use the tablet formulation of Relistor[®]; and
10. The 12mg single-use vials, syringes, or kits will be the preferred products. Criteria for consideration of 8mg single-use syringes:
 - a. Weight range of 38kg to 62kg; and/or
 - b. Caregiver unable to draw up dose from vial.
11. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
12. A quantity limit of 30 units per month will apply.

¹ Relistor[®] Prescribing Information, Valeant Pharmaceuticals. Available online at: <https://shared.salix.com/shared/pi/relistor-pi.pdf?id=811664a>. Last revised 07/2016. Last accessed 09/23/2016.

² Relistor[®] Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/relistor-2/>. Last revised 07/31/2016. Last accessed 09/23/2016.



Appendix E



Vote to Prior Authorize Xeljanz® XR (Tofacitinib Extended-Release), Taltz® (Ixekizumab), Inflectra™ (Infliximab-dyyb), Erelzi™ (Etanercept-szszs), & Amjevita™ (Adalimumab-atto)

Oklahoma Health Care Authority
November 2016

Introduction^{1,2,3,4,5,6,7,8,9,10,11,12,13,14}

- **Xeljanz® XR [tofacitinib extended-release (ER)]** is an inhibitor of Janus kinases (JAKs) indicated for the treatment of adult patients with moderately-to-severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Tofacitinib ER is available as 11mg oral tablets and the recommended dose of tofacitinib ER is 11mg by mouth once daily. The immediate-release formulation is dosed 5mg twice daily.
- **Taltz® (ixekizumab)** is a humanized IL-17A antagonist indicated for the treatment of adults with moderate-to-severe psoriasis (PsO) who are candidates for systemic therapy or phototherapy. Ixekizumab is available as 80mg/mL single-dose, prefilled autoinjectors and syringes. Ixekizumab is administered as a subcutaneous injection into the upper arms, thighs, or abdomen. Injection sites should be rotated. The recommended dosing of ixekizumab is 160mg (two 80mg injections) at Week 0, followed by 80mg at weeks 2, 4, 6, 8, 10, and 12, then 80mg every four weeks.
- **Inflectra™ (infliximab-dyyb)** is a biosimilar to Remicade® (infliximab). Infliximab-dyyb is a tumor necrosis factor (TNF)-blocker indicated for Crohn's disease (CD), ulcerative colitis (UC), RA, ankylosing spondylitis (AS), psoriatic arthritis (PsA), and PsO. Inflectra™ is indicated for all Remicade® indications except pediatric UC. Infliximab-dyyb is supplied as 100mg infliximab-dyyb in a 20mL vial intended to be administered by intravenous (IV) infusion over two hours. The recommended dosing varies by disease state but ranges from 3mg/kg to 10mg/kg every four to eight weeks.
- **Erelzi™ (etanercept-szszs)** is a biosimilar to Enbrel® (etanercept). Etanercept-szszs is a TNF-blocker indicated for RA, polyarticular juvenile idiopathic arthritis (JIA), PsA, AS, and PsO. Erelzi™ is indicated for all Enbrel® indications. Etanercept-szszs is supplied as 25mg/0.5mL and 50mg/mL prefilled syringes and 50mg/mL prefilled Sensoready® pens intended for subcutaneous injection. The recommended dosing varies by disease state, but is typically 50mg once weekly.
- **Amjevita™ (adalimumab-atto)** is a biosimilar to Humira® (adalimumab). Adalimumab-atto is a TNF-blocker indicated for RA, polyarticular JIA, PsA, AS, CD, UC, and PsO. Amjevita™ is indicated for all Humira® indications except pediatric CD, polyarticular JIA in pediatric patients 2 to 4 years, hidradenitis suppurativa (HS), and uveitis. Adalimumab-atto is supplied as 40mg/0.8mL and 20mg/0.4mL prefilled syringes and 40mg/0.8mL prefilled SureClick® autoinjectors intended for subcutaneous injection. The recommended dosing varies by disease state but is typically 40mg every other week.
- In July 2016, AbbVie announced the U.S. Food and Drug Administration (FDA) approval of **Humira® (adalimumab) for the treatment of patients with noninfectious intermediate**

and posterior uveitis and panuveitis. Humira® is the only FDA-approved non-corticosteroid therapy for intermediate uveitis, posterior uveitis, and panuveitis. The new indication is in addition to nine other indications for use of Humira® including PsA, AS, moderate-to-severe RA, polyarticular JIA, CD, HS, UC, and PsO.

- In July 2016, Bristol-Myers Squibb Company announced the launch of **Orencia® ClickJect™ (abatacept)**, an autoinjector that can be used for self-administration of 125mg of subcutaneous abatacept. Orencia® is also available as an IV infusion and prefilled syringe.
- In September 2016, the FDA approved **three new indications for Ilaris® (canakinumab)**, an interleukin-1-β inhibitor. The three new indications include tumor necrosis factor receptor-associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD), and familial Mediterranean fever (FMF). All three indications are inherited conditions characterized by intermittent attacks of fever, inflammation, and severe muscle pain. Ilaris® is the first approved therapy for TRAPS and HIDS/MKD, and was previously approved for cryopyrin-associated periodic syndromes (CAPs) and active systemic JIA.

Recommendations

The College of Pharmacy recommends the addition of Orencia® ClickJect™ (abatacept autoinjector), Xeljanz® XR (tofacitinib extended-release), Taltz® (ixekizumab), Inflectra™ (infliximab-dyyb), Erelzi™ (etanercept-szszs), and Amjevita™ (adalimumab-atto) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category.

Current Tier-3 approval criteria for this category will apply.

- If the net cost of Inflectra™ (infliximab-dyyb), Erelzi™ (etanercept-szszs), and Amjevita™ (adalimumab-atto) is determined to be greater than the net cost of the reference product formulations of Inflectra™, Erelzi™, and Amjevita™ authorization would also require a patient-specific, clinically significant reason why the member could not use the reference product formulations of Inflectra™, Erelzi™, and Amjevita™.
- If the net cost of Xeljanz® XR (tofacitinib extended-release) and Orencia® ClickJect™ (abatacept autoinjector) is determined to be greater than the net cost of the immediate-release formulation of Xeljanz® XR or the prefilled syringe formulation of Orencia® ClickJect™ authorization would also require a patient-specific, clinically significant reason why the member could not use the immediate-release formulation of Xeljanz® XR or the prefilled syringe formulation of Orencia® ClickJect™.

Additionally, the College of Pharmacy recommends the following criteria for Humira® (adalimumab) for a diagnosis of noninfectious intermediate and posterior uveitis or panuveitis:

Humira® (Adalimumab) for Noninfectious Intermediate and Posterior Uveitis or Panuveitis

Approval Criteria:

1. A diagnosis of noninfectious intermediate uveitis, posterior uveitis, or panuveitis in adults; and
2. A failed trial with a corticosteroid injection or systemic corticosteroid in which member has had an inadequate response; or
3. A patient-specific, clinically significant reason a trial of corticosteroid treatment is inappropriate for the member.

Lastly, the College of Pharmacy recommends the following criteria for Ilaris® (canakinumab) for a diagnosis of tumor necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD), or familial Mediterranean fever (FMF):

Ilaris® (Canakinumab) for Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF) Approval Criteria:

1. A diagnosis of tumor necrosis factor receptor associated periodic syndrome (TRAPS) with chronic or recurrent disease activity defined as six flares per year; or
2. A diagnosis of hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD); or
3. A diagnosis of familial Mediterranean fever (FMF) with documented active disease despite colchicine therapy or documented intolerance to effective doses of colchicine; and
4. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Targeted Immunomodulator Agents*		
Tier-1 (DMARDs appropriate to disease state)	Tier-2*	Tier-3
6-mercaptopurine	adalimumab (Humira®)	abatacept (Orencia®)
azathioprine	etanercept (Enbrel®)	adalimumab-atto (Amjevita™)
hydroxychloroquine		alefacept (Amevive®)
leflunomide		anakinra (Kineret®)
mesalamine		apremilast (Otezla®)
methotrexate		canakinumab (Ilaris®)‡
minocycline		certolizumab pegol (Cimzia®)
NSAIDs		etanercept-szsz (Erelzi™)
oral corticosteroids		golimumab (Simponi® & Simponi® Aria™)
		infliximab (Remicade®)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		rituximab (Rituxan®)
		secukinumab (Cosentyx®)
		tocilizumab (Actemra®)
		tofacitinib (Xeljanz® & Xeljanz® XR)
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

*Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable. Tier-2 drugs subject to move to Tier-3. Appropriate laboratory monitoring must be verified by the prescriber prior to approval.

DMARDs = Disease modifying antirheumatic drugs; NSAIDs = Nonsteroidal anti-inflammatory drugs

‡Unique criteria applies for a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF).

Tier-2 Approval Criteria:

1. An FDA approved diagnosis; and
2. A trial of at least one Tier-1 medication in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. For a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) authorization of a Tier-2 product requires history of failure of a mesalamine product (does not have to be within the last 90 days) and a trial of one Tier-1 in the last 90 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
4. Prior stabilization on the Tier-2 medication documented within the last 100 days.

Tier-3 Approval Criteria:

1. An FDA approved diagnosis; and
2. Recent trials of one Tier-1 medication and all available Tier-2 medications that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
3. Prior stabilization on the Tier-3 medication documented within the last 100 days; or
4. A unique FDA-approved indication not covered by Tier-2 products.

Humira® (Adalimumab) for Hidradenitis Suppurativa Approval Criteria:

1. A diagnosis of moderate-to-severe hidradenitis suppurativa (HS); and
2. Hurley Stage II or III disease; and
3. The member must have at least 3 abscesses or inflammatory nodules; and
4. Previous failure of at least two of the following: topical or systemic antibiotics, oral or intralesional corticosteroids, dapsone, cyclosporine, antiandrogens (spironolactone or oral contraceptives), finasteride, or surgery.

Ilaris® (Canakinumab) Approval Criteria [Cryopyrin-Associated Periodic Syndromes (CAPS) Diagnosis]:

1. An FDA approved indication of Cryopyrin-Associated Periodic Syndromes (CAPS) verified by genetic testing. This includes Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 years of age and older; and
2. The member must not be using a tumor necrosis factor blocking agent (e.g. adalimumab, etanercept, and infliximab) or anakinra; and
3. Ilaris® should not be initiated in patients with active or chronic infection including hepatitis B, hepatitis C, human immunodeficiency virus, or tuberculosis; and
4. The following dosing requirements must be met:
 - a. Dosing should not be more often than once every 8 weeks; and
 - b. Dosing (requires recent weight in kilograms):
 - i. Body weight greater than 40kg: 150mg
 - ii. Body weight 15kg to 40kg: 2mg/kg. If inadequate response, may be increased to 3mg/kg.
5. Approvals will be for the duration of one year.

-
- ¹ Xeljanz® Product Information. Pfizer Laboratories. Available online at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=959>. Last revised 02/2016. Last accessed 10/18/2016.
- ² Taltz® Product Information. Eli Lilly and Company. Available online at: <http://uspl.lilly.com/taltz/taltz.html#pi>. Last revised 03/2016. Last accessed 10/18/2016.
- ³ Inflectra™ Product Information. Manufactured by Celltrion for Hospira. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125544s000lbl.pdf. Last revised 04/2016. Last accessed 10/18/2016.
- ⁴ U.S. Food and Drug Administration (FDA). FDA approves Inflectra, a biosimilar to Remicade. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm494227.htm>. Issued 04/05/2016. Last accessed 10/18/2016.
- ⁵ Erelzi™ Product Information. Sandoz Inc. Available online at: http://www.us.sandoz.com/cs/www.us.sandoz.com.wls10/assets/media/shared/documents/Erelzi_PI_MG_IFU.pdf. Last revised 08/2016. Last accessed 10/18/2016.
- ⁶ U.S. Food and Drug Administration (FDA). FDA approves Erelzi, a biosimilar to Enbrel. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518639.htm>. Issued 08/30/2016. Last accessed 10/18/2016.
- ⁷ Brown T. FDA Ok's Biosimilar to Adalimumab for Inflammatory Diseases. *Medscape*. Available online at: http://www.medscape.com/viewarticle/869221?nlid=109442_3901&src=wnl_newsalert_160923_MSCPEDIT&uac=163910MN&mpID=1202938&faf=1. Issued 09/23/2016. Last accessed 10/18/2016.
- ⁸ Amjevita™ Product Information. Amgen Inc. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761024lbl.pdf. Last revised 09/2016. Last accessed 10/18/2016.
- ⁹ U.S. Food and Drug Administration. FDA approves Amjevita, a biosimilar to Humira. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm522243.htm>. Issued 09/23/2016. Last accessed 10/18/2016.
- ¹⁰ Brooks M. FDA Clears Adalimumab (Humira) for Uveitis. *Medscape*. Available online at: <http://www.medscape.com/viewarticle/865654>. Issued 07/01/2016. Last accessed 10/18/2016.
- ¹¹ Humira Product Information. Abbvie inc. Available online at: <http://www.rxabbvie.com/pdf/humira.pdf>. Last revised 07/2016. Last accessed 10/18/2016.
- ¹² Bristol-Myers Squibb Company. Bristol-Myers Squibb Announces Availability of FDA-Approved Orencia® (abatacept) ClickJect™. *American Pharmaceutical Review*. Available online at: <http://www.americanpharmaceuticalreview.com/1315-News/189302-Bristol-Myers-Squibb-Announces-Availability-of-FDA-Approved-ORENCIA-abatacept-ClickJect/>. Issued 07/21/2016. Last accessed 10/18/2016.
- ¹³ Brooks M. Canakinumab (Ilaris) Gets FDA Nod for Three Rare Periodic Fever Syndromes. *Medscape*. Available online at: http://www.medscape.com/viewarticle/869226_print. Issued 09/26/2016. Last accessed 10/18/2016.
- ¹⁴ Ilaris® Product Information. Novartis Pharmaceuticals. Available online at: <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/ilaris.pdf>. Last revised 09/2016. Last accessed 10/18/2016.



Appendix F



Vote to Prior Authorize Synera® (Lidocaine/Tetracaine Topical Patch)

Oklahoma Health Care Authority
November 2016

Introduction^{1,2}

Synera® was approved by the U.S. Food and Drug Administration (FDA) on June 23, 2005. It was previously covered as a medical benefit for SoonerCare members. In March 2014, the FDA approved a supplemental new drug application for labeling changes to Synera®. The patient *Instructions for Use* section of the label was revised to ensure proper use of Synera® in the home setting, and “Not for Home Use by Patient” statements were deleted from the package insert and the carton and container labels.

Synera® is a combination amide and ester local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodesiccation, and shave biopsy of skin lesions. Synera® is a topical patch containing 70mg of lidocaine and 70mg of tetracaine. One patch is applied to intact skin for 20 to 30 minutes then removed prior to the procedure. The wholesale acquisition cost (WAC) of Synera® is \$14.95 per patch resulting in a treatment cost of \$29.90. EMLA® (lidocaine/prilocaine 2.5%/2.5%) cream includes the same FDA approved indications (in addition to other approved indications) and the national average drug acquisition cost (NADAC) is \$0.94 per gram resulting in a treatment cost of \$4.70. The above costs for treatment are based on the maximum dose recommended for minor dermal procedures and do not reflect rebated prices or net costs. WAC was used when NADAC was unavailable.

Recommendations

The College of Pharmacy recommends the prior authorization of Synera® (lidocaine/tetracaine topical patch) with the following criteria:

Synera® (Lidocaine/Tetracaine Topical Patch) Approval Criteria:

1. Member must be 3 years of age or older; and
2. Member must have an FDA approved need for local dermal analgesia for superficial venous access or superficial dermatological procedures; and
3. A patient-specific, clinically significant reason why the member cannot use EMLA® (lidocaine/prilocaine) cream, which is available without a prior authorization, must be provided; and
4. The total number of procedures must be provided on the prior authorization request; and
5. A quantity limit of two patches per day will apply.

¹ Synera® Prescribing Information. Galen US, Inc. Available online at: http://www.synera.com/wp-content/uploads/2015/03/SYNERA_PI.pdf. Last revised 05/2014. Last accessed 10/2016.

² U.S. Food and Drug Administration (FDA): Drug Databases. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/applletter/2014/021623Orig1s015,s017ltr.pdf. Issued 03/10/2014. Last accessed 10/2016.



Appendix G



Vote to Prior Authorize Prior Authorize Ultravate® (Halobetasol Propionate 0.05% Lotion), Sernivo™ (Betamethasone Dipropionate 0.05% Spray), & Flurandrenolide 0.05% Cream and Lotion

Oklahoma Health Care Authority
November 2016

Introduction^{1,2,3}

- Ultravate® (halobetasol 0.05% lotion) is indicated for the topical treatment of plaque psoriasis in patients 18 years of age and older. Treatment beyond two weeks is not recommended, and the total dosage should not exceed 50 grams per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.
- Sernivo™ (betamethasone dipropionate 0.05% topical spray) is indicated for the treatment of mild-to-moderate plaque psoriasis in patients 18 years of age and older.
- Flurandrenolide 0.05% cream and lotion is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Recommendations

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

1. The placement of Ultravate® (halobetasol 0.05% lotion) into Tier-2 of the ultra-high to high potency category; and
2. The placement of Sernivo™ (betamethasone dipropionate 0.05% topical spray), flurandrenolide 0.05% cream, and flurandrenolide 0.05% lotion into Tier-2 of the medium-high to medium potency category; and
3. Move Beta-Val® (betamethasone valerate 0.1% ointment and lotion) to Tier-1 of the medium-high to medium potency category; and
4. Move hydrocortisone butyrate 0.1% solution and Lidex E® (fluocinonide emollient) cream to Tier-2 of the medium-high to medium potency category; and
5. Move Temovate® (clobetasol propionate 0.05% gel and solution) to Tier-2 of the ultra-high to high potency category; and
6. Move Diprolene® (augmented betamethasone dipropionate gel) to Tier-1 of the ultra-high to high potency category.

Topical Corticosteroids	
Tier-1	Tier-2
Ultra-High to High Potency	
augmented betamethasone dipropionate (Diprolene AF®) C	amcinonide C, O, L
augmented betamethasone dipropionate (Diprolene®) G	augmented betamethasone dipropionate (Diprolene®) O, L
betamethasone dipropionate (Diprosone®) O	betamethasone dipropionate (Diprosone®) C
fluocinonide 0.05% C, O, So	clobetasol propionate 0.05% (Clobex®) L, Sh, Spr; (Olux®) F, (Olux-E®) F
halobetasol propionate (Ultravate®) C	clobetasol propionate 0.05% (Temovate®) C, O
	clobetasol propionate 0.05% (Temovate®) G, So
	desoximetasone 0.25% (Topicort®) C, O, Spr
	desoximetasone 0.05% (Topicort®) G
	diflorasone diacetate 0.05% (Apexicon®) C (Apexicon E®) C, O
	fluocinonide 0.05% G
	fluocinonide 0.1% (Vanos®) C
	halcinonide (Halog®) C, O
	halobetasol propionate 0.05% (Ultravate®) O
	halobetasol propionate 0.05% (Ultravate®) L
	halobetasol propionate/lactic acid (Ultravate® X) C
Medium-High to Medium Potency	
betamethasone dipropionate (Betanate®) L	betamethasone dipropionate 0.05% (Sernivo™) Spr
betamethasone valerate 0.1% (Beta-Val®) C	betamethasone dipropionate/calcipotriene (Taclonex®) O, Sus, Spr
fluocinonide emollient (Lidex E®) C	betamethasone valerate 0.12% (Luxiq®) F
fluticasone propionate (Cutivate®) C, O	calcipotriene/betamethasone dipropionate (Enstilar®) F
mometasone furoate (Elocon®) C, L	desoximetasone 0.05% (Topicort LP®) C
betamethasone valerate 0.1% (Beta-Val®) O, L	fluocinolone acetonide 0.025% (Synalar®) C, O
	fluocinonide emollient (Lidex E®) C
	flurandrenolide tape (Cordran®)
	flurandrenolide 0.05% C, L
	fluticasone propionate (Cutivate®) L
	hydrocortisone butyrate 0.1% So
	hydrocortisone butyrate 0.1% C, O
	hydrocortisone probutate (Pandel®) C
	hydrocortisone valerate 0.2% C, O
	hydrocortisone valerate (Westcort®) C, O
	mometasone furoate 0.1% O
	prednicarbate (Dermatop®) O, C
	triamcinolone acetonide (Kenalog®) Spr

Low potency	
alclometasone dipropionate (Aclovate [®]) C, O	clocortolone pivalate (Cloderm [®]) C
fluocinolone acetonide 0.01% (Synalar [®]) C	desonide 0.05% C,O
hydrocortisone acetate 2.5% C, O, L	desonide 0.05% (Desonate [®]) G
hydrocortisone/urea (U-Cort [®]) C	desonide 0.05% (Verdeso [®]) F, L
	desonide/emollient (Desowyn [®] kit) C, O
	fluocinolone acetonide 0.01% (Capex [®]) Sh
	fluocinolone acetonide 0.01% (Synalar [®]) So , (Derma-Smooth [®] ; Derma-Smooth FS [®]) Oil
	hydrocortisone 2.5% (Texacort [®]) So
	hydrocortisone/pramoxine (Pramosone [®]) C, L

C= Cream; O = Ointment; L = Lotion; G = Gel; Sh = Shampoo; So = Solution; Spr = Spray;
Sus = Suspension; F = Foam

¹ Ultravate[®] (halobetasol propionate lotion) New Formulation. Available online at: https://hcp-prod.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals/Ultravate_2015-1113.pdf. Last revised 11/2015. Last accessed 10/2016.

² Sernivo[™] (betamethasone dipropionate topical spray, 0.05%) Prescribing Information. Promius Pharma, LLC. Available online at: <http://sernivo.com/documents/sernivo-pi.pdf>. Last revised 02/2016. Last accessed 10/2016.

³ Cordran[®] (flurandrenolide) Prescribing Information. Aqua Pharmaceuticals. Available online at: http://www.aquapharm.com/pdf/CordranPI2013Aug_CrmOintmnt.pdf. Last revised 08/2013. Last accessed 10/2016.



Appendix H



Fiscal Year 2016 Annual Review of Orkambi® (Lumacaftor/Ivacaftor) & Kalydeco® (Ivacaftor)

Oklahoma Health Care Authority
November 2016

Current Prior Authorization Criteria

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the *F508del* mutation in the CFTR gene detected by genetic testing; and
2. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the CFTR gene; and
3. Orkambi® will not be approved for patients with CF other than those homozygous for the *F508del* mutation; and
4. Member must be 12 years of age or older; and
5. Members using Orkambi® must be supervised by a pulmonary specialist; and
6. The prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi®, every three months during the first year of treatment, and annually thereafter; and
7. Members must not be taking any of the following medications concomitantly with Orkambi®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
8. A quantity limit of four tablets per day or 112 tablets per 28 days will apply.
9. Initial approval will be for the duration of three months, after which time compliance will be required for continued approval. After six months of utilization, compliance and information regarding efficacy, such as improvement in FEV₁, will be required for continued approval.

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved indication of cystic fibrosis (CF) with a *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *R117H*, *S1251N*, *S1255P*, *S549N*, or *S549R* mutation in the CFTR gene detected by genetic testing; and
2. Member must be age 6 years of age or older; and
3. A quantity limit of two tablets per day, or 56 tablets per 28 days will apply.
4. Initial approval will be for six months, after which time compliance and information regarding efficacy, such as improvement in FEV₁, will be required for continued approval.

Utilization of Orkambi® and Kalydeco®: Fiscal Year 2016

Comparison of Fiscal Years

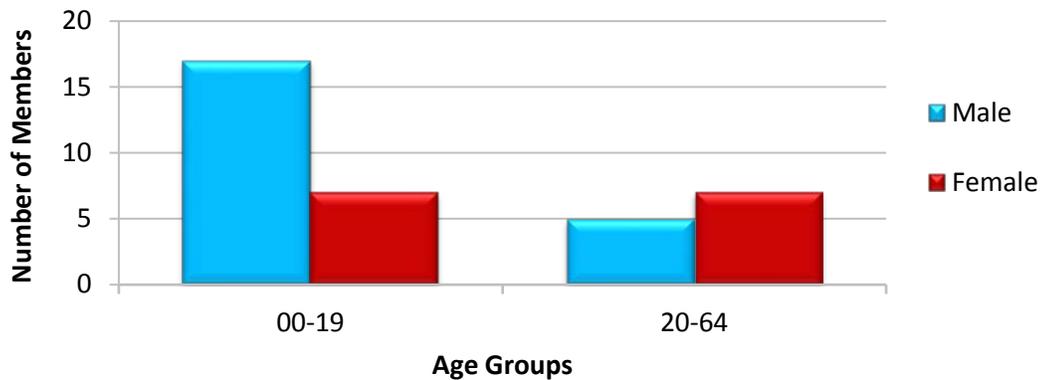
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	7	46	\$1,103,321.47	\$23,985.25	\$829.57	2,660	1,330
2016	33	197	\$4,274,100.28	\$21,695.94	\$774.01	18,200	5,522
% Change	371.40%	328.30%	287.40%	-9.50%	-6.70%	584.20%	315.20%
Change	26	151	\$3,170,778.81	-\$2,289.31	-\$55.56	15,540	4,192

*Total number of unduplicated members.

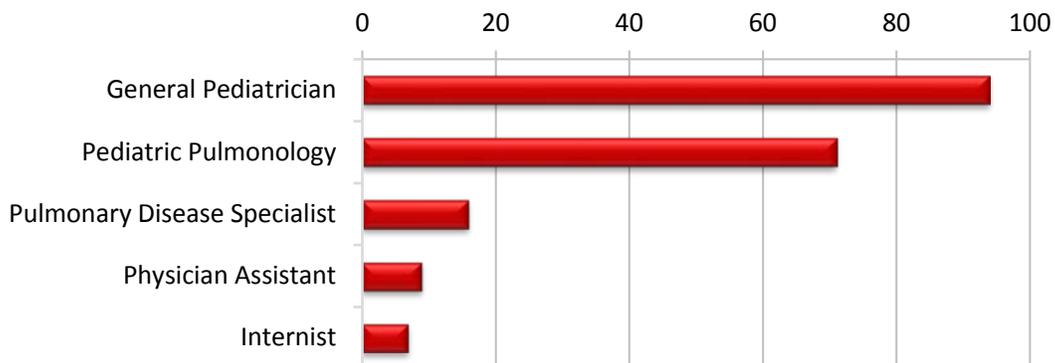
Costs do not reflect rebated prices or net costs.

- Orkambi® (lumacaftor/ivacaftor) was FDA approved July 2015 and had no utilization in fiscal year 2015.

Demographics of Members Utilizing Orkambi® and Kalydeco®



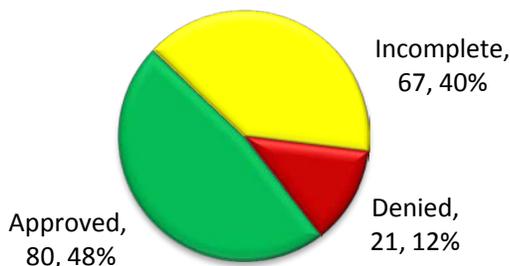
Top Prescriber Specialties of Orkambi® and Kalydeco® by Number of Claims



Prior Authorization of Orkambi® and Kalydeco®

There were 168 prior authorization requests submitted for Orkambi® and Kalydeco® during fiscal year 2016. The following chart shows the status of the submitted petitions.

Status of Petitions



Market News and Updates^{1,2,3,4,5,6}

Anticipated Patent Expirations:

- Kalydeco® (ivacaftor): May 2027
- Orkambi® (lumacaftor/ivacaftor): December 2030
- Kalydeco® (ivacaftor granules): February 2033

News:

- **March 2015:** The U.S. Food and Drug Administration (FDA) expanded the indicated age for Kalydeco® (ivacaftor) for use in ages 2 years of age and older in CF patients who have one of ten mutations in the cystic transmembrane conductance regulator (CFTR) gene (*G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, *S549R* and *R117H*). Previously, Kalydeco® was indicated in 6 years of age and older. A new weight-based oral granule formulation of Kalydeco® 50mg and 75mg that can be mixed in soft foods or liquids was created to meet the needs of children in this age group who may be unable to swallow a tablet. The approval is based on results of an open-label 24-week Phase 3 study that was designed to evaluate the safety and pharmacokinetics of weight-based dosing of Kalydeco® (50mg or 75mg twice daily) in children ages 2 to 5 years.
- **July 2016:** The United Kingdom's National Institute for Health and Care Excellence (NICE) published guidance on Orkambi® (lumacaftor/ivacaftor) and stated it was unable to recommend Orkambi® for treating CF. The guidance concluded that compared to the current standard of care, the benefit Orkambi® offered did not justify its considerable cost.
- **August 2016:** Vertex Pharmaceuticals Inc. provided an update on its ongoing Phase 3 development program of its investigational compound VX-661 in combination with Kalydeco®, which includes four studies anticipated to enroll over 1,000 patients with CF. Results from Part A of the Phase 3 study in people with one copy of the *F508del* mutation and one copy of a mutation that results in minimal CFTR protein function (*F508del het/min*) did not support continuation of the study based on efficacy analysis by an independent board. There were no safety concerns noted for the study discontinuation.

- **September 2016:** The FDA announced the approval of an age expansion for Orkambi® (lumacaftor/ivacaftor) to now include ages 6 to 11 years in addition to the already approved ages of 12 years and older in CF patients who have two copies of the *F508del* mutation. The approval is based on data from a previously announced open-label Phase 3 clinical safety study of Orkambi® presented at the 39th European Cystic Fibrosis Society Conference in June 2016.

Cost Comparison:

Medication	Cost Per Unit*	Cost Per Month [†]	Cost Per Year [‡]
Orkambi® 200mg/125mg	\$177.89	\$19,923.68	\$239,084.16
Kalydeco® 150mg	\$426.72	\$23,896.32	\$286,755.84

Costs do not reflect rebated prices or net costs.

*Costs are based on WAC (wholesale acquisition cost) pricing.

[†]Cost based on recommended dosing for 28 day month.

[‡]Cost per year based on twelve 28-day months.

Kalydeco® is not indicated in the *F508del* mutation in the CFTR gene, but is indicated in the following CFTR mutations: *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *R117H*, *S1251N*, *S1255P*, *S549N*, or *S549R*.

Recommendations

The College of Pharmacy recommends updating the Orkambi® (lumacaftor/ivacaftor) and Kalydeco® (ivacaftor) approval criteria to reflect the new FDA approved age expansions:

Orkambi® (Lumacaftor/Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the *F508del* mutation in the CFTR gene detected by genetic testing; and
2. If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the CFTR gene; and
3. Orkambi® will not be approved for patients with CF other than those homozygous for the *F508del* mutation; and
4. Member must be **6 years of age or older**; and
5. Members using Orkambi® must be supervised by a pulmonary specialist; and
6. The prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Orkambi®, every three months during the first year of treatment, and annually thereafter; and
7. Members must not be taking any of the following medications concomitantly with Orkambi®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John’s wort; and
8. A quantity limit of four tablets per day or 112 tablets per 28 days will apply.
9. Initial approval will be for the duration of three months, after which time compliance will be required for continued approval. After six months of utilization, compliance and information regarding efficacy, such as improvement in FEV₁, will be required for continued approval.

Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved indication of cystic fibrosis (CF) with a *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *R117H*, *S1251N*, *S1255P*, *S549N*, or *S549R* mutation in the CFTR gene detected by genetic testing; and
2. Member must be age **2 years of age or older**; and
3. A quantity limit of two tablets per day, or 56 tablets per 28 days will apply.
4. Initial approval will be for six months, after which time compliance and information regarding efficacy, such as improvement in FEV₁, will be required for continued approval.

Utilization Details of Orkambi® and Kalydeco®: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	PERCENT COST
IVACAFTOR PRODUCTS						
KALYDECO 150MG TAB	57	7	\$1,277,960.55	\$797.73	\$22,420.36	29.90%
KALYDECO TAB 75MG	12	2	\$302,856.02	\$901.36	\$25,238.00	7.09%
SUBTOTAL	69	9	\$1,580,816.57	\$849.55	\$23,829.18	36.99%
LUMACAFTOR/IVACAFTOR PRODUCTS						
ORKAMBI 200-125MG	128	25	\$2,693,283.71	\$751.47	\$21,041.28	63.01%
SUBTOTAL	128	25	\$2,693,283.71	\$751.47	\$21,041.28	63.01%
TOTAL	197	33*	\$4,274,100.28	\$774.01	\$21,695.94	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1>. Last revised 09/2016. Last accessed 10/2016.

² Vertex Pharmaceuticals Inc. Press Release: Vertex Receives U.S. Food and Drug Administration Approval of KALYDECO® (ivacaftor) for Children with Cystic Fibrosis Ages 2 to 5 who have Specific Mutations in the CFTR Gene. Available online at: <http://investors.vrtx.com/releasedetail.cfm?ReleaseID=902211>. Issued 03/2015. Last accessed 10/2016.

³ Vertex Pharmaceuticals Inc. Press Release: Vertex Provides Update on Ongoing Phase 3 Program for VX-661 in Combination with Ivacaftor for the Treatment of Cystic Fibrosis. Available online at: <http://investors.vrtx.com/releasedetail.cfm?releaseid=984388>. Issued 08/2016. Last accessed 10/2016.

⁴ Vertex Pharmaceuticals Inc. Press Release: U.S. Food and Drug Administration Approves ORKAMBI® (lumacaftor/ivacaftor) for Use in Children with Cystic Fibrosis Ages 6 through 11 who have Two Copies of the F508del Mutation. Available at: <http://investors.vrtx.com/releasedetail.cfm?ReleaseID=991350>. Issued 09/2016. Last accessed 10/2016.

⁵ National Institute for Health and Care Excellence (NICE). Cost of cystic fibrosis treatment too high for benefit offered, says NICE. Available at: <https://www.nice.org.uk/news/press-and-media/cost-of-cystic-fibrosis-treatment-too-high-for-benefit-offered-says-nice>. Issued 06/2016. Last accessed 10/2016.

⁶ National Institute for Health and Care Excellence (NICE) Guideline: Lumacaftor-ivacaftor for treating cystic fibrosis homozygous for the F508del mutation. Available at: <https://www.nice.org.uk/guidance/ta398/resources/lumacaftorivacaftor-for-treating-cystic-fibrosis-homozygous-for-the-f508del-mutation-82602916891333>. Issued 07/2016. Last accessed 10/2016.



Appendix I



Fiscal Year 2016 Annual Review of Hepatitis C Medications and 30-Day Notice to Prior Authorize Viekira XR™ (Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir) and Epclusa® (Sofosbuvir/Velpatasvir)

Oklahoma Health Care Authority
November 2016

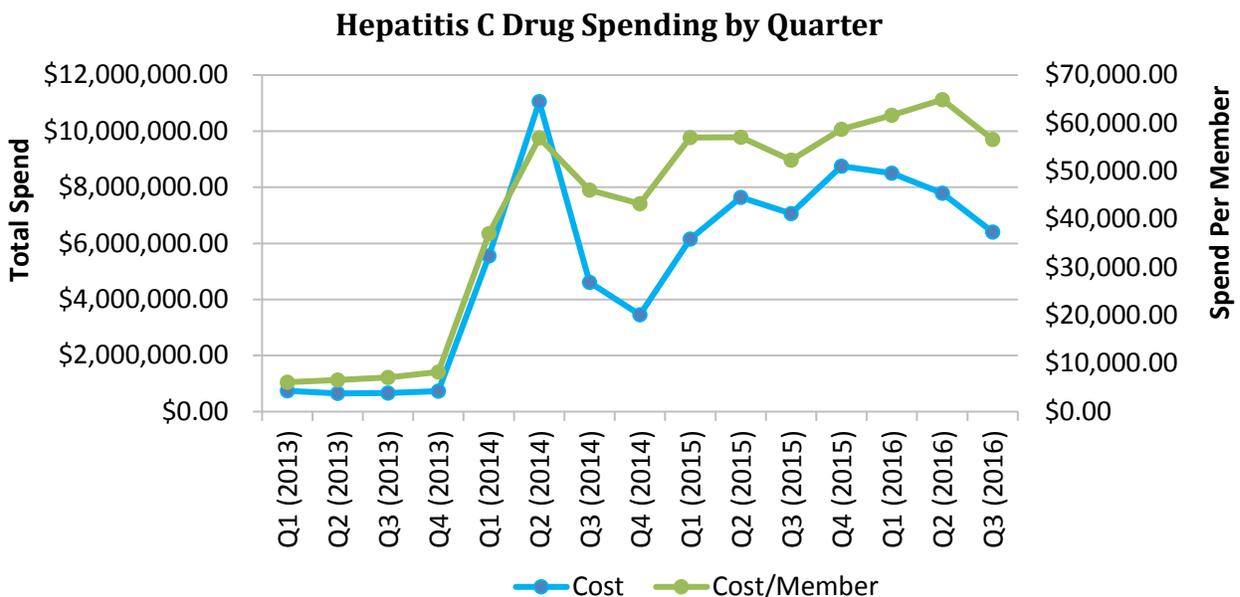
Introduction

Sovaldi® (sofosbuvir) and Olysio® (simeprevir), both approved by the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2013, were previously restricted under Oklahoma law, preventing prior authorization management by the Oklahoma Health Care Authority. The state law was changed in May of 2014 allowing for prior authorization implementation of the hepatitis C medications effective July 1, 2014.

As new direct-acting antivirals (DAAs) were FDA approved they were subsequently reviewed and recommended to be prior authorized by the DUR board. Harvoni® (ledipasvir/sofosbuvir) was reviewed in November 2014, Viekira Pak™ (dasabuvir/ombitasvir/paritaprevir/ritonavir) was reviewed in January 2015, Daklinza™ (daclatasvir) and Technivie™ (ombitasvir/paritaprevir/ritonavir) were reviewed in December 2015, and Zepatier™ (elbasvir/grazoprevir) was reviewed in April 2016. The newer treatment regimens correlated with an increase in cost ranging from \$54,600.00 to \$297,356.64 per regimen.

	Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015	Fiscal Year 2016
Total Hepatitis C Drug Spending	\$2,990,929.48	\$17,993,807.47	\$21,863,385.60	\$32,105,818.63

Costs do not reflect rebated prices or net costs.



Current Prior Authorization Criteria

Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), Harvoni® (sofosbuvir/ledipasvir), Sovaldi® (sofosbuvir), and Zepatier™ (elbasvir/grazoprevir) are the preferred direct-acting antivirals for treatment of chronic hepatitis C genotype-1. Use of Sovaldi® (sofosbuvir) and Olysio® (simeprevir) in combination, Olysio® (simeprevir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (daclatasvir) in combination for treatment of HCV genotype-1 requires patient-specific, clinically significant reasoning why Viekira Pak™, Harvoni®, Sovaldi® with peginterferon and ribavirin, or Zepatier™ (elbasvir/grazoprevir) are not appropriate for the member. Detailed prior authorization criteria similar to the currently prior authorized medications can be found at the end of this report in the recommendations section.

Utilization of Hepatitis C Medications: Fiscal Year 2016

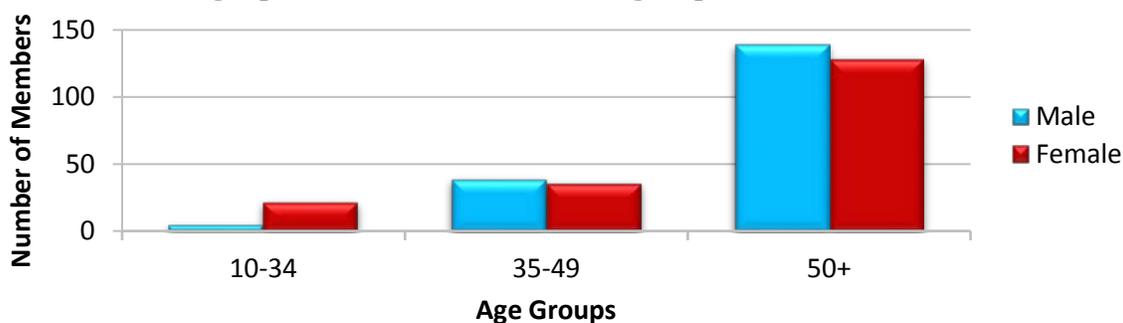
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	291	1,272	\$21,863,385.60	\$17,188.20	\$615.61	90,199	35,515
2016	371	1,355	\$32,105,818.63	\$23,694.33	\$847.57	75,856	37,880
% Change	27.50%	6.50%	46.80%	37.90%	37.70%	-15.90%	6.70%
Change	80	83	\$10,242,433.03	\$6,506.13	\$231.96	-14,343	2,365

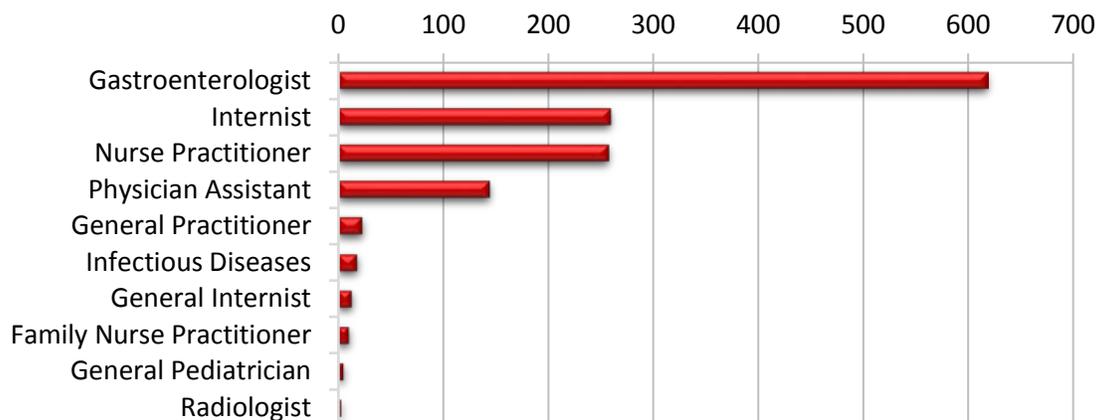
*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Hepatitis C Medications



Top Prescriber Specialties of Hepatitis C Medications by Number of Claims



Hepatitis C Summary Statistics for Treated Members*

Parameter	Details
Number of Unduplicated Treated Members*	824 Unduplicated Members
Genotype	Genotype-1: 69.0% Genotype-2: 15.6% Genotype-3: 14.8% Genotype-4: 0.6%
Fibrosis Score	Average: 3.06 F2: 33.8% F3: 21.4% F4: 42.8% Decompensated: 0.3% Other: 1.8%
Pre-Treatment Viral Load (HCV RNA)	Average: 4,533,205 IU/mL
Prior Treatment Experience	Treatment-Experienced Members: 18.3% Treatment-Naïve Members: 81.7%
Treatment Length	Average: 12.8 weeks 8 weeks: 21.7% 12 weeks: 63.8% 16 weeks: 1.4% 24 weeks: 13.0%
Compliance[‡]	Before PA: 18.8% of members noncompliant After PA: 2.4% of members noncompliant
SVR Cure Rate/Cost Per Cure	92.2% Cure Rate [†] Based on cure rate and drug spending during allotted time frame (12/01/2013-03/31/2016), the estimated cost per cure in the SoonerCare population is \$99,685.88-\$205,887.18. Range due to partial SVR response rate.

*Table includes data collected from 07/01/2014 to 10/14/2016; total number of unduplicated members treated includes data from 12/01/2013 to 10/05/2016 (treated members are those with at least one paid claim).
HCV RNA = Hepatitis C Virus Ribonucleic Acid; PA = Prior Authorization; SVR = Sustained Virologic Response at least 12 weeks after therapy completion

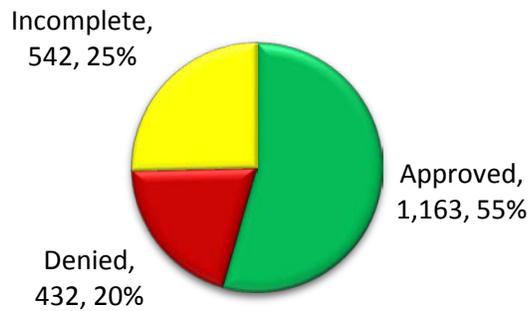
[‡]Compliance before prior authorization was defined as an appropriate regimen length of 12 or 24 weeks.

[†]SVR Cure rate includes data from members who started therapy from 12/01/2013-03/31/2016. The cure rate is based only on members for whom SoonerCare was able to obtain SVR responses (SVR response rate: 55.6%).

Prior Authorization of Hepatitis C Medications

There were 2,137 prior authorization requests submitted for 592 unique members for hepatitis C medications during fiscal year 2016. Approvals are granted for 28 days of therapy each time, so members will have a prior authorization request for each refill of therapy. 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}

Anticipated Patent Expiration(s):

- Olysio® (simeprevir): September 2029
- Sovaldi® (sofosbuvir): December 2030
- Zepatier™ (elbasvir/grazoprevir): May 2031
- Daklinza™ (daclatasvir): June 2031
- Technivie™ (ombitasvir/paritaprevir/ritonavir): April 2032
- Harvoni® (ledipasvir/sofosbuvir): September 2032
- Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir): September 2032

New FDA Approval(s):

- **June 2016:** The FDA approved Epclusa® (sofosbuvir/velpatasvir), an oral combination of a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor and an HCV NS5A inhibitor, for the treatment of all six major genotypes of chronic hepatitis C. Epclusa® is indicated in patients with and without cirrhosis, and in combination with ribavirin for patients with decompensated cirrhosis.
- **July 2016:** The FDA approved Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir), a once-daily version of Viekira Pak™, for the treatment of patients with genotype-1 chronic hepatitis C. Viekira XR™ is dosed as three tablets once daily with a meal. Previously approved Viekira Pak™ is dosed as two tablets containing ombitasvir, paritaprevir, and ritonavir in the morning, along with one dasabuvir tablet in the morning and one in the evening, each time with a meal.

New Indication(s):

- **April 2016:** AbbVie announced the FDA approval of their supplemental New Drug Application (sNDA) for use of Viekira Pak™ without ribavirin in patients with genotype-1b chronic hepatitis C and compensated cirrhosis. The approval was based on results from the TURQUOISE-III study in which Viekira Pak™ demonstrated a 100% SVR rate in genotype-1b patients with compensated cirrhosis.

Safety Update(s):

- **October 2016:** The FDA released a drug safety communication regarding the risk of hepatitis B virus (HBV) reactivation in patients treated with DAAs for hepatitis C who have a current or had a previous HBV infection. Some cases of HBV reactivation resulted

in serious liver problems or death. The FDA is requiring the addition of a boxed warning to the DAA drug labels. It is recommended that prescribers screen and monitor for HBV in all patients receiving DAA treatment. The SoonerCare prior authorization criteria for DAAs requires documentation of initiation of immunization with HBV vaccines or screening for HBV prior to approval.

Pipeline News:

- **April 2016:** AbbVie announced positive results for its investigational, pan-genotypic regimen of ABT-493 and ABT-530 used in the treatment of genotype-1 patients who have failed previous treatment with DAAs. The regimen in combination with ribavirin achieved a 91% SVR12 rate after 12 weeks of treatment.
- **April 2016:** A pilot study presented at the 2016 International Liver Congress revealed a 100% SVR12 rate after treatment with only six weeks of Harvoni® (ledipasvir/sofosbuvir). The study was conducted in 20 patients with acute HCV genotype-1. The authors concluded that a shorter treatment duration did not appear to hinder efficacy.
- **July 2016:** A phase 2a study of three weeks of treatment with an NS3 protease inhibitor and dual NS5A inhibitor-NS5B nucleotide analogue in non-cirrhotic patients with chronic HCV genotype-1b demonstrated a 100% SVR12 rate. Patients were only included in the three week treatment group if they achieved an ultrarapid virologic response defined as plasma HCV RNA <500 IU/mL by day two. The authors concluded that shortening the duration of therapy was effective and could reduce costs and adverse events.
- **September 2016:** Achillion Pharmaceuticals announced positive interim results from a phase 2a study of odalasvir and AL-335 with or without simeprevir for six or eight weeks in treatment-naïve patients with genotype-1 chronic HCV infection. The combination with simeprevir demonstrated a 100% SVR24 rate after 8 weeks of treatment.

Regimen Comparison^{11,12,13,14,15,16,17,18,19}

The following table shows the current FDA approved or American Association for the Study of Liver Disease (AASLD)/Infectious Diseases Society of America (IDSA) guidance recommended regimens of DAA medications for the treatment of chronic HCV infection in treatment-naïve patients with or without compensated cirrhosis. The table is not all-inclusive and may exclude regimens where a shorter treatment duration is recommended in the guidance or FDA approved labeling. Specific regimens are used in particular patient populations depending on comorbidities, pre-treatment viral load, prior hepatitis C treatment experience, fibrosis stage, cirrhosis status, and baseline viral polymorphisms. Regimens marked with a star are not currently FDA approved, but are recommended by the AASLD/IDSA treatment guidance. Many non-FDA approved regimens were only studied in very small treatment populations with limited SVR data. SVR rates found in clinical studies should not be compared across studies, but can be used as a measure of clinical efficacy for each regimen. SVR rates were obtained from studies cited in the AASLD/IDSA treatment guidance or from an individual product's package labeling. SVR rates may vary across studies even when used in similar patient populations. Some SVR percentages in the following table may contain treatment-experienced patients or combined cirrhotic and non-cirrhotic patients if the study did not differentiate. Overall SVR percentages for genotypic subtypes may be reported together if the study did not differentiate.

Genotype	Host Factors	Treatment Regimen	Total Cost	SVR**
Genotype-1a ^o	Treatment-naïve, Non-cirrhotic	DAC + SOF 12 wks	\$142,710.12	98% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	\$54,600.00-\$73,324.16	92%-100% [†]
		LED/SOF 8 or 12 wks	\$60,804.80-\$91,207.20	93% or 96%
		PAR/RIT/OMB/DAS + RBV 12 wks	\$83,711.88	96%-97%
		SIM + SOF 12 wks	\$148,285.20	97% (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	\$93,652.44	92% [‡]
	Treatment-naïve, Cirrhotic	VEL/SOF 12 wks	\$74,760.00	98% [‡]
		DAC + SOF 12 weeks	\$142,710.12	91% (1a & 1b)
		EBR/GZR +/- RBV 12 or 16 wks	\$54,600.00-\$73,324.16	92%-100% [†]
		LED/SOF 12 wks	\$91,207.20	94% (1a & 1b)
		PAR/RIT/OMB/DAS + RBV 24 wks	\$167,423.76	95%
		SIM + SOF +/- RBV 24 wks	\$296,570.40-\$297,356.64	100%
Genotype-1b ^o	Treatment-naïve, Non-cirrhotic	SOF + RBV + PEG IFN 12 wks	\$93,652.44	79%-92% [‡] (1a & 1b)
		VEL/SOF 12 wks	\$74,760.00	98% [‡]
		DAC + SOF 12 wks	\$142,710.12	98% (1a & 1b)
		EBR/GZR 12 wks	\$54,600.00	98%
		LED/SOF 8 or 12 wks	\$60,804.80-\$91,207.20	98%
		PAR/RIT/OMB/DAS 12 wks	\$83,318.76	100%
	Treatment-naïve, Cirrhotic	SIM + SOF 12 wks	\$148,285.20	95 [†] (1a & 1b)
		SOF + RBV + PEG IFN 12 wks	\$93,652.44	83% [‡]
		VEL/SOF 12 wks	\$74,760.00	99% [‡]
		DAC + SOF 12 wks	\$142,710.12	91% (1a & 1b)
		EBR/GZR 12 wks	\$54,600.00	98%
		LED/SOF 12 wks	\$91,207.20	94% (1a & 1b)
Genotype-2	Treatment-naïve, Non-cirrhotic	PAR/RIT/OMB/DAS 12 wks	\$83,318.76	100%
		SIM + SOF +/- RBV 24 wks	\$296,570.40-\$297,356.64	100%
		SOF + RBV + PEG IFN 12 wks	\$93,652.44	79%-83% [‡] (1a & 1b)
	Treatment-naïve, Cirrhotic	VEL/SOF 12 wks	\$74,760.00	98% [‡]
		*DAC + SOF 12 wks	\$142,710.12	100%
		SOF + RBV 12 wks	\$82,318.32	97%
Genotype-3	Treatment-naïve, Non-cirrhotic	VEL/SOF 12 wks	\$74,760.00	99%-100% [‡]
		*DAC + SOF 16 or 24 wks	\$190,280.16-\$285,420.24	Not Available
		SOF + RBV 12 wks	\$82,318.32	83%
	Treatment-naïve, Cirrhotic	VEL/SOF 12 wks	\$74,760.00	99%-100% [‡]
		DAC + SOF 12 wks	\$142,710.12	97%
		SOF + RBV 24 wks	\$164,636.64	93%
Genotype-4 ^o	Treatment-naïve, Non-cirrhotic	VEL/SOF 12 wks	\$74,760.00	98%
		DAC + SOF + RBV 12 wks	\$143,103.24	83%
		SOF + RBV 24 wks	\$164,636.64	92%
		VEL/SOF 12 wks	\$74,760.00	93%
	Treatment-naïve, Cirrhotic	EBR/GZR 12 wks	\$54,600.00	97%
		LED/SOF 12 wks	\$91,207.20	93%
		*PAR/RIT/OMB + RBV 12 wks	\$77,046.48	96%-97%
		SOF + RBV + PEG IFN 12 wks	\$93,652.44	79%-96% [‡]
Genotype-5 or 6	Treatment-naïve, Cirrhotic & Non	VEL/SOF 12 wks	\$74,760.00	100% [‡]
		LED/SOF 12 wks	\$91,207.20	GT5: 93%, GT6: 96%

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

[†]Percentage includes cirrhotic & non-cirrhotic patients. For SOF regimen lower % may include genotype-4 and both -1a and -1b subtypes.

[‡]Lower % accounts for those with baseline resistance associated variants (RAVs) & some cirrhotic patients; lower % shown is for 12 weeks without RBV.

^oSimeprevir + PEG IFN + RBV for 12 weeks followed by 12 or 36 additional weeks PEG IFN + RBV excluded for genotypes 1 and 4.

Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

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

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

RBV dosing based on >75kg patient (1200mg).

Viekira XR™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir) Product Summary¹²

FDA Approval: July 2016

Indications: Viekira XR™ [ombitasvir (OMB)/paritaprevir (PAR)/ritonavir (RIT)/dasabuvir (DAS)] is a fixed-dose combination of DAS, a HCV non-nucleoside NS5B polymerase inhibitor, OMB, a HCV NS5A inhibitor, PAR, a HCV NS3/4A protease inhibitor, and RIT, a CYP3A inhibitor. OMB/PAR/RIT/DAS is indicated for patients with genotype-1b infection without cirrhosis or with compensated cirrhosis and genotype-1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin.

Dosing:

- Viekira XR™ is available as 200mg DAS/8.33mg OMB/50mg PAR/33.3mg RIT extended-release oral tablets. It is dispensed in a carton for a total of 28 days of therapy. Each monthly carton contains four weekly cartons, and each weekly carton contains seven daily dose packs. Each daily dose pack contains three Viekira XR™ tablets.
- The recommended dosage of OMB/PAR/RIT/DAS is three tablets by mouth once daily. OMB/PAR/RIT/DAS must be taken with a meal because administration under fasting conditions may result in reduced virologic response and possible development of resistance. Patients should swallow tablets whole. The recommended treatment regimens and duration can be found in the following table:

Patient Population	Treatment	Duration
Genotype-1a, w/o cirrhosis	OMB/PAR/RIT/DAS + RBV	12 weeks
Genotype-1a, w/ compensated cirrhosis	OMB/PAR/RIT/DAS + RBV	24 weeks
Genotype-1b, with or w/o compensated cirrhosis	OMB/PAR/RIT/DAS	12 weeks

w/o = without; w/ = with; PAR = paritaprevir; RIT = ritonavir; OMB = ombitasvir; DAS = dasabuvir; RBV = ribavirin

- OMB/PAR/RIT/DAS may be used in combination with ribavirin. The recommended dose of ribavirin when administered with OMB/PAR/RIT/DAS is based on weight (1000mg per day for patients less than 75kg and 1200mg per day for those weighing at least 75kg).

Mechanism of Action: OMB/PAR/RIT/DAS combines three direct-acting HCV antiviral agents with distinct mechanisms of action and non-overlapping resistance profiles to target HCV at multiple steps in the viral lifecycle.

- DAS is an inhibitor of HCV RNA-dependent RNA polymerase encoded by the NS5B gene, which is essential for replication of the viral genome.
- OMB is an inhibitor of HCV NS5A, which is essential for viral RNA replication and virion assembly.
- PAR is an inhibitor of HCV NS3/4A protease, which is necessary for the proteolytic cleavage of the HCV encoded polyprotein and is essential for viral replication.
- RIT is not active against HCV. RIT is a potent CYP3A inhibitor that increases peak and trough plasma concentrations of PAR and overall drug exposure.

Contraindications:

- When OMB/PAR/RIT/DAS is administered with ribavirin the contraindications to ribavirin also apply to the combination regimen.

- OMB/PAR/RIT/DAS is contraindicated in moderate-to-severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity.
- OMB/PAR/RIT/DAS is contraindicated in patients with known hypersensitivity to ritonavir (e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome).
- OMB/PAR/RIT/DAS is contraindicated when taken with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events (*see table below*).
- OMB/PAR/RIT/DAS is contraindicated when taken with drugs that are moderate or strong inducers of CYP3A and strong inducers of CYP2C8 and may lead to reduced efficacy of OMB/PAR/RIT/DAS (*see table below*).
- OMB/PAR/RIT/DAS is contraindicated when taken with drugs that are strong inhibitors of CYP2C8 and may increase DAS plasma concentrations and the risk of QT prolongation (*see table below*).

Drugs that are Contraindicated with Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir		
Concomitant Drug Class	Drug(s) within Class that are Contraindicated	Clinical Comment(s)
Alpha 1-Adrenoreceptor Antagonist	alfuzosin HCl	Potential for hypotension.
Anti-Anginal	ranolazine	Potential for serious reactions.
Antiarrhythmic	dronedarone	Potential for serious reactions such as cardiac arrhythmias.
Anticonvulsants	carbamazepine, phenytoin, phenobarbital	OMB/PAR/RIT/DAS exposures may decrease leading to a potential loss of therapeutic activity.
Anti-Gout	colchicine	Potential for serious and/or life-threatening reactions in patients with renal and/or hepatic impairment.
Antihyperlipidemic	gemfibrozil	Increase in DAS concentrations by 10-fold which may increase the risk of QT prolongation.
Antimycobacterial	rifampin	OMB/PAR/RIT/DAS exposures may decrease leading to a potential loss of therapeutic activity.
Antipsychotic	lurasidone, pimozide	Lurasidone: potential for serious reactions. Pimozide: potential for serious reactions such as cardiac arrhythmias.
Ergot Derivatives	ergotamine, dihydroergotamine, methylergonovine	Acute ergot toxicity characterized by vasospasm and tissue ischemia has been associated with co-administration of RIT and ergot derivatives.
Ethinyl Estradiol-Containing Products	ethinyl estradiol containing-medications such as combined oral contraceptives	Potential for ALT elevations.
GI Motility Agent	cisapride	Potential for serious reactions such as cardiac arrhythmias.
Herbal Products	St. John's wort	OMB/PAR/RIT/DAS exposures may decrease leading to a potential loss of therapeutic activity.
HMG-CoA Reductase Inhibitors	lovastatin, simvastatin	Potential for myopathy including rhabdomyolysis.
Non-Nucleoside Reverse Transcriptase Inhibitors	efavirenz	Co-administration of efavirenz with PAR, RIT was poorly tolerated and resulted in liver enzyme elevations.
PDE5 inhibitor	sildenafil when dosed for the treatment of pulmonary arterial hypertension	Increased potential for sildenafil-associated adverse events such as visual disturbances, hypotension, priapism, and syncope.

Drugs that are Contraindicated with Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir		
Concomitant Drug Class	Drug(s) within Class that are Contraindicated	Clinical Comment(s)
Sedatives/Hypnotics	triazolam, orally administered midazolam	Triazolam and orally administered midazolam are extensively metabolized by CYP3A4. Co-administration of triazolam or orally administered midazolam with OMB/PAR/RIT/DAS may cause increases in concentration of these benzodiazepines. The potential exists for serious events such as prolonged or increased sedation or respiratory depression.

Table modified from: Viekira XR™ Product Information. AbbVie Inc.

PAR = paritaprevir; RIT = ritonavir; OMB = ombitasvir; DAS = dasabuvir; GI = gastrointestinal; ALT = alanine transaminase; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A; PDE5 = phosphodiesterase-5

Warnings and Precautions:

- **Risk of Hepatic Decompensation and Hepatic Failure in Patients with Cirrhosis:** Hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, have been reported in patients treated with OMB/PAR/RIT/DAS. Most patients with these severe outcomes had evidence of advanced cirrhosis prior to initiating therapy. Reported cases typically occurred within one to four weeks of initiating therapy and were characterized by the acute onset of rising direct serum bilirubin levels without ALT elevations in association with clinical signs and symptoms of hepatic decompensation.
- **Increased Risk of Alanine Transaminase (ALT) Elevations:** During clinical trials with OMB/PAR/RIT/DAS, elevations of ALT to greater than five times the upper limit of normal (ULN) occurred in approximately 1% of subjects. ALT elevations were typically asymptomatic, occurred in the first four weeks of treatment, and declined within two to eight weeks of onset with continued dosing.
 - These ALT elevations were significantly more frequent in female subjects who were using ethinyl estradiol-containing medications. Ethinyl estradiol-containing medications should be discontinued prior to starting treatment with OMB/PAR/RIT/DAS. Alternative methods of contraception are recommended.
 - Hepatic laboratory testing should be performed during the first four weeks of starting treatment and as clinically indicated thereafter.
- **Risks Associated with Ribavirin Combination Treatment:** The warnings and precautions for ribavirin, in particular the pregnancy avoidance warning, apply to this combination regimen.
- **Risks of Adverse Reactions or Reduced Therapeutic Effect Due to Drug Interactions:** The concomitant use of OMB/PAR/RIT/DAS and certain other drugs may result in known or potentially significant drug interactions, some of which may lead to loss of therapeutic effect of OMB/PAR/RIT/DAS and possible development of resistance, or possible clinically significant adverse reactions from greater exposures of concomitant drugs or components of OMB/PAR/RIT/DAS (*see drug interactions section*).
- **Risk of HIV-1 Protease Inhibitor Drug Resistance in HCV/HIV-1 Co-Infected Patients:** The ritonavir component of OMB/PAR/RIT/DAS is also an HIV-1 protease inhibitor and can select for HIV-1 protease inhibitor resistance-associated substitutions. Any HCV/HIV-1 co-infected patients treated with OMB/PAR/RIT/DAS should also be on a suppressive

antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.

Adverse Reactions: The most common adverse reactions ($\geq 5\%$) reported during OMB/PAR/RIT/DAS clinical trials include the following:

- Asthenia
- Nausea
- Pruritus
- Fatigue
- Insomnia
- Skin Reactions

Use in Special Populations:

- **Pregnancy:** There are no adequate and well-conducted studies in pregnant women. When OMB/PAR/RIT/DAS is administered with ribavirin, the combination is contraindicated in pregnant women and in men whose female partners are pregnant.
- **Nursing Mothers:** It is not known whether any of the components of OMB/PAR/RIT/DAS are present in human milk. Unchanged OMB, PAR and its hydrolysis product, and DAS were the predominant components observed in the milk of lactating rats.
- **Females and Males of Reproductive Potential:** If OMB/PAR/RIT/DAS is administered with ribavirin, the information for ribavirin with regard to pregnancy testing, contraception, and infertility also applies to this combination regimen.
- **Pediatric Use:** The safety and effectiveness of OMB/PAR/RIT/DAS in pediatric patients have not been established.
- **Geriatric Use:** No dosage adjustment of OMB/PAR/RIT/DAS is warranted in geriatric patients. Of the total number of subjects in clinical studies of OMB/PAR/RIT/DAS, 8.5% were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.
- **Renal Impairment:** No dosage adjustment of OMB/PAR/RIT/DAS is required for patients with mild, moderate, or severe renal impairment including those on dialysis.

Drug Interactions:

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	Effect on Concentration	Clinical Comment and Labeling Recommendations
ARBs valsartan, losartan, candesartan	Increased ARBs	Decrease ARB dose and monitor for hypotension and/or worsening renal function.
Antiarrhythmics amiodarone, bepridil, disopyramide, flecainide, lidocaine (systemic), mexiletine, propafenone, quinidine	Increased antiarrhythmics	Concentration monitoring is recommended for antiarrhythmics.
Antidiabetic Medications metformin	No metformin change	Monitor for lactic acidosis and worsening renal function. Concomitant use in patients with renal insufficiency or hepatic impairment is not recommended.
Antifungals ketoconazole, voriconazole	Increased ketoconazole Decreased voriconazole	The maximum daily dose of ketoconazole limited to 200mg. Co-administration with voriconazole is not recommended.

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	Effect on Concentration	Clinical Comment and Labeling Recommendations
Antipsychotics quetiapine	Increased quetiapine	Consider alternative anti-HCV therapy to avoid increases in quetiapine exposures. If co-administration is necessary, reduce quetiapine dose to 1/6 th of current dose & monitor.
CCBs amlodipine, nifedipine, diltiazem, verapamil	Increased CCBs	Decrease dose of CCB (amlodipine should be decreased by ≥50%). Monitoring for edema and hypotension is recommended.
Corticosteroids (Inhaled/Nasal) fluticasone	Increased fluticasone	Alternative corticosteroids should be considered.
Diuretics furosemide	Increased furosemide	Monitoring is recommended.
HIV-Antiviral Agents atazanavir/RIT, darunavir/RIT, lopinavir/RIT, rilpivirine	Increased PAR with atazanavir & lopinavir Decreased darunavir Increased rilpivirine	Atazanavir 300mg should only be given in morning. Co-administration with darunavir/RIT, lopinavir/RIT, or rilpivirine is not recommended.
HMG CoA Reductase Inhibitors pravastatin, rosuvastatin	Increased pravastatin Increased rosuvastatin	Pravastatin dose should not exceed 40mg per day. Rosuvastatin dose should not exceed 10mg per day.
Immunosuppressants cyclosporine, tacrolimus	Increased cyclosporine Increased tacrolimus	The dose of cyclosporine should be reduced to 1/5 th of the current dose. The dose of tacrolimus should be reduced.
LABA salmeterol	Increased salmeterol	Co-administration is not recommended.
Narcotic Analgesics hydrocodone/acetaminophen, buprenorphine/naloxone	Increased hydrocodone Increased buprenorphine	Decrease dose of hydrocodone by 50% and monitor for respiratory depression and sedation. Buprenorphine patients should be monitored for sedation and cognitive effects.
Sedatives/Hypnotics alprazolam	Increased alprazolam	Clinical monitoring and a potential need for a decrease in alprazolam dose is recommended.

Table modified from: Viekira XR™ Product Information. AbbVie Inc.

Not all drug interactions from prescribing information are included in above table. Consult the prescribing information for a detailed list of clinically significant drug interactions.

ARBs = angiotensin receptor blockers; CCBs = calcium channel blockers; PAR = paritaprevir; RIT = ritonavir; HIV = human immunodeficiency virus; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A; LABA = Long-Acting Beta-Adrenoceptor Agonist

Epclusa® (Sofosbuvir/Velpatasvir) Product Summary¹⁹

FDA Approval: June 2016

Indications: Epclusa® (sofosbuvir [SOF]/velpatasvir [VEL]) is a fixed-dose combination of SOF, a HCV nucleotide analog NS5B polymerase inhibitor, and VEL, a HCV NS5A inhibitor, indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection with or without compensated cirrhosis and in decompensated cirrhosis in combination with ribavirin.

Dosing:

- Epclusa® is available as a fixed-dose oral tablet containing 400mg of SOF and 100mg of VEL. It is dispensed in a monthly bottle for a total of 28 days of therapy.
- The recommended dosage of SOF/VEL is one tablet by mouth once daily with or without food. The recommended treatment regimens and duration can be found in the following table.

Patient Population	Treatment Regimen and Duration
Patients w/o cirrhosis and patients w/ compensated cirrhosis	SOF/VEL for 12 weeks
Patients w/ decompensated cirrhosis	SOF/VEL + ribavirin for 12 weeks

w/o = without; w/ = with; SOF = sofosbuvir; VEL = velpatasvir

- When SOF/VEL is used in combination with ribavirin, the recommended dose of ribavirin is based on weight (1000mg per day for patients less than 75kg and 1200mg per day for those weighing at least 75kg).
- No dosage regimen of SOF/VEL can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] less than 30 mL/min/1.73 m²) or with end stage renal disease (ESRD) due to higher exposures (up to 20-fold) of the SOF metabolite.

Mechanism of Action:

- SOF is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication. SOF is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate (GS-461203), which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator.
- VEL is an inhibitor of the HCV NS5A protein, which is required for viral replication.

Contraindications:

- When SOF/VEL is taken in combination with ribavirin, the contraindications to ribavirin also apply to the combination regimen.

Warnings and Precautions:

- Serious Symptomatic Bradycardia When SOF Is Co-administered with Amiodarone and Another HCV DAA: Postmarketing cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is co-administered with SOF in combination with DAC or simeprevir (SIM). Bradycardia has generally occurred within hours to days, but cases have been observed up to two weeks after initiating HCV

treatment. Bradycardia generally resolved after discontinuation of HCV treatment. Co-administration of amiodarone with SOF/VEL is not recommended.

- Risk of Reduced Therapeutic Effect Due to Concomitant Use of SOF/VEL with Inducers of P-glycoprotein (P-gp) and/or Moderate-to-Potent Inducers of Cytochrome (CYP) P450: Drugs that are inducers of P-gp and/or moderate-to-potent inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., rifampin, St. John's wort, carbamazepine) may significantly decrease plasma concentrations of SOF and/or VEL, leading to potentially reduced therapeutic effect of SOF/VEL. The use of these agents with SOF/VEL is not recommended.
- Risks Associated with Ribavirin Combination Treatment: If SOF/VEL is administered with ribavirin, the warnings and precautions for ribavirin, in particular the pregnancy avoidance warning, apply to this combination regimen.

Adverse Reactions: The most common adverse reactions (≥5%) reported during SOF/VEL clinical trials include the following:

- Headache
- Nausea
- Insomnia
- Fatigue
- Asthenia

Use in Special Populations:

- Pregnancy: No adequate human data are available to establish whether or not SOF/VEL poses a risk to pregnancy outcomes. In animal reproduction studies, no evidence of adverse developmental outcomes was observed with SOF/VEL at exposures greater than those in humans. When SOF/VEL is administered with ribavirin, the combination is contraindicated in pregnant women and in men whose female partners are pregnant.
- Nursing Mothers: It is not known whether SOF/VEL and its metabolites are present in human breast milk, affect human milk production, or have effects on the breastfed infant. The predominant circulating metabolite of SOF (GS-331007) was the primary component observed in the milk of lactating rats, without effect on nursing pups.
- Females and Males of Reproductive Potential: If SOF/VEL is administered with ribavirin, the information for ribavirin with regard to pregnancy testing, contraception, and infertility also applies to this combination regimen.
- Pediatric Use: The safety and effectiveness of SOF/VEL in pediatric patients have not been established.
- Geriatric Use: No overall differences in safety or effectiveness have been observed between geriatric subjects and younger subjects in SOF/VEL clinical trials.
- Renal Impairment: No dosage adjustment of SOF/VEL is required for patients with mild or moderate renal impairment. The safety and efficacy of SOF/VEL have not been established in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m²) or ESRD requiring hemodialysis.
- Hepatic Impairment: No dosage adjustment of SOF/VEL is required for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C). Clinical and hepatic laboratory monitoring (including direct bilirubin), as clinically indicated, is recommended for patients with decompensated cirrhosis receiving treatment with SOF/VEL and ribavirin.

Drug Interactions:

Established and Other Potentially Significant Drug Interactions		
Concomitant Drug Class	Effect on Concentration	Clinical Comment
Acid Reducing Agents antacids, H ₂ -receptor antagonists, proton pump inhibitors	Decreased VEL	Drugs that increase gastric pH are expected to decrease concentration of VEL. Antacids should be separated by 4 hours. H ₂ -receptor antagonists may be administered simultaneously with or 12 hours apart at a dose that does not exceed equivalent to famotidine 40mg twice daily. Co-administration of omeprazole or other proton-pump inhibitors is not recommended.
Antiarrhythmics digoxin, amiodarone	Increased digoxin Effect on amiodarone, SOF, and VEL unknown	Monitor of serum digoxin levels. Co-administration with amiodarone is not recommended.
Anticancers topotecan	Increased topotecan	Co-administration is not recommended.
Anticonvulsants carbamazepine, phenytoin, phenobarbital, oxcarbazepine	Decreased SOF Decreased VEL	Co-administration is not recommended.
Antimycobacterials rifabutin, rifampin, rifapentine	Decreased SOF Decreased VEL	Co-administration is not recommended.
HIV-Antiviral Agents efavirenz, tipranavir/ritonavir, tenofovir DF	Decreased VEL with efavirenz or tipranavir/ritonavir Increased tenofovir DF	Co-administration with efavirenz or tipranavir/ritonavir is not recommended. Monitor for tenofovir-associated adverse reactions.
Herbal Supplements: St. John's wort	Decreased SOF Decreased VEL	Co-administration is not recommended.
HMG CoA Reductase Inhibitors rosuvastatin, atorvastatin	Increased rosuvastatin Increased atorvastatin	Co-administration with rosuvastatin or atorvastatin may significantly increase the concentration of rosuvastatin or atorvastatin, which is associated with increased risk of myopathy, including rhabdomyolysis. Rosuvastatin may be administered at a dose that does not exceed 10mg. Atorvastatin patients should be monitored closely for myopathy and rhabdomyolysis.

Table modified from: Eplusa® Product Information. Gilead Sciences Inc.

Not all drug interactions from prescribing information are included in above table. Consult the prescribing information for a detailed list of clinically significant drug interactions.

SOF = sofosbuvir; VEL = velpatasvir; H₂ = histamine-2; HIV = human immunodeficiency virus; DF = disproxil fumarate;

HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A

Recommendations

The College of Pharmacy recommends the prior authorization of Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir) and Eplusa® (sofosbuvir/velpatasvir) with criteria similar to the other prior authorized hepatitis C medications. The following table highlights the preferred regimens for each genotype in treatment-naïve and PEG-IFN and RBV-experienced members (listed in alphabetical order). Additional regimens other than those listed may be considered based on patient-specific clinical situations.

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

Genotype	Patient Factors	Preferred Regimen(s)
2	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 12 weeks
2	Treatment-experienced, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 12 weeks
Genotype-3		
3	Treatment-naïve, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-naïve, cirrhotic	Epclusa® for 12 weeks (with RBV if decompensated) Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, non-cirrhotic	Epclusa® for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
3	Treatment-experienced, cirrhotic	Epclusa® + RBV for 12 weeks Sovaldi® + RBV for 24 weeks (only if can't use Epclusa®)
Genotype-4		
4	Treatment-naïve, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-naïve, cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ for 12 weeks
4	Treatment-experienced, non-cirrhotic	Harvoni® for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
4	Treatment-experienced, cirrhotic	Harvoni® + RBV for 12 weeks Sovaldi® + RBV + PEG IFN for 12 weeks Technivie™ + RBV for 12 weeks Zepatier™ + RBV for 16 weeks
Genotype-5 or 6		
5 or 6	Treatment-naïve or experienced, non-cirrhotic or cirrhotic	Harvoni® for 12 weeks

Not all regimens included are FDA approved.

All regimens are either FDA approved, recommended in AASLD/IDSA treatment guidance, or have study data indicating efficacy.

If not specified, regimen applies to all genotypic subtypes.

RBV = Ribavirin; PEG IFN = peginterferon alfa; RAV= resistance-associated polymorphisms

Preferred regimens based on clinical efficacy data, guideline recommendations, supplemental rebate participation, and/or National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

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

Viekira Pak™ and Viekira XR™ (Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir)

Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Viekira Pak™ or **Viekira XR™** must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated by a gastroenterologist, infectious disease specialist, or transplant specialist for hepatitis C therapy within the last three months; and
5. Hepatitis C Virus (HCV) genotype/subtype testing must be confirmed and indicated on prior authorization request; and
6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on prior treatment experience, genotypic subtype, and cirrhosis will apply:
 - a. **Genotype 1a, without cirrhosis:**
 - i. Viekira Pak™ or **Viekira XR™** with weight-based ribavirin for 12 weeks
 - b. **Genotype 1a, with compensated cirrhosis:**
 - i. Viekira Pak™ or **Viekira XR™** with weight-based ribavirin for 24 weeks
 - ii. Viekira Pak™ or **Viekira XR™** with weight-based ribavirin for 12 weeks may be considered for some patients based on prior treatment history.
 - c. **Genotype 1b, without cirrhosis or with compensated cirrhosis:**
 - i. Viekira Pak™ or **Viekira XR™** for 12 weeks
 - d. New regimens will apply as approved by the FDA
8. Member must not have previously failed treatment with a hepatitis C protease inhibitor (non-responder or relapsed); and
9. Member must sign and submit the Hepatitis C Intent to Treat contract; and
10. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and

11. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Viral Response (SVR-12); and
12. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
13. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
14. Member must not have decompensated cirrhosis or moderate-to-severe hepatic impairment (Child-Pugh B and C); and
15. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for those on ribavirin); and
16. The prescriber must verify that the member's ALT levels will be monitored during the first four weeks of starting treatment and as clinically indicated thereafter; and
17. Member must not be taking the following medications: alfuzosin, ranolazine, carbamazepine, phenytoin, phenobarbital, colchicine, gemfibrozil, rifampin, lurasidone, pimozide, ergotamine, dihydroergotamine, methylergonovine, ethinyl estradiol, cisapride, St. John's wort, lovastatin, simvastatin, efavirenz, sildenafil, triazolam, oral midazolam, darunavir/ritonavir, lopinavir/ritonavir, rilpivirine, and salmeterol; and
18. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight management, severe concurrent medical diseases, such as but not limited to, retinal disease or autoimmune thyroid disease; and
19. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
20. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
21. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month, and for 24 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Epclusa® (Sofosbuvir/Velpatasvir) Approval Criteria:

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of Chronic Hepatitis C (CHC) genotype-1, genotype-2, genotype-3, genotype-4, genotype-5, or genotype-6; and
3. Member must have a METAVIR fibrosis score of F2 or greater or equivalent scoring with an alternative test. Fibrosis testing type and scoring must be indicated on prior authorization request; and
4. Epclusa® must be prescribed by a gastroenterologist, infectious disease specialist, or transplant specialist or the member must have been evaluated for hepatitis C treatment by a gastroenterologist, infectious disease specialist, or transplant specialist within the last three months; and
5. Hepatitis C Virus (HCV) genotype testing must be confirmed and indicated on prior authorization request; and

6. Pre-treatment viral load (HCV-RNA) must be confirmed and indicated on the petition. Viral load should have been taken within the last three months; and
7. The following regimens and requirements based on cirrhosis status will apply:
 - a. **Genotype-1, -2, -3, -4, -5, -6:**
 - i. **Treatment-naïve or treatment-experienced without cirrhosis or with compensated cirrhosis (Child-Pugh A):**
 1. Epclusa® for 12 weeks
 - ii. **Treatment-naïve or treatment-experienced with decompensated cirrhosis (Child-Pugh B and C):**
 1. Epclusa® + weight-based ribavirin for 12 weeks
 - b. New regimens will apply as approved by the FDA
8. Member must sign and submit the Hepatitis C Intent to Treat contract; and
9. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
10. The prescriber must verify that they will provide SoonerCare with all necessary labs to evaluate hepatitis C therapy efficacy including Sustained Virologic Response (SVR-12); and
11. Prescriber must agree to counsel members on potential harms of illicit IV drug use or alcohol use and member must agree to no illicit IV drug use or alcohol use while on treatment and post-therapy; and
12. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
13. Member must not have severe renal impairment (estimated Glomerular Filtration Rate [eGFR] <30mL/min/1.73m²); and
14. Female members must not be pregnant and must have a pregnancy test immediately prior to therapy initiation. Male and female members must be willing to use two forms of non-hormonal birth control while on therapy (and for six months after therapy completion for ribavirin users); and
15. Member must not be taking the following medications: H2-receptor antagonists at doses greater than 40mg famotidine equivalent, amiodarone, omeprazole or other proton pump inhibitors, topotecan, rifampin, rifabutin, rifapentine, carbamazepine, eslicarbazepine, phenytoin, phenobarbital, oxcarbazepine, efavirenz, tenofovir disoproxil fumarate, tipranavir/ritonavir, St. John's wort, and rosuvastatin doses exceeding 10mg; and
16. If member is using antacids they must agree to separate antacid and Epclusa® administration by four hours; and
17. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease.
18. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
19. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy.
20. Approvals for treatment regimen initiation for 12 weeks of therapy will not be granted prior to the 10th of a month in order to prevent prescription limit issues from affecting the member's compliance.

Utilization Details of Hepatitis C Medications: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	% COST	COST/CLAIM
SOFOBUVIR PRODUCTS						
SOVALDI 400MG TAB	320	105	\$9,461,859.18	3.05	29.47%	\$29,568.31
Subtotal	320	105	\$9,461,859.18	3.05	29.47%	\$29,568.31
SOFOBUVIR/LEDIPASVIR PRODUCTS						
HARVONI 400/90MG TAB	585	246	\$19,459,629.97	2.38	60.61%	\$33,264.32
Subtotal	585	246	\$19,459,629.97	2.38	60.61%	\$33,264.32
DACLATASVIR PRODUCTS						
DAKLINZA 60MG TAB	107	36	\$2,372,858.81	2.97	7.39%	\$22,176.25
Subtotal	107	36	\$2,372,858.81	2.97	7.39%	\$22,176.25
OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR PRODUCTS						
VIEKIRA PAK 12.5/75/50/250MG	24	11	\$703,879.62	2.18	2.19%	\$29,328.32
Subtotal	24	11	\$703,879.62	2.18	2.19%	\$29,328.32
ELBASVIR/GRAZOPREVIR PRODUCTS						
ZEPATIER 50/100MG	3	1	\$48,356.36	3	0.15%	\$16,118.79
Subtotal	3	1	\$48,356.36	3	0.15%	\$16,118.79
RIBAVIRIN PRODUCTS						
RIBAVIRIN TAB 200MG	186	69	\$18,041.04	2.7	0.06%	\$96.99
RIBASPHERE TAB 200MG	65	25	\$7,455.82	2.6	0.02%	\$114.70
RIBAVIRIN CAP 200MG	33	10	\$5,445.91	3.3	0.02%	\$165.03
MODERIBA TAB 200MG	24	10	\$2,515.70	2.4	0.01%	\$104.82
RIBASPHERE CAP 200MG	1	1	\$96.01	1	0.00%	\$96.01
Subtotal	309	107	\$33,554.48	2.89	0.11%	\$108.59
PEGINTERFERON PRODUCTS						
PEGASYS INJ	4	1	\$14,639.56	4	0.05%	\$3,659.89
PEG-INTRON KIT 150 RP	2	1	\$7,363.10	2	0.02%	\$3,681.55
PEGINTRON KIT 150MCG	1	1	\$3,677.55	1	0.01%	\$3,677.55
Subtotal	7	3	\$25,680.21	2.33	0.08%	\$3,668.60
TOTAL	1,355	371*	\$32,105,818.63	3.65	100%	\$23,694.33

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

-
- ¹ U.S. Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 09/2016. Last accessed 10/19/2016.
- ² U.S. Food and Drug Administration (FDA). FDA approved Epclusa for treatment of chronic Hepatitis C virus infection. Available online at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm508915.htm>. Issued 06/28/2016. Last accessed 10/19/2016.
- ³ Epclusa® Product Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf. Last revised 06/2016. Last accessed 10/19/2016.
- ⁴ Lowes, R. FDA Approves Once-Daily Viekira XR for Hepatitis C. *Medscape*. Available online at: <http://www.medscape.com/viewarticle/866680>. Issued 07/2016. Last accessed 10/19/2016.
- ⁵ AbbVie. AbbVie Receives U.S. FDA Approval of Supplemental New Drug Application for Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets) without Ribavirin in Genotype 1b Chronic Hepatitis C Patients with Compensated Cirrhosis. Available online at: <https://news.abbvie.com/news/abbvie-receives-us-fda-approval-supplemental-new-drug-application-for-viekira-pak-ombitasvir-paritaprevir-and-ritonavir-tablets-dasabuvir-tablets-without-ribavirin-in-genotype-1b-chronic-hepatitis-c-patients-with-compensated-cirrhosis.htm>. Issued 04/25/2016. Last accessed 10/19/2016.
- ⁶ U.S. Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. Available online at: <http://www.fda.gov/Drugs/DrugSafety/ucm522932.htm>. Issued 10/04/2016. Last accessed 10/19/2016.
- ⁷ AbbVie. AbbVie's Investigational, Pan-Genotypic Regimen of ABT-493 and ABT-530 Shows High SVR Rates in Genotype 1 Hepatitis C Patients Who Failed Previous Therapy with Direct-Acting Antivirals. Available online at: <https://news.abbvie.com/news/abbvies-investigational-pan-genotypic-regimen-abt-493-and-abt-530-shows-high-svr-rates-in-genotype-1-hepatitis-c-patients-who-failed-previous-therapy-with-direct-acting-antivirals.htm>. Issued 04/15/2016. Last accessed 10/19/2016.
- ⁸ Cara, E. 6 Weeks of Antiviral Treatment May Be Enough Time To Cure Hepatitis C Patients: Study. *Medical Daily*. Available online at: <http://www.medicaldaily.com/antiviral-treatment-hepatitis-c-cure-382313>. Issued 04/17/2016. Last accessed 10/19/2016.
- ⁹ Lau G, Benhamou Y, Chen G, et al. Efficacy and safety of 3-week response-guided triple direct-acting antiviral therapy for chronic hepatitis C infection: a phase 2, open-label, proof-of-concept study. *Lancet* 2016; 1(2): 97-104.
- ¹⁰ Achillion Pharmaceuticals Inc. Achillion Announces 100% SVR Reported in Janssen's Phase 2a Trial Evaluating Triple Combination of Odalasvir, AL-335, and Simeprevir for Genotype 1 Treatment-Naive HCV. *GlobeNewswire*. Available online at: <https://globenewswire.com/news-release/2016/09/09/870753/0/en/Achillion-Announces-100-SVR-Reported-in-Janssen-s-Phase-2a-Trial-Evaluating-Triple-Combination-of-Odalasvir-AL-335-and-Simeprevir-for-Genotype-1-Treatment-Naive-HCV.html>. Issued 09/09/2016. Last accessed 10/19/2016.
- ¹¹ American Association For The Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA). Recommendations for testing, managing, and treating hepatitis C. Available online at: <http://www.hcvguidelines.org>. Last revised 09/27/2016. Last accessed 10/19/2016.
- ¹² Viekira XR™ Product Information. AbbVie Inc. Available online at: http://www.rxabbvie.com/pdf/viekiraxr_pi.pdf. Last revised 07/2016. Last accessed 10/20/2016.
- ¹³ Harvoni® Product Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf. Last revised 06/2016. Last accessed 10/20/2016.
- ¹⁴ Olysio™ Product Information. Janssen Therapeutics, LP. Available online at: www.olsio.com/shared/product/olsio/prescribing-information.pdf. Last revised 05/2016. Last accessed 10/20/2016.
- ¹⁵ Sovaldi® Product Information. Gilead Sciences, Inc. Available online at: www.gilead.com/~media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf. Last revised 08/2015. Last accessed 10/20/2016.
- ¹⁶ Daklinza™ Product Information. Bristol-Myers Squibb Company. Available online at: http://packageinserts.bms.com/pi/pi_daklinza.pdf. Last revised 04/2016. Last accessed 10/20/2015.
- ¹⁷ Technivie™ Product Information. AbbVie Inc. Available online at http://www.rxabbvie.com/pdf/technivie_pi.pdf. Last revised 06/2016. Last accessed 10/20/2016.
- ¹⁸ Zepatier™ Product Information. Merck and Co. Inc. Available online at: http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf. Last revised 01/2016. Last accessed 10/20/2016.
- ¹⁹ Epclusa® Product Information. Gilead Sciences, Inc. Available online at: http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/epclusa/epclusa_pi.pdf. Last revised 06/2016. Last accessed 10/20/2016.



Appendix J



30-Day Notice to Prior Authorize Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone)

Oklahoma Health Care Authority
November 2016

Introduction^{1,2,3,4}

The human body has no active mechanism for the excretion of iron; iron homeostasis thus relies on the amount that is absorbed from the small intestine. During normal physiology, the amount of iron absorbed (1 to 2mg/day) is lost by sloughing of intestinal mucosa and skin, as well as small amounts in the urine and bile. The day-to-day iron requirements, as iron is needed by virtually all body cells and especially erythrocytes, are met by recycling between various compartments.

In some patients who may become transfusion-dependent and receive excess iron with each transfusion, iron gradually accumulates in various tissues, causing morbidity and mortality. This may include patients with β -thalassemia major, sickle cell disease, myelodysplastic syndrome, aplastic anemia, or hemolytic anemia. Each unit of transfused blood has approximately 250mg of iron. The dynamics of iron regulation in the body is multifaceted and is altered in transfusion-induced iron overload.

Patients with non-transfusion-dependent thalassemia (NTDT) do not require lifelong regular transfusions for survival, although they may require occasional or even frequent transfusions in certain clinical settings and for defined periods of time. However, patients with NTDT are susceptible to iron overload. Their intestinal iron absorption is continuously being upregulated, triggered by a cascade initiated by ineffective erythropoiesis (which is characteristic of thalassemia disorders) and results in anemia and hypoxia, which influence the expression of the serum protein hepcidin, a key regulator of intestinal iron absorption.

In patients with iron overload, the excess iron is stored in major organs, especially the liver, and can cause severe damage that may lead to organ failure and chronic diseases, such as cirrhosis, diabetes, and heart failure. Unlike patients with primary hemochromatosis and some other causes of secondary iron overload, patients with transfusion-induced iron overload or patients with NTDT are already anemic, and therapeutic phlebotomy is not usually an option. Patients with transfusion-dependent iron overload or NTDT can be given iron chelation therapy to remove excess iron from the body. The goal of iron chelation therapy is to reduce the body's burden of iron, especially iron within labile compartments in plasma as well as in various tissues. By decreasing iron in these sites, the specific aim is to minimize the production of reactive oxygen species, thus reducing damage to critical organs such as the liver, heart, and endocrine organs, resulting in reduced morbidity and improved survival.

Currently, there are three iron chelating agents in wide use and a number of ways in which iron chelation therapy can be given to patients with iron overload. However, no agent or

combination of agents is considered the gold standard of therapy, and long-term, randomized, prospective, comparative studies are lacking. Deferoxamine is administered as a nightly 10 to 12 hour continuous subcutaneous infusion using a small battery-driven pump, and should be administered approximately 250 nights each year in order to be effective. Deferiprone and deferasirox are both administered orally, and are discussed in more detail in the following pages.

Utilization of Oral Iron Chelating Agents: Fiscal Year 2016

Comparison of Fiscal Years: Oral Iron Chelating Agents

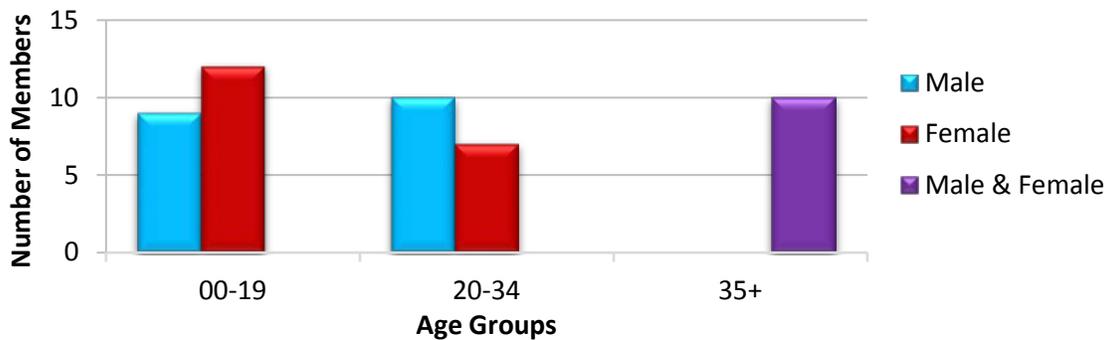
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2014	34	213	\$1,323,705.88	\$6,214.58	\$207.67	16,666	6,374
2015	44	240	\$1,917,738.41	\$7,990.58	\$262.34	19,646	7,310
2016	48	249	\$1,914,074.72	\$7,687.05	\$255.72	19,861	7,485
% Change	41.20%	16.90%	44.60%	23.70%	23.10%	19.20%	17.40%
Change	14	36	\$590,368.84	\$1,472.47	\$48.05	3,195	1,111

*Total number of unduplicated members.

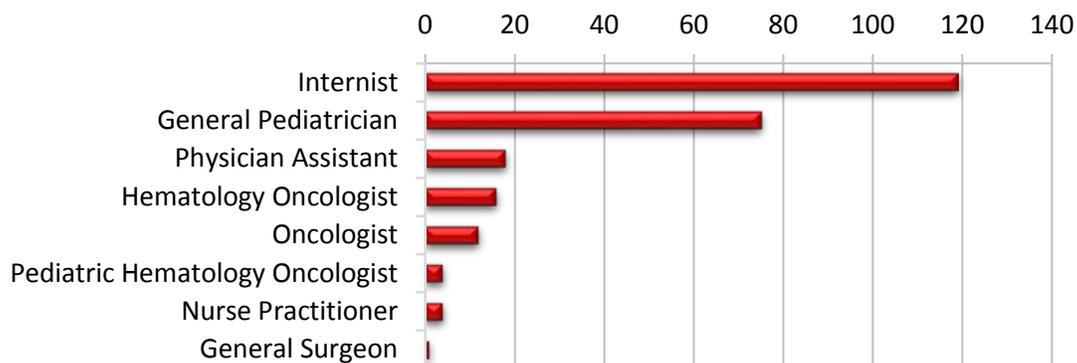
Costs do not reflect rebated prices or net costs.

Percentage change and actual change compare fiscal year 2016 to fiscal year 2014.

Demographics of Members Utilizing Oral Iron Chelating Agents



Top Prescriber Specialties of Oral Iron Chelating Agents by Number of Claims



Market News and Updates⁵

Anticipated Patent Expirations:

- Exjade® (deferasirox tablets for oral suspension): April 2019
- Ferriprox® (deferiprone tablets): June 2021
- Ferriprox® (deferiprone oral solution): October 2029
- Jadenu™ (deferasirox tablets): November 2034

Oral Iron Chelating Agents Summary^{6,7,8,9,10}

Comparison of Oral Iron Chelating Agents

Medication Name and Dosage Form	FDA Approval	Dosing Regimen [^]	Cost/ Month*	Clinical Comments
Exjade® (deferasirox) 125mg, 250mg, and 500mg tablets for oral suspension	2005	20mg/kg PO Q day (max dose 40mg/kg PO Q day)	\$10,683.90 - \$11,655.00 ⁺	<ul style="list-style-type: none"> ▪ Doses should be calculated to the nearest whole tablet ▪ Tablets must be dispersed in water, orange juice, or apple juice to obtain a suspension prior to taking (do not chew or swallow tablets whole) ▪ Binds iron with high affinity in a 2:1 ratio; iron excretion produced by deferasirox is primarily fecal ▪ Boxed warning: renal failure, hepatic failure, and gastrointestinal hemorrhage ▪ FDA approved for ages 2 years and older for transfusion-induced iron overload and for ages 10 years and older for NTD syndromes ▪ Pregnancy category C
Ferriprox® (deferiprone) 500mg oral tablets and 100mg/mL oral solution	2011 (tablets); 2015 (solution)	25mg/kg PO TID (max dose 33mg/kg PO TID)	\$15,636.60 - \$15,639.75 [¥]	<ul style="list-style-type: none"> ▪ Dose should be rounded to the nearest 250mg (half-tablet) or nearest 2.5mL ▪ Binds ferric ions (iron III) to form neutral 3:1 (deferiprone:iron) complexes that are stable over a wide range of pH values ▪ Boxed warning: agranulocytosis and neutropenia ▪ FDA approved for transfusion-induced iron overload due to thalassemia syndromes when current chelation therapy is inadequate ▪ Not FDA approved for pediatric use ▪ Pregnancy category D

Medication Name and Dosage Form	FDA Approval	Dosing Regimen [^]	Cost/ Month [*]	Clinical Comments
Jadenu™ (deferasirox) 90mg, 180mg, and 360mg oral tablets	2015	14mg/kg PO Q day (max dose 28mg/kg PO Q day)	\$10,678.20 - \$11,655.00 ⁺	<ul style="list-style-type: none"> ▪ Jadenu™ dose should be approximately 30% lower than Exjade® dose ▪ Doses should be calculated to the nearest whole tablet ▪ Binds iron with high affinity in a 2:1 ratio; iron excretion produced by deferasirox is primarily fecal ▪ Boxed warning: renal failure, hepatic failure, and gastrointestinal hemorrhage ▪ There are no clinical data in patients taking Jadenu™; FDA approval was based on Exjade® clinical trials, as they contain the same active ingredient ▪ FDA approved for ages 2 years and older for transfusion-induced iron overload and for ages 10 years and older for NTDT syndromes ▪ Pregnancy category C

TID = Three times daily; Q day = Once daily; PO = By mouth; FDA = Food and Drug Administration;

NTDT = Non-transfusion-dependent thalassemia

[^]Dosing regimen based on treatment of transfusion-induced iron overload in adult patients.

^{*}Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable, and recommended dosing regimen for a 70kg patient. Costs do not reflect rebated prices or net costs.

⁺Cost/month range based on using one tablet strength or multiple tablet strengths to achieve recommended dose.

[¥]Cost/month range based on using tablets or oral solution to achieve recommended dose.

Estimated Cost Savings

Exjade® was FDA approved in 2005 and has significant federal rebates, making it much more cost efficient than Jadenu™ or Ferriprox®. The estimated annual cost savings, based on SoonerCare fiscal year 2016 utilization data and the average net cost per claim for Exjade® after taking into account federal rebates, if members using Jadenu™ or Ferriprox® switched to Exjade® would be approximately \$712,922.49.

Recommendations

Based on the low net cost of Exjade® (deferasirox) and significant cost savings if members using Jadenu™ (deferasirox) or Ferriprox® (deferiprone) switched to Exjade® (deferasirox), the College of Pharmacy recommends the prior authorization of Jadenu™ (deferasirox) and Ferriprox® (deferiprone) with the following criteria:

Jadenu™ (Deferasirox) and Ferriprox® (Deferiprone) Approval Criteria:

1. An FDA approved diagnosis; and
2. A patient-specific, clinically significant reason other than convenience why member cannot use Exjade® (deferasirox) must be provided; and
3. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.

Utilization Details of Oral Iron Chelating Agents: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
DEFERASIROX PRODUCTS						
JADENU TAB 360MG	142	36	\$1,217,018.85	\$284.15	\$8,570.56	63.58%
JADENU TAB 180MG	56	10	\$287,775.63	\$171.30	\$5,138.85	15.03%
EXJADE TAB 500MG	32	8	\$311,693.93	\$327.41	\$9,740.44	16.28%
JADENU TAB 90MG	12	2	\$43,726.26	\$121.46	\$3,643.86	2.28%
EXJADE TAB 250MG	2	2	\$10,777.35	\$179.62	\$5,388.68	0.56%
SUBTOTAL	244	47*	\$1,870,992.02	\$255.08	\$7,668.00	97.75%
DEFERIPRONE PRODUCTS						
FERRIPROX TAB 500MG	5	1	\$43,082.70	\$287.22	\$8,616.54	2.25%
SUBTOTAL	5	1*	\$43,082.70	\$287.22	\$8,616.54	2.25%
TOTAL	249	48*	\$1,914,074.72	\$255.72	\$7,687.05	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

-
- ¹ Mir MA. Transfusion-Induced Iron Overload. *Medscape*. Available online at: <http://emedicine.medscape.com/article/1389732-overview>. Last revised 03/10/2014. Last accessed 10/11/2016.
- ² Schrier SL, Bacon BR. Chelation Therapy for Thalassemia and Other Iron Overload States. *UpToDate*. Available online at: http://www.uptodate.com/contents/chelation-therapy-for-thalassemia-and-other-iron-overload-states?source=search_result&search=chronic+iron+overload&selectedTitle=1%7E150. Last revised 09/26/2016. Last accessed 10/11/2016.
- ³ Taher A, Viprakasit V, Musallam K, Cappellini M. Treating Iron Overload in Patients with Non-Transfusion-Dependent Thalassemia. *American Journal of Hematology*. Available online at (doi): [10.1002/ajh.23405](https://doi.org/10.1002/ajh.23405). Issued 02/06/2013. Last accessed 10/11/2016.
- ⁴ Musallam K, Rivella S, Vichinsky E, Rachmilewitz E. Non-Transfusion-Dependent Thalassemias. *Haematologica*. Available online at (doi): [10.3324/haematol.2012.066845](https://doi.org/10.3324/haematol.2012.066845). Issued 06/2013. Last accessed 10/11/2016.
- ⁵ U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 08/2016. Last accessed 10/11/2016.
- ⁶ Exjade® Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/exjade-1/>. Last revised 08/12/2016. Last accessed 10/11/2016.
- ⁷ Ferriprox® Tablets Prescribing Information, ApoPharma USA, Inc. Available online at: http://www.ferriprox.com/us/pdf/ferriprox_full_pi.pdf. Last revised 02/2015. Last accessed 10/11/2016.
- ⁸ Ferriprox® Solution Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/ferriprox/>. Last revised 09/30/2015. Last accessed 10/11/2016.
- ⁹ Jadenu™ Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/jadenu/>. Last revised 08/12/2016. Last accessed 10/11/2016.
- ¹⁰ Micromedex 2.0: Drug Comparison (Deferiprone and Deferasirox). Available online at: <http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.ShowDrugCompareResults>. Last revised 10/07/2016. Last accessed 10/11/2016.



Appendix K



Fiscal Year 2016 Annual Review of Various Antibiotics and 30-Day Notice to Prior Authorize Acticlate® (Doxycycline Hyclate)

Oklahoma Health Care Authority
November 2016

Current Prior Authorization Criteria

Oral Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the immediate release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.

Ofloxacin 400mg Tablet and Moxifloxacin 400mg Tablet Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, and/or other cost effective therapeutic equivalent medication(s).

Tetracycline 250mg and 500mg Capsule Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the member requires tetracycline and cannot use doxycycline, minocycline capsules, and/or other cost effective therapeutic equivalent medication(s).

Suprax® (Cefixime), Cedax® (Ceftibuten), and Spectracef® (Cefditoren) Approval Criteria:

1. Indicated diagnosis or infection known to be susceptible to requested agent; and
2. Patient-specific, clinically significant reason why member cannot use cephalixin, cefdinir, or other cost effective therapeutic equivalent medication(s).

Sivextro® (Tedizolid) Tablet Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use Zyvox® (linezolid) or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of six tablets per six days will apply.

Dalvance® (Dalbavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid), or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of three vials per seven days will apply.

Orbactiv® (Oritavancin) Approval Criteria:

1. An indicated diagnosis or infection known to be susceptible to requested agent and resistant to the cephalosporin-class of antibiotics and other antibiotics commonly used for diagnosis or infection; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, Zyvox® (linezolid), or other cost effective therapeutic equivalent medication(s).
3. A quantity limit of three vials per 30 days will apply.

Avycaz® (Ceftazidime/Avibactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
 - a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
 - b. Complicated urinary tract infections (cUTI), including pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Avycaz® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin-beta lactamase inhibitor combination (e.g. piperacillin-tazobactam), a carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), a cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Zerbaxa® (Ceftolozane/Tazobactam) Approval Criteria:

1. An FDA approved diagnosis of one of the following infections caused by designated susceptible microorganisms:
 - a. Complicated intra-abdominal infections (cIAI), used in combination with metronidazole; or
 - b. Complicated urinary tract infections (cUTI), including pyelonephritis; and
2. Member must be 18 years of age or older; and
3. For the diagnosis of cIAI, Zerbaxa® must be used in combination with metronidazole; and
4. A patient-specific, clinically significant reason why the member cannot use an appropriate penicillin-beta lactamase inhibitor combination (e.g. piperacillin-tazobactam), a carbapenam (e.g. ertapenem, meropenem, imipenem-cilastatin), a cephalosporin (e.g. ceftriaxone, ceftazidime) in combination with metronidazole, or other cost effective therapeutic equivalent medication(s).
5. A quantity limit of 42 vials per 14 days will apply.

Utilization of Various Antibiotics: Fiscal Year 2016

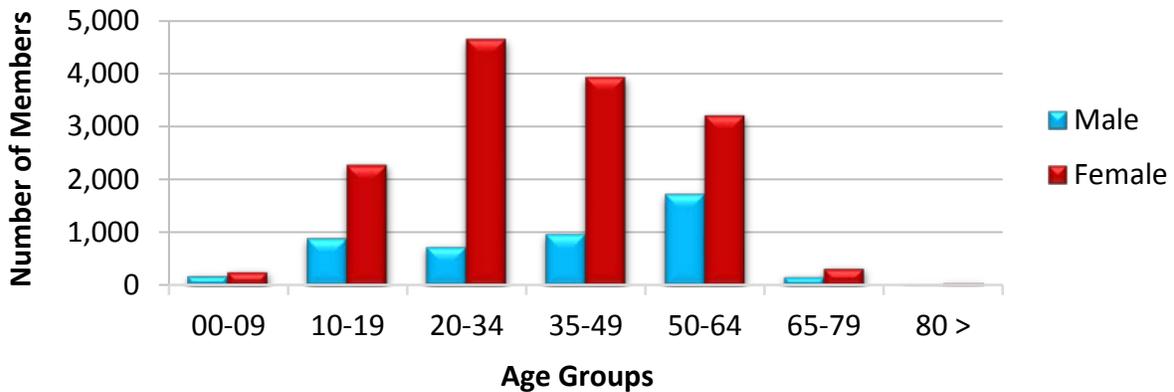
Please note, the following utilization data only includes antibiotics that currently require prior authorization; antibiotics available without prior authorization are not included in the data.

Comparison of Fiscal Years: Various Antibiotics

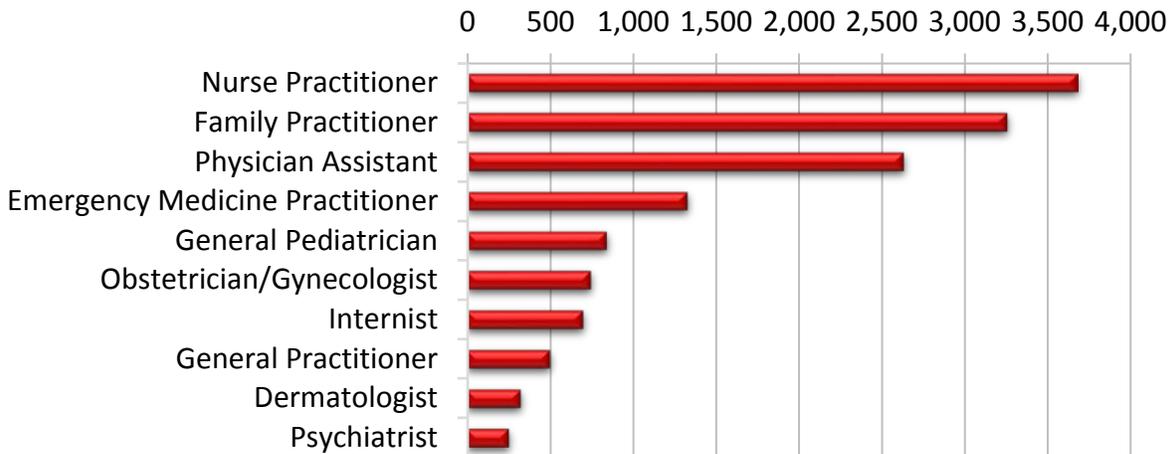
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	522	643	\$108,179.35	\$168.24	\$10.55	19,091	10,254
2016	294	392	\$96,621.55	\$246.48	\$16.51	12,603	5,853
% Change	-43.70%	-39.00%	-10.70%	46.50%	56.50%	-34.00%	-42.90%
Change	-228	-251	-\$11,557.80	\$78.24	\$5.96	-6,488	-4,401

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

Demographics of Members Utilizing Various Antibiotics

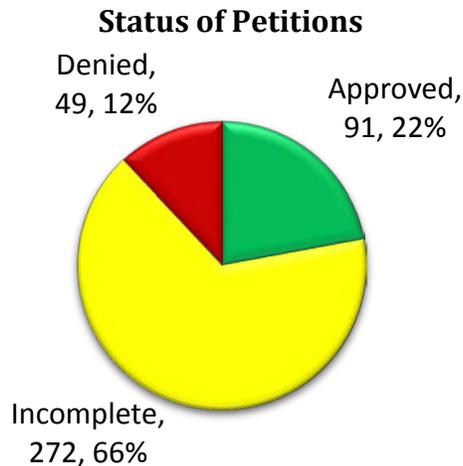


Top Prescriber Specialties of Various Antibiotics by Number of Claims



Prior Authorization of Various Antibiotics

There were 412 prior authorization requests submitted for various antibiotics during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}

Anticipated Patent Expirations:

- Dalvance[®] (dalbavancin): December 2023
- Suprax[®] (cefixime 500mg/5mL oral suspension): December 2028
- Orbactiv[®] (oritavancin): August 2029
- Sivextro[®] (tedizolid): December 2030
- Avycaz[®] (ceftazidime/avibactam): June 2032
- Zerbaxa[®] (ceftolozane/tazobactam): May 2034

New FDA Approvals and Indications:

- **April 2015:** The U.S. Food and Drug Administration (FDA) approved an abbreviated new drug application (ANDA) for cefixime 100mg/5mL and 200mg/5mL oral suspension (generic Suprax[®]).
- **May 2015:** The FDA approved an ANDA for linezolid tablets (generic Zyvox[®]), with multiple other ANDA approvals from different pharmaceutical companies following. Linezolid oral suspension received FDA approval shortly after in June 2015, but is currently only approved and available from one pharmaceutical company.
- **January 2016:** The FDA approved a supplemental new drug application (sNDA) for Dalvance[®] (dalbavancin) to update the label to include a single dose administered as a 30-minute intravenous (IV) infusion for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible Gram-positive bacteria in adults, including infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA).
- **April 2016:** The FDA approved Acticlate[®] (doxycycline hyclate 75mg capsules) for various indications, including for the treatment of Rickettsial infections, sexually transmitted infections, respiratory tract infections, specific bacterial infections, ophthalmic infections, anthrax, including inhalational anthrax (post-exposure); as an alternative treatment for select infections when penicillin is contraindicated; as an adjunctive treatment for acute intestinal amebiasis and severe acne; and for the prophylaxis of malaria. Acticlate[®] 75mg and 150mg tablets were FDA approved in 2014. Acticlate[®] capsules are not currently available on the market; therefore, cost information is not yet available. Generic

doxycycline hyclate 20mg, 50mg, and 100mg capsules and tablets are available without prior authorization.

- **May 2016:** The FDA approved a sNDA for Doryx® MPC (doxycycline hyclate delayed-release 60mg and 120mg tablets) to provide for a modified formulation and two new product strengths (60mg and 120mg tablets). Doryx® 75mg and 100mg delayed-release tablets were first FDA approved in 2005.
- **June 2016:** The FDA approved a sNDA for Avycaz® (ceftazidime/avibactam) to revise the *Indications and Usage* section of the label to remove the following statement under complicated intra-abdominal infections (cIAI): “As only limited clinical safety and efficacy data for Avycaz® are currently available, reserve Avycaz® for use in patients who have limited or no alternative treatment options.” In addition, this sNDA updates the *Adverse Reactions and Clinical Studies* sections to include Phase 3 clinical data evaluating the safety and efficacy of Avycaz® (in combination with metronidazole) in patients with cIAI. This approval follows the FDA granting priority review for the sNDA in February 2016.

Guidelines and Other News:

- **March 2016:** The American College of Physicians (ACP) and the Centers for Disease Control and Prevention (CDC) published clinical guidelines regarding the appropriate prescribing of antibiotics for adult patients with acute respiratory tract infection (ARTI). The article states that antibiotics are often inappropriately prescribed for patients with ARTI, and inappropriate use of antibiotics for ARTI is an important factor contributing to the spread of antibiotic-resistant infections, which is a public health threat. Significant recommendations and conclusions from the guidelines include:
 - Clinicians should not perform testing or initiate antibiotic therapy in patients with bronchitis unless pneumonia is suspected.
 - Clinicians should test patients with symptoms suggestive of group A streptococcal pharyngitis by rapid antigen detection test and/or culture for group A *Streptococcus*. Clinicians should treat patients with antibiotics only if they have confirmed streptococcal pharyngitis.
 - Clinicians should reserve antibiotic treatment for acute rhinosinusitis for patients with persistent symptoms for more than ten days, onset of severe symptoms or signs of high fever (> 39°C) and purulent nasal discharge or facial pain lasting for at least three consecutive days, or onset of worsening symptoms following a typical viral illness that lasted five days that was initially improving (double sickening).
 - Clinicians should not prescribe antibiotics for patients with the common cold.
- **April 2016:** The Infectious Disease Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) published clinical guidelines for implementing an antibiotic stewardship program. Initially, antibiotic stewardship was more focused on cost savings; however, the most important benefit is that it improve patient outcomes and reduce the emergence of antibiotic resistance. The guidelines note that more research needs to be done to determine how to ensure antibiotic stewardship is most effective. Significant recommendations and conclusions from the guidelines include:

- **Preauthorization or prospective audit and feedback:** Targeted antibiotics, such as those that treat emerging drug-resistant infections, should require preauthorization. Prospective audit and feedback can be an alternate strategy or combined with preauthorization and allows antibiotic stewards to engage the prescribing clinician after the antibiotic has been used, typically after two or three days, to optimize antibiotic treatments. Both methods can reduce antibiotic misuse and decrease the development of resistance.
- **Syndrome-specific interventions:** Multifaceted interventions for the treatment of specific syndrome are recommended, rather than trying to improve treatment of all infections at once. For example, the hospital's antibiotic stewardship program may look closely at the management of pneumonia during winter, including making recommendations to shorten the amount of time people are treated and switching to an oral agent more quickly, and then measuring the results of those interventions. In the fall, the program may focus on urinary tract infections and then several months later, switch to skin and soft tissue infections. This method makes stewardship more manageable and provides a targeted and clear treatment message rather than trying to disseminate multiple different infections at the same time.
- **Rapid Diagnosis Testing:** Rapid diagnosis testing of respiratory specimens can help determine if the cause is viral and therefore reduce the inappropriate use of antibiotics. It is also noted that rapid testing of blood cultures in addition to conventional culture is helpful, but should be guided by the antibiotic stewardship team for maximum benefit to the patient.
- **May 2016:** An article was published in the Journal of the American Medical Association (JAMA) regarding the appropriateness of outpatient antibiotic prescribing in the U.S. Data was evaluated from 2010 and 2011 from two annual surveys funded by the CDC, and it was estimated that approximately 30% of antibiotics prescribed for outpatients (across all conditions) may have been inappropriate. These findings highlight the need to set a new goal for antibiotic stewardship in the ambulatory setting.
- **July 2016:** The FDA updated warnings for oral and injectable fluoroquinolone antibiotics due to disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system that can occur together in the same patient. The FDA revised fluoroquinolones' Boxed Warning to address these serious safety concerns and also added new warnings and updated other parts of the drug label. The FDA determined that fluoroquinolones should be reserved for use in patients who have no other treatment options for acute bacterial sinusitis (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTI) because the risk of these serious side effects generally outweighs the benefits in these patients. For some serious bacterial infections, the benefits of fluoroquinolones outweigh the risks, and it is appropriate for them to remain available as a therapeutic option.

Recommendations

The College of Pharmacy recommends the prior authorization of Acticlate® (doxycycline hyclate) 75mg capsules with the following criteria:

Oral Antibiotic Special Formulation Approval Criteria:

1. Member must have a patient-specific, clinically significant reason why the immediate release formulation and/or other cost effective therapeutic equivalent medication(s) cannot be used.

Utilization Details of Various Antibiotics: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
MOXIFLOXACIN PRODUCTS						
MOXIFLOXACIN TAB 400MG	157	131	\$18,547.16	\$11.23	\$118.13	19.20%
SUBTOTAL	157	131	\$18,547.16	\$11.23	\$118.13	19.20%
TETRACYCLINE PRODUCTS						
TETRACYCLINE CAP 250MG	76	34	\$19,218.68	\$9.70	\$252.88	19.89%
TETRACYCLINE CAP 500MG	66	52	\$23,688.10	\$20.40	\$358.91	24.52%
SUBTOTAL	142	86	\$42,906.78	\$13.65	\$302.16	44.41%
CEFIXIME PRODUCTS						
CEFIXIME SUS 200/5ML	22	20	\$8,668.96	\$40.13	\$394.04	8.97%
CEFIXIME SUS 100/5ML	10	10	\$1,956.87	\$20.60	\$195.69	2.03%
SUPRAX CAP 400MG	8	7	\$1,553.74	\$24.28	\$194.22	1.61%
SUPRAX SUS 200/5ML	3	3	\$1,687.72	\$51.14	\$562.57	1.75%
SUPRAX CHW 200MG	1	1	\$416.06	\$41.61	\$416.06	0.43%
SUPRAX SUS 100/5ML	1	1	\$243.25	\$24.33	\$243.25	0.25%
SUBTOTAL	45	42	\$14,526.60	\$33.94	\$322.81	15.03%
CIPROFLOXACIN PRODUCTS						
CIPROFLOXACIN TAB 500MG ER	17	14	\$988.62	\$7.78	\$58.15	1.02%
CIPROFLOXACIN TAB 1000MG ER	3	3	\$203.59	\$7.27	\$67.86	0.21%
CIPROFLOXACIN TAB 100MG	1	1	\$364.79	\$12.16	\$364.79	0.38%
SUBTOTAL	21	18	\$1,557.00	\$8.42	\$74.14	1.61%
CEFTIBUTEN PRODUCTS						
CEFTIBUTEN SUS 180/5ML	9	8	\$4,417.06	\$36.21	\$490.78	4.57%
CEDAX SUS 180/5ML	6	6	\$3,442.90	\$57.38	\$573.82	3.56%
SUBTOTAL	15	14	\$7,859.96	\$43.19	\$524.00	8.13%
MINOCYCLINE PRODUCTS						
SOLODYN TAB 65MG	7	1	\$7,679.49	\$36.74	\$1,097.07	7.95%
SUBTOTAL	7	1	\$7,679.49	\$36.74	\$1,097.07	7.95%
AMOXICILLIN/CLAVULANATE POTASSIUM PRODUCTS						
AMOX-POT CLA ER 1000-62.5MG	3	3	\$644.11	\$14.31	\$214.70	0.67%
SUBTOTAL	3	3	\$644.11	\$14.31	\$214.70	0.67%
TEDIZOLID PRODUCTS						
SIVEXTRO TAB 200MG	2	2	\$2,900.45	\$322.27	\$1,450.23	3.00%

SUBTOTAL	2	2	\$2,900.45	\$322.27	\$1,450.23	3.00%
TOTAL	392	294*	\$96,621.55	\$16.51	\$246.48	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Please note, the above utilization details only include antibiotics that currently require prior authorization; antibiotics available without prior authorization are not included in the above data.

¹ U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 08/2016. Last accessed 10/14/2016.

² FDA ANDA Approval: Cefixime 100mg/5mL and 200mg/5mL Oral Suspension. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 04/14/2015. Last accessed 10/14/2016.

³ FDA ANDA Approval: Linezolid 600mg Oral Tablets. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 05/18/2015. Last accessed 10/14/2016.

⁴ FDA ANDA Approval: Linezolid 100mg/5mL Oral Suspension. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 06/03/2015. Last accessed 10/14/2016.

⁵ PR Newswire: Allergan Announces FDA Approval of Updated Label for New Dosing Regimen for Dalvance® (Dalbavancin). Available online at: <http://www.prnewswire.com/news-releases/allergan-announces-fda-approval-of-updated-label-for-new-dosing-regimen-for-dalvance-dalbavancin-300207674.html>. Issued 01/21/2016. Last accessed 10/14/2016.

⁶ FDA NDA Approval: Acticlate (Doxycycline Hyclate) Capsules. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 04/26/2016. Last accessed 10/14/2016.

⁷ Acticlate® Package Insert. Medlibrary.org. Available online at: <http://medlibrary.org/lib/rx/meds/acticlate/>. Last revised 05/19/2016. Last accessed 10/14/2016.

⁸ FDA sNDA Approval: Doryx® MPC (Doxycycline Hyclate) 60mg and 120mg Delayed-Release Oral Tablets. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 05/20/2016. Last accessed 10/14/2016.

⁹ Allergan News Release: Allergan Announces FDA Approval of Supplemental New Drug Application (sNDA) for Avycaz® (Ceftazidime and Avibactam). Available online at: <http://www.allergan.com/investors/news/thomson-reuters/allergan-announces-fda-approval-of-supplemental-ne>. Issued 06/23/2016. Last accessed 10/14/2016.

¹⁰ FDA sNDA Approval: Avycaz® (Ceftazidime and Avibactam) Injection. Available online at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Issued 06/22/2016. Last accessed 10/14/2016.

¹¹ PR Newswire: FDA Accepts and Grants Priority Review for Avycaz® (Ceftazidime and Avibactam) Supplemental New Drug Application (sNDA). Available online at: <http://www.prnewswire.com/news-releases/fda-accepts-and-grants-priority-review-for-avycaz-ceftazidime-and-avibactam-supplemental-new-drug-application-snda-300225138.html>. Issued 02/24/2016. Last accessed 10/14/2016.

¹² Harris A, Hicks L, Qaseem A. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. *Annals of Internal Medicine*. Available online at (doi): 10.7326/M15-1840. Issued 03/15/2016. Last accessed 10/14/2016.

¹³ Barlam T, Cosgrove S, Abbo L, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Disease Society of America and the Society for Healthcare Epidemiology of America. *Clinical Infectious Diseases*. Available online at (doi): 10.1093/cid/ciw118. Issued 04/26/2016. Last accessed 10/14/2016.

¹⁴ Tamma P, Cosgrove S. Addressing the Appropriateness of Outpatient Antibiotic Prescribing in the United States. *JAMA*. Available online at (doi): 10.1001/jama.2016.4286. Issued 05/03/2016. Last accessed 10/14/2016.

¹⁵ Swift D. One Third of Outpatient Antibiotic Rxs May Be Inappropriate. *Medscape*. Available online at: <http://www.medscape.com/viewarticle/862785>. Issued 05/03/2016. Last accessed 10/14/2016.

¹⁶ FDA Drug Safety Communication: FDA Updates Warnings for Oral and Injectable Fluoroquinolone Antibiotics Due to Disabling Side Effects. Available online at: <http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm>. Issued 07/26/2016. Last accessed 10/14/2016.



Appendix L



Fiscal Year 2016 Annual Review of Pancreatic Enzyme Products and 30-Day Notice to Prior Authorize Pancreaze® (Pancrelipase), Pertzye® (Pancrelipase), and Viokace® (Pancrelipase)

Oklahoma Health Care Authority
November 2016

Introduction^{1,2,3,4,5}

Exocrine pancreatic insufficiency (EPI) is a condition associated with diseases affecting the pancreas, such as chronic pancreatitis and cystic fibrosis (CF). The leading cause of EPI is chronic pancreatitis. The most common cause of EPI in children is CF. Malnutrition, steatorrhea, and weight loss may develop in patients with EPI. The main treatment for EPI is pancreatic enzyme replacement therapy (PERT). Pancreatic enzyme products (PEPs) are extracts of porcine pancreas and contain a combination of lipase, protease, and amylase. PEPs act like digestive enzymes physiologically secreted by the pancreas by catalyzing the hydrolysis of fats, proteins, and starches. PEPs have been used for several decades. They were available prior to the 1938 Food, Drug, and Cosmetic Act therefore the safety and efficacy of generic pancrelipase products were never formally established. Several years ago the U.S. Food and Drug Administration (FDA) became aware that unapproved PEPs may contain varying amounts of lipase, amylase, and protease, resulting in lack of effectiveness due to under-dosing or adverse effects due to over-dosing. In 1991, the FDA initially notified manufacturers that PEPs must be approved and a New Drug Application (NDA) would need to be submitted for marketed products. As of April 2010, unapproved PEPs were no longer allowed to be manufactured or distributed. There are currently five FDA-approved PEPs available. These products are not interchangeable.

Utilization of Pancreatic Enzyme Products: Fiscal Year 2016

Comparison of Fiscal Years for Pancreatic Enzyme Products

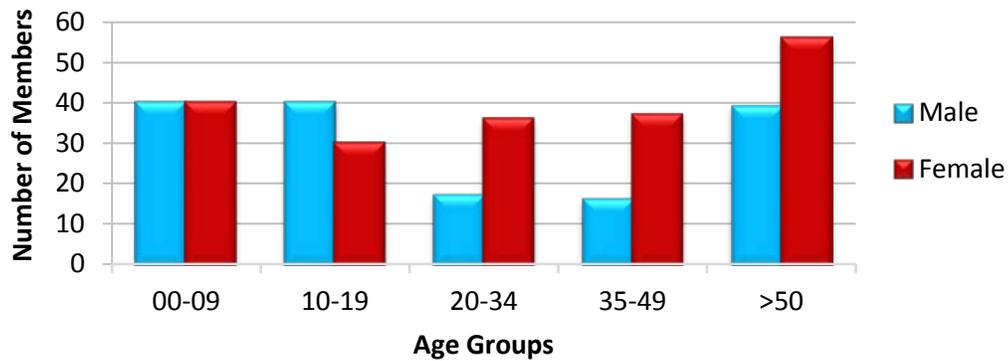
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	337	1,652	\$1,881,270.60	\$1,138.78	\$40.26	545,973	46,726
2016	351	1,720	\$2,172,151.19	\$1,262.88	\$44.17	524,473	49,180
% Change	4.20%	4.10%	15.50%	10.90%	9.70%	-3.90%	5.30%
Change	14	68	\$290,880.59	\$124.10	\$3.91	-21,500	2,454

*Total number of unduplicated members.

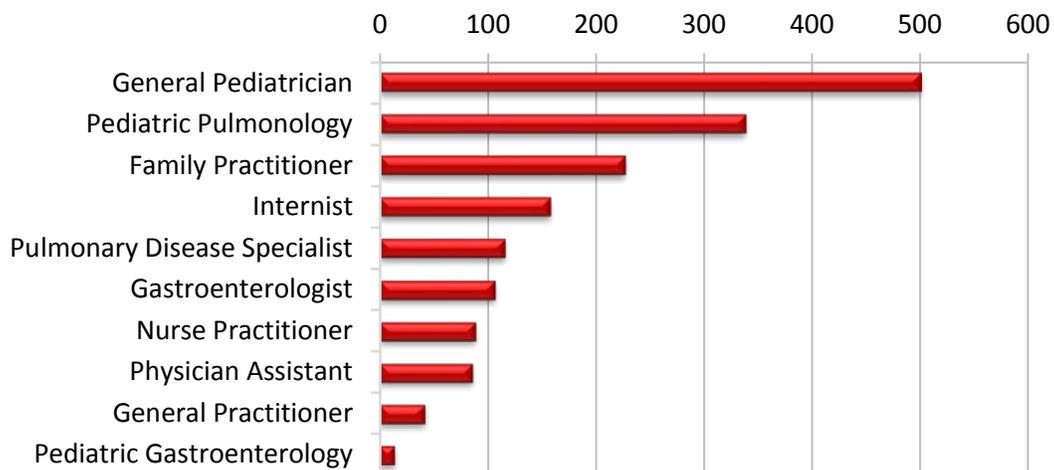
Costs do not reflect rebated prices or net costs.

Pancreatic enzyme products do not currently require prior authorization.

Demographics of Members Utilizing Pancreatic Enzyme Products



Top Prescriber Specialties of Pancreatic Enzyme Products by Number of Claims



Market News and Updates^{6,7}

Patent Expiration(s):

- Pancreaze® (pancrelipase), Pertzeye® (pancrelipase), and Viokace® (pancrelipase): There are no unexpired patents; however, no generic formulations are available at this time.
- Zenpep® (pancrelipase): February 2028
- Creon® (pancrelipase): February 2030

Update(s):

- **October 2016:** Digestive Care, Inc. and Chiesi USA, Inc. announced the FDA approval for a new infant-specific formulation and capsule strength of Pertzeye® containing 4,000 USP lipase units. The new strength expands the use of Pertzeye® to infants (up to 12 months of age) with EPI due to CF or other conditions.

Pancreatic Enzyme Product Summaries^{3,8,9,10,11,12}

Comparison of Pancreatic Enzyme Products

Brand Name	Initial FDA Approval	FDA Approved Indications	Available Strengths (units of lipase/protease/amylase)
Creon®	2009	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions	Delayed-release capsules: 3,000/9,500/15,000 6,000/19,000/30,000 12,000/38,000/60,000 24,000/76,000/120,000 36,000/114,000/180,000
Zenpep®	2009	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions	Delayed-release capsules: 3,000/10,000/16,000 5,000/17,000/27,000 10,000/34,000/55,000 15,000/51,000/82,000 20,000/68,000/109,000 25,000/85,000/136,000 40,000/136,000/218,000
Pancreaze®	2010	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions	Delayed-release capsules: 4,200/10,000/17,500 10,500/25,000/43,750 16,800/40,000/70,000 21,000/37,000/61,000
Pertzye®	2012	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions	Delayed-release capsules: 4,000/14,375/15,125 8,000/28,750/30,250 16,000/57,500/60,500
Viokace®	2012	Treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy, in combination with a proton pump inhibitor	Immediate-release tablets: 10,440/39,150/39,150 20,880/78,300/78,300

Dosing:

- The recommended initial dosing for patients 4 years of age or older with CF is 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g of fat ingested per day.
- Manufacturer dosing recommendations are similar across all products as dosage recommendations for PEPs were published according to the Cystic Fibrosis Foundation Consensus Conferences.
- Slight differences may exist in dosing recommendations for infants and children due to the lowest strength available for the particular medication.

Mechanism of Action: The pancreatic enzymes catalyze the hydrolysis of fats to monoglycerides, glycerol, and free fatty acids, proteins into peptides and amino acids, and starches into dextrins and short chain sugars, thereby acting like digestive enzymes physiologically secreted by the pancreas.

Contraindications: None.

Warnings and Precautions:

- **Fibrosing Colonopathy:** Fibrosing colonopathy is a rare, serious adverse reaction initially described in association with use of high-dose pancreatic enzymes, usually over a prolonged period of time. It is most commonly reported in pediatric patients with CF.
- **Potential for Oral Mucosa Irritation:** The medication should not be retained in the mouth or chewed.
- **Potential Risk of Hyperuricemia:** Porcine-derived PEPs contain purines that may increase blood uric acid levels, therefore caution should be exercised when prescribing PEPs to patients with gout, renal impairment, or hyperuricemia.
- **Potential Viral Exposure from the Product Source:** The presence of porcine viruses that might infect humans cannot be excluded; however, no cases of transmission of an infectious illness associated with the use of porcine pancreatic extracts have been reported.
- **Allergic Reactions:** PEPs should be administered with caution to patients with a known allergy to proteins of porcine origin. Severe allergic reactions including anaphylaxis, asthma, hives, and pruritus have been rarely reported with PEPs.

Adverse Reactions: The most commonly reported adverse reactions vary among the different products.

The most common adverse reactions of **Creon®** reported during clinical trials in patients with CF (≥4% of patients) include:

- Vomiting
- Dizziness
- Cough

The most common adverse reactions of **Creon®** reported during clinical trials in patients with chronic pancreatitis or pancreatectomy (≥4% of patients) include:

- Hyperglycemia
- Flatulence
- Nasopharyngitis
- Hypoglycemia
- Frequent Bowel Movements
- Abdominal Pain

The most common adverse reactions of **Zenpep®** reported during clinical trials (≥6% of patients) include:

- Abdominal Pain
- Cough
- Contusion
- Flatulence
- Decreased Weight
- Headache
- Early Satiety

The most common adverse reactions of **Pancreaze®** reported during clinical trials (≥10% of patients) include:

- Abdominal Pain
- Flatulence
- Diarrhea

- Abnormal Feces
- Fatigue

The most common adverse reactions of **Pertzye**[®] reported during clinical trials (≥10% of patients) include:

- Diarrhea
- Dyspepsia
- Cough

The most common adverse reactions of **Viokace**[®] reported during clinical trials (≥7% of patients) include:

- Biliary Tract Stones
- Anal Pruritus

Use in Special Populations:

- Pregnancy: The pancreatic enzymes are Pregnancy Category C. There are no animal reproduction studies conducted with pancrelipase.
- Nursing Mothers: It is unknown whether pancrelipase is excreted into human milk. Caution should be exercised if administered to a nursing woman.
- Pediatric Use: Creon[®], Pancreaze[®], Pertzye[®], and Zenpep[®] are approved for use in children and infants of all ages. The safety and efficacy of Viokace[®] have not been established in children.
- Geriatric Use: Clinical experience with pancrelipase has not identified differences in responses between the elderly and younger patients.

Efficacy: There are currently limited clinical studies available and the studies that have been conducted have enrolled relatively few patients and have often been of short duration. There is also a lack of head-to-head comparisons between commercial products.

Estimated Cost Savings

Creon[®] and Zenpep[®] were FDA approved in 2009 and have significant federal and supplemental rebates, making them more cost efficient than Pancreaze[®], Pertzye[®], or Viokace[®]. The estimated annual cost savings would be approximately \$160,000 if members using Pancreaze[®], Pertzye[®], or Viokace[®] switched to Creon[®] or Zenpep[®], based on SoonerCare fiscal year 2016 utilization data and the average cost per claim for Creon[®] and Zenpep[®] after taking into account federal and supplemental rebates.

Recommendations

The College of Pharmacy recommends the prior authorization of Pancreaze[®], Pertzye[®], and Viokace[®] with the following criteria:

Pancreaze[®], Pertzye[®], and Viokace[®] Approval Criteria:

1. An FDA approved diagnosis of pancreatic insufficiency; and
2. Documented trials of inadequate response to Creon[®] and Zenpep[®] or a patient-specific, clinically significant reason why the member cannot use Creon[®] or Zenpep[®].

Based on the lower net cost of Creon[®] and Zenpep[®], the College of Pharmacy does not recommend the prior authorization of Creon[®] or Zenpep[®] at this time.

Utilization Details of Pancreatic Enzyme Products: Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
CREON®						
CREON CAP 24000 UNT	447	94	\$736,284.14	\$56.55	\$1,647.17	33.90%
CREON CAP 12000 UNT	295	74	\$183,267.60	\$22.70	\$621.25	8.44%
CREON CAP 36000 UNT	205	58	\$446,654.59	\$74.43	\$2,178.80	20.56%
CREON CAP 6000 UNT	96	24	\$31,658.80	\$11.34	\$329.78	1.46%
CREON CAP 3000 UNT	31	13	\$8,644.48	\$10.44	\$278.85	0.40%
SUBTOTAL	1,074	263	\$1,406,509.61	\$45.79	\$1,309.60	64.76%
ZENPEP®						
ZENPEP CAP 20000 UNT	89	26	\$170,065.43	\$65.33	\$1,910.85	7.83%
ZENPEP CAP 15000 UNT	67	10	\$68,264.65	\$35.44	\$1,018.88	3.14%
ZENPEP CAP 10000 UNT	66	17	\$31,927.70	\$16.68	\$483.75	1.47%
ZENPEP CAP 25000 UNT	46	8	\$82,759.01	\$62.93	\$1,799.11	3.81%
ZENPEP CAP 5000 UNT	39	17	\$9,523.74	\$8.59	\$244.20	0.44%
ZENPEP CAP 40000 UNT	8	2	\$19,677.34	\$83.38	\$2,459.67	0.91%
ZENPEP CAP 3000 UNT	3	3	\$383.89	\$2.56	\$127.96	0.02%
SUBTOTAL	318	83	\$382,601.76	\$41.35	\$1,203.15	17.62%
PERTZYE®						
PERTZYE CAP 16000 UNT	160	31	\$286,474.50	\$61.08	\$1,790.47	13.19%
PERTZYE CAP 8000 UNT	52	11	\$41,339.92	\$28.10	\$795.00	1.90%
SUBTOTAL	212	42	\$327,814.42	\$53.21	\$1,546.29	15.09%
PANCRELIPASE™						
PANCRELIPASE CAP 5000 UNT	34	13	\$5,226.53	\$6.02	\$153.72	0.24%
SUBTOTAL	34	13	\$5,226.53	\$6.02	\$153.72	0.24%
PANCREAZE®						
PANCREAZE CAP 10500 UNT	20	9	\$5,132.84	\$9.97	\$256.64	0.24%
PANCREAZE CAP 4200 UNT	18	4	\$1,609.45	\$4.24	\$89.41	0.07%
PANCREAZE CAP 21000 UNT	12	4	\$18,497.68	\$52.25	\$1,541.47	0.85%
PANCREAZE CAP 16800 UNT	5	3	\$2,216.31	\$14.78	\$443.26	0.10%
SUBTOTAL	55	20	\$27,456.28	\$19.63	\$499.21	1.26%
VIOKACE®						
VIOKACE TAB 20880 UNT	14	3	\$9,266.26	\$22.06	\$661.88	0.43%
VIOKACE TAB 10440 UNT	13	2	\$13,276.33	\$36.47	\$1,021.26	0.61%
SUBTOTAL	27	5	\$22,542.59	\$28.75	\$834.91	1.04%
TOTAL	1,720	351*	\$2,172,151.19	\$44.17	\$1,262.88	100%

*Total number of unduplicated members.

UNT = Unit

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

Pancreatic enzyme products do not currently require prior authorization.

-
- ¹ Nakajima K, Oshida H, Muneyuki T, Kakei M. Pancrelipase: an evidence-based review of its use for treating pancreatic exocrine insufficiency. *Core Evidence*. 2012;7:77-91. doi:10.2147/CE.S26705.
- ² Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: present and future. *Clinical and Experimental Gastroenterology*. 2011;4:55-73. doi:10.2147/CEG.S17634.
- ³ PL Detail-Document, Comparison of Pancreatic Enzyme Products. *Pharmacist's Letter/Prescriber's Letter*. January 2013.
- ⁴ Creon® Package Insert. AbbVie, Inc. Available online at: http://www.rxabbvie.com/pdf/creon_PI.pdf. Last revised 03/2015. Last accessed 09/28/2016.
- ⁵ U.S. Food and Drug Administration (FDA). Updated Questions and Answers for Healthcare Professions and the Public: Use an Approved Pancreatic Enzyme Product (PEP). Available online at: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm204745.htm>. Last revised 05/17/2012. Last accessed 10/05/2016.
- ⁶ U.S. Food and Drug Administration (FDA): Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 08/2016. Last accessed 10/05/2016.
- ⁷ Digestive Care, Inc. Announces FDA Approval of Infant-Specific Dose of PERTZYE® (pancrelipase) Delayed-Release Capsules to Treat Exocrine Pancreatic Insufficiency (EPI) Due to Cystic Fibrosis. Digestive Care, Inc. Available online at: <http://chiesiusa.mwnewsroom.com/press-releases/digestive-care-inc-announces-fda-approval-of-infant-specific-dose-of-pertzeyer-11g117543-001?feed=a2d91aff-5498-44d3-94a2-50d08f0012b1>. Issued 10/11/2016. Last accessed 10/18/2016.
- ⁸ Zenpep® Package Insert. Aptalis Pharma US, Inc. Available online at: http://www.allergan.com/assets/pdf/zenpep_pi. Last revised 03/2014. Last accessed 09/28/2016.
- ⁹ Pancreaze® Package Insert. Janssen Pharmaceuticals, Inc. Available online at: <http://www.pancreaze.net/PDF/PANCREAZE.pdf>. Last revised 11/2013. Last accessed 09/28/2016.
- ¹⁰ Pertzye® Package Insert. Digestive Care, Inc. Available online at: http://chiesiusa.com/wp-content/uploads/PERTZYE_PI.pdf. Last revised 10/2016. Last accessed 10/18/2016.
- ¹¹ Viokace® Package Insert. Aptalis Pharma US, Inc. Available online at: http://www.allergan.com/assets/pdf/viokace_pi. Last revised 03/2012. Last accessed 09/28/2016.
- ¹² Trang T, Chan J, Graham DY. Pancreatic enzyme replacement therapy for pancreatic exocrine insufficiency in the 21st century. *World Journal of Gastroenterology: WJG*. 2014;20(33):11467-11485. doi:10.3748/wjg.v20.i33.11467.



Appendix M



Fiscal Year 2016 Annual Review of Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and 30-Day Notice to Prior Authorize BromSite™ (Bromfenac 0.075% Ophthalmic Solution)

Oklahoma Health Care Authority
November 2016

Current Prior Authorization Criteria

Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	
Tier-1	Tier-2
diclofenac (Voltaren®) 0.1% solution	bromfenac (Bromday™) 0.09% solution
flurbiprofen (Ocufer®) 0.03% solution*	bromfenac (Prolensa™) 0.07% solution
ketorolac (Acular®) 0.5% solution	ketorolac (Acular LS®) 0.4% solution
	ketorolac (Acuvail®) 0.45% solution
	nepafenac (Nevanac™) 0.1% suspension
	nepafenac (Ilevro™) 0.3% suspension

*Not a required Tier-1 trial. Does not have to be attempted for approval of a Tier-2 medication.

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

Ophthalmic Nonsteroidal Anti-Inflammatory Drug (NSAIDs) Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic NSAIDs (from different medication lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier-1 anti-inflammatories lack.

Utilization of Ophthalmic NSAIDs: Fiscal Year 2016

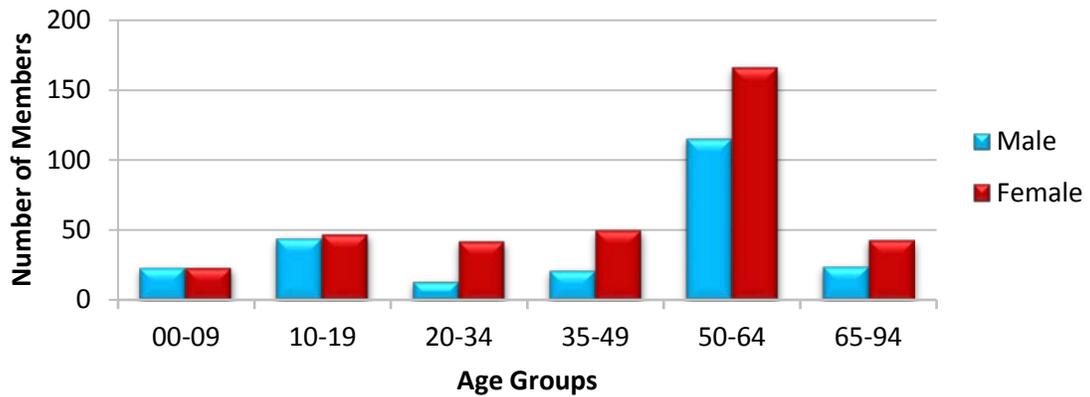
Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2015	534	739	\$17,726.03	\$23.99	\$1.18	3,722	15,084
2016	611	795	\$11,070.49	\$13.93	\$0.68	4,202	16,388
% Change	14.40%	7.60%	-37.50%	-41.90%	-42.40%	12.90%	8.60%
Change	77	56	-\$6,655.54	-\$10.06	-\$0.50	480	1,304

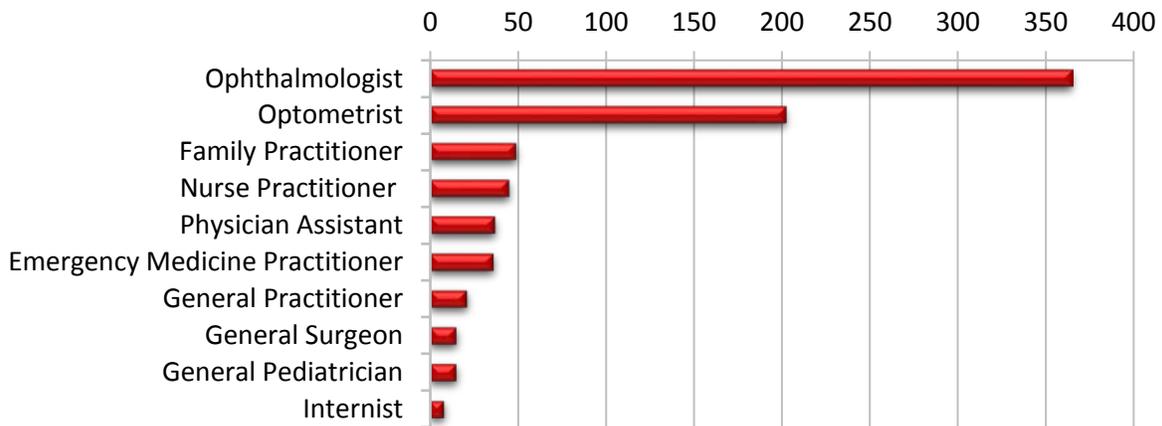
*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

Demographics of Members Utilizing Ophthalmic NSAIDs

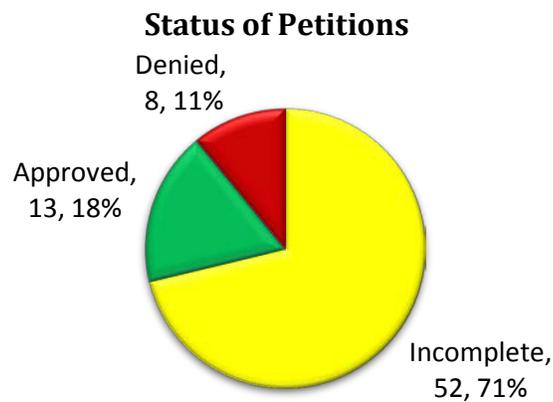


Top Prescriber Specialties of Ophthalmic NSAIDs by Number of Claims



Prior Authorization of Ophthalmic NSAIDs

There were 73 prior authorization requests submitted for the ophthalmic NSAIDs during fiscal year 2016. The following chart shows the status of the submitted petitions.



Market News and Updates¹

Anticipated Patent Expirations:

- Prolensa™ (bromfenac 0.07%): September 2025
- Nevanac™ (nepafenac 0.1%): January 2027
- Acuvail® (ketorolac 0.45%): August 2029
- Ilevro™ (nepafenac 0.3%): March 2032

BromSite™ (Bromfenac Ophthalmic Solution) Product Summary^{2,3,4}

FDA Approved: April 8, 2016

Indications: BromSite™ (bromfenac 0.075% ophthalmic solution) is indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

Dosing:

- BromSite™ is available as a 0.075% ophthalmic solution.
- It is formulated in DuraSite®, a delivery vehicle that stabilizes small molecules in a polymeric mucoadhesive matrix, creating a gel forming drop. This extends the residence time of the drug relative to conventional eye drops.
- BromSite™ is supplied in a 7.5mL plastic dropper-tipped bottle containing 5mL of bromfenac 0.075% ophthalmic solution.
- The recommended dosing is one drop into the affected eye twice daily (morning and evening) one day prior to surgery, the day of surgery, and 14 days post-surgery.
- BromSite™ should be administered at least 5 minutes after instillation of other topical ophthalmic medications. It may be administered in conjunction with other topical ophthalmic medications such as alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics.

Mechanism of Action: Bromfenac is a nonsteroidal anti-inflammatory drug (NSAID) that has anti-inflammatory activity. The mechanism of its action is thought to be due to its ability to block prostaglandin synthesis by inhibiting cyclooxygenase 1 and 2. Prostaglandins have been shown in many animal models to be mediators of certain kinds of intraocular inflammation.

Contraindications: None

Warning and Precautions:

- Slow or Delayed Healing: All topical NSAIDs, including BromSite™, may slow or delay healing. Concomitant use of topical NSAIDs and topical corticosteroids may increase the potential for healing problems.
- Potential for Cross-Sensitivity: There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including BromSite™. It is recommended that BromSite™ be used with caution in individuals who have previously exhibited sensitivities to these drugs.
- Increased Bleeding Time of Ocular Tissue: There have been reports that ophthalmic NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in

conjunction with ocular surgery. It is recommended that BromSite™ be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

- **Keratitis and Corneal Reactions:** Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration, or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including BromSite™, and should be closely monitored for corneal health. Post-marketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.
- **Contact Lens Wear:** BromSite™ should not be administered while wearing contact lenses. The preservative in BromSite™, benzalkonium chloride, may be absorbed by soft contact lenses.

Adverse Reactions: The most commonly reported adverse reactions in 1% to 8% of patients include the following:

- Anterior Chamber Inflammation
- Headache
- Vitreous Floaters
- Iritis
- Eye Pain
- Ocular Hypertension

Use in Special Populations:

- **Pregnancy:** There are no adequate and well-controlled studies in pregnant women to inform any drug-associated risks. Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of BromSite™ during late pregnancy should be avoided.
- **Lactation:** There are no data on the presence of bromfenac in human milk, the effects on the breastfed infant, or the effects on milk production
- **Pediatric Use:** Safety and efficacy in pediatric patients below the age of 18 years have not been established.
- **Geriatric Use:** There is no evidence that the efficacy or safety profiles for BromSite™ differ in patients 65 years of age and older compared to younger adult patients.

Efficacy: Clinical efficacy was evaluated in two multi-centered, randomized, double-masked, parallel group, placebo-controlled trials in which subjects requiring cataract surgery were assigned to receive BromSite™ or vehicle. Patients undergoing cataract surgery self-administered BromSite™ or vehicle twice daily, beginning one day prior to surgery, continuing the day of surgery and for 14 days after surgery. Clearance of ocular inflammation was assessed on Days 1, 8, 15, and 29 using slit lamp biomicroscopy. The primary efficacy endpoint was the proportion of subjects with anterior chamber cell (ACC) grade 0 at Day 15. The secondary efficacy endpoint was the proportion of subjects who were pain free after cataract surgery as assessed using a Visual Analog Scale.

- **Anterior Chamber Cell Grading with Slit Lamp Biomicroscopy:** Inflammation in the anterior segment of the eye causes breakdown of the blood-aqueous barrier and results in an increase in the number of cells and the protein concentration of the aqueous humor. Examination of the aqueous humor by slit-lamp biomicroscopy is the primary method used to evaluate the severity of anterior segment inflammation. Various systems have been reported to quantify the cell number and estimate the amount of protein in the anterior chamber. The slit-lamp cell grading system utilizes ordinal levels to represent a hierarchy of increasing cell numbers. The grading scale is not linear and is only semi-quantitative. The current clinical standard, established by the Standardization of Uveitis Nomenclature (SUN) Working Group grading scheme for ACC, includes criteria of less than one cell in the field for a Grade 0.

No data was provided in the prescribing information for clearance of ocular inflammation on Days 1 and 29. For the secondary endpoint, subjects who were pain free after cataract surgery, the prescribing information only included data from Day 1.

- **Study 1:** On Day 8, the proportion of patients with cleared ocular inflammation after cataract surgery was 32.1% with BromSite™ and 7.8% with the vehicle, a difference of 23.9%. On Day 15, the BromSite™ group was 57.1% while the vehicle group was 18.8%, a difference of 38.3%. The proportion of patients who were pain free after cataract surgery on Day 1 were 76.8% for the BromSite™ group and 48.2% for the vehicle group. This is a difference of 28.6%.
- **Study 2:** The proportion of patients with cleared ocular inflammation after cataract surgery on Day 8, was 23.8% for the BromSite™ group and 9.4% for the vehicle group, a difference of 14.4%. On Day 15, the BromSite™ group was 38.1% while the vehicle group was 22.4%, a difference of 15.7%. The proportion of patients who were pain free after cataract surgery on Day 1 were 82.1% for the BromSite™ group and 62.4% for the vehicle group. This is a difference of 19.8%.

Cost Comparison:

Medication	Cost per mL	Cost per Bottle
BromSite™ (bromfenac) 0.075% solution	Unknown	Unknown
Bromday™ (bromfenac) 0.09% solution	\$51.49	\$87.53
Prolensa™ (bromfenac) 0.07% solution	\$68.23	\$204.69
Voltaren® (diclofenac) 0.1% solution	\$2.55	\$12.75

Costs do not reflect rebated prices or net costs.

Costs based on National Average Drug Acquisition Costs (NADAC), or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

Recommendations

The College of Pharmacy recommends the placement of BromSite™ (bromfenac 0.075% ophthalmic solution) into Tier-2 of the Ophthalmic Nonsteroidal Anti-Inflammatory Drugs Product Based Prior Authorization Category (PBPA). Current Tier-2 criteria for this category will apply.

Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	
Tier-1	Tier-2
diclofenac (Voltaren®) 0.1% solution	bromfenac (Bromday™) 0.09% solution
flurbiprofen (Ocufen®) 0.03% solution*	bromfenac (BromSite™) 0.075% solution
ketorolac (Acular®) 0.5% solution	bromfenac (Prolensa™) 0.07% solution
	ketorolac (Acular LS®) 0.4% solution
	ketorolac (Acuvail®) 0.45% solution
	nepafenac (Nevanac™) 0.1% suspension
	nepafenac (Ilevro™) 0.3% suspension

*Not a required Tier-1 trial. Does not have to be attempted for approval of a Tier-2 medication.

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

Ophthalmic Nonsteroidal Anti-Inflammatory Drug (NSAIDs) Tier-2 Approval Criteria:

1. Documented trials of all Tier-1 ophthalmic NSAIDs (from different medication lines) in the last 30 days that did not yield adequate relief of symptoms or resulted in intolerable adverse effects; or
2. Contraindication to all lower tiered medications; or
3. A unique indication for which the Tier-1 anti-inflammatories lack.

Utilization Details of Ophthalmic Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): Fiscal Year 2016

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM	% COST
TIER-1 UTILIZATION						
KETOROLAC SOL 0.5% OP	546	424	\$7,952.17	\$0.69	\$14.56	71.83%
DICLOFENAC SOL 0.1% OP	241	182	\$2,395.99	\$0.51	\$9.94	21.65%
FLURBIPROFEN SOL 0.03% OP	5	4	\$36.62	\$0.36	\$7.32	0.33%
TIER-1 SUBTOTAL	792	610	\$10,384.78	\$0.64	\$13.11	93.81%
TIER-2 UTILIZATION						
NEVANAC SUS 0.1%	1	1	\$237.31	\$11.87	\$237.31	2.14%
ACULAR LS SOL 0.4%	1	1	\$225.08	\$7.50	\$225.08	2.03%
PROLENSA SOL 0.07%	1	1	\$223.32	\$5.58	\$223.32	2.02%
TIER-2 SUBTOTAL	3	3	\$685.71	\$7.62	\$228.57	6.19%
TOTAL	795	611*	\$11,070.49	\$0.68	\$13.93	100.00%

*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

¹ U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Last revised 08/2016. Last accessed 10/05/2016.

² U.S. Food and Drug Administration (FDA). BromSite™ Prescribing Information. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/206911s000lbl.pdf. Last revised 04/2016. Last accessed 10/07/16.

³ Li Y, Lowder C, Zhang X, Haung D. Anterior Chamber Cell Grading by Optical Coherence Tomography. Invest Ophthalmol Vis Sci. 2013 Jan; 54(1): 258-265.

⁴ DuraSite® Core Technology. Available online at: <http://www.insitevision.com/durasite.html>. Last accessed 10/07/2016.



Appendix N



Fiscal Year 2016 Annual Review of Keveyis™ (Dichlorphenamide)

Oklahoma Health Care Authority
November 2016

Hyperkalemic and Hypokalemic Periodic Paralysis Background Information^{1,2,3,4}

Periodic paralysis is a rare muscle disorder related to a defect in muscle ion channels characterized by episodes of painless muscle weakness. Periodic paralysis affects approximately 5,000 Americans and the two most common types of this disorder are classified as either hyperkalemic or hypokalemic. Hyperkalemic periodic paralysis occurs when episodes can be induced by elevated potassium and hypokalemic periodic paralysis episodes occur in association with low potassium blood levels.

Hyperkalemic periodic paralysis is rare with an estimated prevalence of 1 in 200,000 affecting women and men equally. Symptoms usually start within the first decade of life, but can affect individuals as early as the first year with generalized weakness. The attack of weakness can affect only one limb, but generalized weakness with hypotonia is more common. Triggers of hyperkalemic periodic paralysis attacks include rest after exercise, fasting, stress, or the ingestion of potassium-rich food. Acute attacks usually are brief and do not require treatment. Mild exercise or sugar intake can abort attacks for some patients. In severe symptomatic attacks accompanied by severe hyperkalemia, thiazide diuretics, inhaled beta adrenergic agonists, and intravenous calcium can be used. Dietary modifications can prevent attacks by avoiding foods rich in potassium, but also avoiding fasting. Avoiding strenuous activity is recommended. In patients with disabling attacks that are not responsive to nonpharmacological measures, pharmacological preventative treatment include thiazide diuretics (hydrochlorothiazide) and carbonic anhydrase inhibitors (acetazolamide or dichlorphenamide).

Hypokalemic periodic paralysis is the most common of the periodic paralyses, but is still quite rare, with an estimated prevalence of 1 in 100,000 and is three to four times more common in men than women. Attacks begin in late childhood or teenage years and vary in frequency and duration. Attacks usually last several hours, but range from minutes to days and may be triggered by rest after vigorous exercise, stress, or high-carbohydrate meals. These triggers are often associated with an increased release of epinephrine or insulin, both of which cause movement of potassium ions into cells and low potassium blood levels. Acute treatment involves oral administration of 60 to 120 mEq of potassium chloride given incrementally. Nonpharmacological interventions including low-carbohydrate diet and refraining from vigorous exercise are recommended for preventative treatment. If lifestyle changes are not sufficiently effective in preventing attacks, pharmacological treatment including symptomatic potassium supplementation, potassium-sparing diuretics (spironolactone or triamterene), and carbonic anhydrase inhibitors (acetazolamide or dichlorphenamide) may be effective.

The mechanism whereby carbonic anhydrase inhibitors are effective in hypokalemic periodic paralysis is not well understood. Animal model studies suggest that these agents trigger calcium-activated potassium channels on skeletal muscle. These agents can cause side effects such as malaise and fatigue which limit tolerability in some patients. Kidney stones are also a potential complication of treatment with these agents. Keveyis™ (dichlorphenamide), a carbonic anhydrase inhibitor, is the first drug approved by the U.S. Food and Drug Administration (FDA) to treat primary periodic paralysis. Dichlorphenamide was previously available under the brand name Daranide® for the treatment of elevated intraocular pressure, but in June of 2002 was withdrawn from the market by the manufacturer. In 2007, the FDA determined that Daranide® was not withdrawn from sale for reasons of safety or effectiveness and could be approved under an abbreviated new drug application (ANDA).

Current Prior Authorization Criteria

- Can be found in the recommendations section at the end of this report.

Utilization of Keveyis™ (Dichlorphenamide): Fiscal Year 2016

- There has been no utilization of Keveyis™ (dichlorphenamide) since it was FDA approved in August 2015 to current date.

Market News and Updates^{5,6}

Anticipated Patent Expiration(s):

- Keveyis™ (dichlorphenamide): August 2022

News:

- **May 2016:** Taro Pharmaceuticals announced Keveyis™ (dichlorphenamide) will now be available to distributors at no cost for the treatment of primary periodic paralysis. As a result, Taro ceased commercial sales and related promotional activities for Keveyis™ and will bear all costs associated with its manufacture. Although Taro expected to treat only a few hundred patients with Keveyis™, it became clear that reaching such a small pool of people is more difficult than previously anticipated. Among the 5,000 people estimated to be living with periodic paralysis in the United States, less than 1,500 are believed to be diagnosed. Among these patients, a mix of lifestyle modifications and medicines prescribed off-label are often used to manage their disease. Taro reports sales have been less than one million dollars since launch. Given the high costs and resources required to identify and reach a limited number of viable patients, Taro decided that it cannot sustain its current level of investment. Based on these learnings, Taro now believes that it can better serve all stakeholders, including patients, by ceasing commercial sales and related promotional activities for Keveyis™.

Recommendations

The College of Pharmacy recommends no changes to the current Keveyis™ (dichlorphenamide) prior authorization criteria.

Keveyis™ (Dichlorphenamide) Approval Criteria:

1. An FDA approved indication for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, or related variants; and
2. Prescriber documentation that all non-pharmacological treatments failed including the following:
 - a. Hyperkalemic periodic paralysis:
 - i. Acute attacks can be aborted with sugar or mild exercise
 - ii. Avoiding foods rich in potassium
 - iii. Avoiding fasting
 - iv. High-carbohydrate diet
 - v. Avoiding strenuous activity
 - vi. Avoiding prolonged cold exposure
 - b. Hypokalemic periodic paralysis:
 - i. Low-carbohydrate diet (avoiding carbohydrate loading)
 - ii. Avoiding vigorous exercise (some mild attacks can be aborted by low level exercise)
3. Prescriber documentation of frequent and severe attacks requiring pharmacological treatment (at least one attack per week but no more than three attacks per day); and
4. A four-week trial within the last 90 days of acetazolamide in combination with
 - a. Spironolactone or triamterene in hypokalemic periodic paralysis; or
 - b. Hydrochlorothiazide in hyperkalemic periodic paralysis
5. A quantity limit of four tablets per day will apply.

¹ Gutmann L, Conwit R. Hyperkalemic periodic paralysis. *UpToDate*. Available online at:

http://www.uptodate.com/contents/hyperkalemic-periodic-paralysis?source=search_result&search=hyperkalemic+periodic+paralysis&selectedTitle=1%7E12. Last revised 09/2016. Last accessed 10/2016.

² Hypokalemic periodic paralysis. *UpToDate*. Available online at: http://www.uptodate.com/contents/hypokalemic-periodic-paralysis?source=search_result&search=hypokalemic+periodic+paralysis&selectedTitle=1%7E20. Last revised 09/2016. Last accessed 10/2016.

³ Keveyis™ (dichlorphenamide) New Orphan Drug Approval. OptumRx. Available online at: https://www.optumrx.com/vgnlive/HCP/Assets/RxNews/Drug%20Approvals_Keveyis_2015-0812.pdf. Last accessed 10/2016.

⁴ U.S. Food and Drug Administration. HHS: Determination That Daranide (Dichlorphenamide) Tablets, 50 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness. Available online at: <http://www.gpo.gov/fdsys/pkg/FR-2007-08-06/pdf/E7-15230.pdf>. Issued 08/2007. Last accessed 10/2016.

⁵ U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm?resetfields=1>. Last revised 09/2016. Last accessed 10/2016.

⁶ Taro Pharmaceutical Industries Inc. News Release: Taro to Make Keveyis™ Available to Distributors Free of Cost. Available online at: <http://phx.corporate-ir.net/phoenix.zhtml?c=114698&p=irol-newsArticle&ID=2163726>. Issued 05/2016. Last accessed 10/2016.



Appendix O



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

FDA NEWS RELEASE

For Immediate Release: October 19th, 2016

FDA grants accelerated approval to new treatment for advanced soft tissue sarcoma

The U.S. Food and Drug Administration granted accelerated approval to Lartruvo (olaratumab) with doxorubicin to treat adults with certain types of soft tissue sarcoma (STS), which are cancers that develop in muscles, fat, tendons or other soft tissues. Lartruvo is approved for use with the FDA-approved chemotherapy drug doxorubicin for the treatment of patients with STS who cannot be cured with radiation or surgery and who have a type of STS for which an anthracycline (chemotherapy) is an appropriate treatment. The National Cancer Institute estimates that 12,310 new cases of STS and nearly 5,000 deaths are likely to occur from the disease in 2016. The most common treatment for STS that cannot be removed by surgery is treatment with doxorubicin alone or with other drugs. STS includes a wide variety of tumors arising in the muscle, fat, blood vessels, nerves, tendons or the lining of the joints.

Lartruvo is a platelet-derived growth factor (PDGF) receptor-alpha blocking antibody. When stimulated, PDGF receptors cause tumor growth. Lartruvo works by blocking these receptors, which may help slow or stop tumor growth.

The safety and efficacy of Lartruvo were studied in a randomized clinical trial involving 133 patients with more than 25 different subtypes of metastatic STS. Patients received either Lartruvo with doxorubicin or doxorubicin alone. This trial measured the length of time patients lived after treatment (overall survival), the length of time tumors did not grow after treatment (progression-free survival) and the percentage of patients who experienced shrinkage of their tumors (overall response rate). Patients in this trial who received Lartruvo with doxorubicin had a statistically significant improvement in overall survival: the median survival was 26.5 months compared to 14.7 months for patients who received doxorubicin alone. Patients who received Lartruvo with doxorubicin had a median progression-free survival of 8.2 months compared to 4.4 months for patients who received doxorubicin alone. Tumor shrinkage was 18.2 percent for patients who received Lartruvo with doxorubicin and 7.5 percent for those who received doxorubicin alone.

Lartruvo has serious risks including infusion-related reactions and embryo-fetal harm. Infusion-related reactions include low blood pressure, fever, chills and rash. The most common side effects of treatment with Lartruvo are nausea, fatigue, low levels of white blood cells (neutropenia), musculoskeletal pain, inflammation of the mucous membranes (mucositis), hair loss (alopecia), vomiting, diarrhea, decreased appetite, abdominal pain, nerve damage (neuropathy) and headache.

The FDA granted the Lartruvo application fast track designation, breakthrough therapy designation and priority review status because preliminary clinical evidence indicated that it may offer a substantial improvement in effectiveness in the treatment of a serious or life-threatening disease or condition. The FDA is approving Lartruvo under the agency's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease or condition based on clinical data showing the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The sponsor is conducting a larger study, which is currently underway, to further explore the effectiveness of Lartruvo across the multiple subtypes of STS.

Lartruvo also received orphan drug designation, which provides incentives such as tax credits, user fee waivers and eligibility for exclusivity to assist and encourage the development of drugs intended to treat rare diseases.

Lartruvo is marketed by Eli Lilly and Company based in Indianapolis, Indiana.

Safety Announcements

FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C

[10-4-2016] The U.S. Food and Drug Administration (FDA) is warning about the risk of hepatitis B virus (HBV) becoming an active infection again in any patient who has a current or previous infection with HBV and is treated with certain direct-acting antiviral (DAA) medicines for hepatitis C virus. In a few cases, HBV reactivation in patients treated with DAA medicines resulted in serious liver problems or death.

As a result, the FDA is requiring a Boxed Warning about the risk of HBV reactivation to be added to the drug labels of these DAAs directing health care professionals to screen and monitor for HBV in all patients receiving DAA treatment. This warning will also be included in the patient information leaflet or Medication Guides for these medicines.

Direct-acting antiviral medicines are used to treat chronic hepatitis C virus (HCV) infection. These medicines reduce the amount of HCV in the body by preventing HCV from multiplying, and in most cases, they cure HCV. Without treatment, HCV can lead to serious liver problems including cirrhosis, liver cancer, and death.

Health care professionals should screen all patients for evidence of current or prior HBV infection before starting treatment with DAAs, and monitor patients using blood tests for HBV flare-ups or reactivation during treatment and post-treatment follow-up. It is currently unknown why the reactivation occurs.

Patients should tell their health care professional if they have a history of hepatitis B infection or other liver problems before being treated for hepatitis C. They should not stop taking their DAA medicine without first talking to their health care professional. Stopping treatment early could result in their virus becoming less responsive to certain hepatitis C medicines. Patients should read the patient information leaflet or Medication Guide that comes with each new prescription because the information may have changed. Patients should contact their health care professional immediately if they develop fatigue, weakness, loss of appetite, nausea and vomiting, yellow eyes or skin, or light-colored stools, as these may be signs of serious liver problems.

The FDA identified 24 cases of HBV reactivation reported to the FDA and from the published literature in HCV/HBV co-infected patients treated with DAAs during the 31 months from November 22, 2013 to July 18, 2016. This number includes only cases submitted to FDA, so there are likely additional cases about which the FDA is unaware. Of the cases reported, two patients died and one required a liver transplant. HBV reactivation was not reported as an adverse event in the clinical trials submitted for the DAA approvals because patients with HBV co-infection were excluded from the trials. The trials excluded these patients in order to specifically evaluate the safety of DAAs, including their effects on the liver, in patients infected with only HCV and without the presence of another virus which affects the liver.

The FDA urges health care professionals and patients to report side effects involving DAAs and other medicines to the FDA MedWatch program.

Safety Announcements

FDA analyses conclude that Xarelto clinical trial results were not affected by faulty monitoring device

[10-11-2016] In July 2016, the Alere INRatio device was recalled due to the potential to generate inaccurate results. This device was used to monitor warfarin therapy in the control group of the ROCKET-AF clinical trial, which provided the primary data to support the 2011 approval of the blood thinner drug Xarelto (rivaroxaban). Xarelto is indicated to reduce the rates of stroke and blood clots in patients with non-valvular atrial fibrillation. Because of the concern about the Alere INRatio device, the FDA has completed a variety of analyses to assess the impact that this faulty monitoring device had on the ROCKET-AF study results. The Agency has determined that effects on strokes or bleeding, including bleeding in the head, were minimal. The FDA concludes that Xarelto is a safe and effective alternative to warfarin in patients with non-valvular atrial fibrillation.

Safety Announcements

FDA approves new changes to testosterone labeling regarding the risks associated with abuse and dependence of testosterone and other anabolic androgenic steroids (AAS)

[10-25-2016] The U.S. Food and Drug Administration (FDA) approved class-wide labeling changes for all prescription testosterone products, adding a new Warning and updating the Abuse and Dependence section to include new safety information from published literature and case reports regarding the risks associated with abuse and dependence of testosterone and other AAS.

The Anabolic Steroids Control Act of 1990 placed AAS, including testosterone, in Schedule III of the Controlled Substances Act. Testosterone and other AAS are abused by adults and adolescents, including athletes and body builders. Abuse of testosterone, usually at doses higher than those typically prescribed and usually in conjunction with other AAS, is associated with serious safety risks affecting the heart, brain, liver, mental health, and endocrine system. Reported serious adverse outcomes include heart attack, heart failure, stroke, depression, hostility, aggression, liver toxicity, and male infertility. Individuals abusing high doses of

testosterone have also reported withdrawal symptoms, such as depression, fatigue, irritability, loss of appetite, decreased libido, and insomnia.

The new Warning will alert prescribers to the abuse potential of testosterone and the serious adverse outcomes, especially those related to heart and mental health that have been reported in association with testosterone/AAS abuse. In addition to the new Warning, all testosterone labeling has been revised to include information in the Abuse and Dependence section about adverse outcomes reported in association with abuse and dependence of testosterone/AAS, and information in the Warning and Precautions section advising prescribers of the importance of measuring serum testosterone concentration if abuse is suspected. Prescription testosterone products are FDA-approved as hormone replacement therapy for men who have low testosterone due to certain medical conditions. Examples of these conditions include failure of the testicles to produce testosterone because of genetic problems, or damage to the testicles from chemotherapy or infection.

The FDA asks health care professionals and consumers to report any adverse reactions with the use of testosterone products to the FDA's MedWatch Adverse Event Reporting program.

Current Drug Shortages Index (as of October 31st, 2016):

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

Acetohydroxamic Acid (Lithostat) Tablets	<i>Currently in Shortage</i>
Ammonium Chloride Injection	<i>Currently in Shortage</i>
Anagrelide Hydrochloride Capsules	<i>Currently in Shortage</i>
Asparaginase Erwinia Chrysanthemi (Erwinaze)	<i>Currently in Shortage</i>
Atropine Sulfate Injection	<i>Currently in Shortage</i>
Bleomycin Sulfate for Injection	<i>Currently in Shortage</i>
Caffeine Anhydrous (125mg/mL); Sodium Benzoate (125mg/mL) Injection	<i>Currently in Shortage</i>
Calcium Chloride Injection, USP	<i>Currently in Shortage</i>
Calcium Gluconate Injection	<i>Currently in Shortage</i>
Cefepime Injection	<i>Currently in Shortage</i>
Cefotaxime Sodium (Claforan) Injection	<i>Currently in Shortage</i>
Cefotetan Disodium Injection	<i>Currently in Shortage</i>
Ceftazidime and Avibactam (AVYCAZ) for Injection, 2.5g	<i>Currently in Shortage</i>
Chloramphenicol Sodium Succinate Injection	<i>Currently in Shortage</i>
Dexamethasone Sodium Phosphate Injection	<i>Currently in Shortage</i>
Dextrose 5% Injection Bags	<i>Currently in Shortage</i>
Dextrose Injection USP, 70%	<i>Currently in Shortage</i>
Dihydroergotamine Mesylate Injection	<i>Currently in Shortage</i>
Disopyramide Phosphate (Norpac) Capsules	<i>Currently in Shortage</i>
Doxorubicin Lyophilized Powder for Injection	<i>Currently in Shortage</i>
Epinephrine Injection	<i>Currently in Shortage</i>
Estradiol Valerate Injection, USP	<i>Currently in Shortage</i>
Ethiodized Oil (Lipiodol) Injection	<i>Currently in Shortage</i>
Etoposide Phosphate (Etopophos) Injection	<i>Currently in Shortage</i>
Fentanyl Citrate (Sublimaze) Injection	<i>Currently in Shortage</i>
Fomepizole Injection	<i>Currently in Shortage</i>
Gemifloxacin Mesylate (Factive) Tablets	<i>Currently in Shortage</i>
Imipenem and Cilastatin for Injection, USP	<i>Currently in Shortage</i>
Indigotindisulfonate Sodium (Indigo Carmine) Injection	<i>Currently in Shortage</i>
Ketoprofen Capsules	<i>Currently in Shortage</i>
L-Cysteine Hydrochloride Injection	<i>Currently in Shortage</i>
Leucovorin Calcium Lyophilized Powder for Injection	<i>Currently in Shortage</i>
Leuprolide Acetate Injection	<i>Currently in Shortage</i>
Lidocaine Hydrochloride (Xylocaine) Injection	<i>Currently in Shortage</i>
Liotrix (Thyrolar) Tablets	<i>Currently in Shortage</i>
Mecasermin [rDNA origin] (Increlex) Injection	<i>Currently in Shortage</i>

Methyldopate Hydrochloride Injection	Currently in Shortage
Methylprednisolone Sodium Succinate for Injection, USP	Currently in Shortage
Multi-Vitamin Infusion (Adult and Pediatric)	Currently in Shortage
Mupirocin Calcium Nasal Ointment	Currently in Shortage
Nimodipine (Nymalize) Oral Solution	Currently in Shortage
Penicillin G Benzathine (Bicillin L-A) Injection	Currently in Shortage
Penicillin G Benzathine and Penicillin G Procaine (Bicillin C-R) Injection	Currently in Shortage
Penicillin G Procaine Injection	Currently in Shortage
Peritoneal Dialysis Solutions	Currently in Shortage
Piperacillin and Tazobactam (Zosyn) Injection	Currently in Shortage
Potassium Chloride Injection	Currently in Shortage
Procainamide Hydrochloride Injection, USP	Currently in Shortage
Sacrosidase (Sucraid) Oral Solution	Currently in Shortage
Scopolamine (Transderm Scop) Transdermal System Patch	Currently in Shortage
Sodium Acetate Injection, USP	Currently in Shortage
Sodium Bicarbonate Injection, USP	Currently in Shortage
Sodium Chloride 0.9% Injection Bags	Currently in Shortage
Sodium Chloride 23.4% Injection	Currently in Shortage
Sufentanil Citrate (Sufenta) Injection	Currently in Shortage
Sumatriptan (Imitrex) Nasal Spray	Currently in Shortage
Technetium Tc99m Succimer Injection (DMSA)	Currently in Shortage
Theophylline Extended Release Tablets and Capsules	Currently in Shortage
Tigecycline (Tygacil) Injection	Currently in Shortage
Tobramycin Injection	Currently in Shortage
Trimipramine Maleate (SURMONTIL) Capsules	Currently in Shortage