

**Drug Utilization Review Board**

Oklahoma  
**Health Care**  
Authority

Wednesday,  
November 14, 2018  
4:00pm

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







# *The University of Oklahoma*

*Health Sciences Center*

COLLEGE OF PHARMACY

PHARMACY MANAGEMENT CONSULTANTS

## MEMORANDUM

TO: Drug Utilization Review (DUR) Board Members

FROM: Bethany Holderread, Pharm.D.

SUBJECT: Packet Contents for DUR Board Meeting – November 14, 2018

DATE: October 26, 2018

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

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

### **Call to Order**

### **Public Comment Forum**

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

**Update on Medication Coverage Authorization Unit/2018 Fall Pipeline Update – Appendix B**

**Action Item – Vote to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib) – Appendix C**

**Action Item – Vote to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix) – Appendix D**

**Action Item – Vote to Prior Authorize Yescarta® (Axicabtagene) and to Update the Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications Approval Criteria – Appendix E**

**Action Item – Vote to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc) – Appendix F**

**Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Hemlibra® (Emicizumab-kxwh), Feiba® (Anti-Inhibitor Coagulant Complex), Novoseven® RT [Coagulation Factor VIIa (Recombinant)], and Jivi® [Antihemophilic Factor (Recombinant), PEGylated-aucl] – Appendix G**

**Action Item – Vote to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablet) – Appendix H**

**Action Item – Vote to Prior Authorize Krystexxa® (Pegloticase) – Appendix I**

**Action Item – Vote to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream) – Appendix J**

**Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Symdeko® (Tezacaftor/Ivacaftor) and Orkambi® (Lumacaftor/Ivacaftor Oral Granules) – Appendix K**

**30-Day Notice to Prior Authorize Onpattro™ (Patisiran) and Tegsedi™ (Inotersen) – Appendix L**

**Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Zemdri™ (Plazomicin), Xerava™ (Eravacycline), Nuzyra™ (Omadacycline), Seysara™ (Sarecycline), and Ximino™ (Minocycline Extended-Release) – Appendix M**

**Annual Review of Hepatitis C Medications – Appendix N**

**30-Day Notice to Prior Authorize Signifor® LAR (Pasireotide) – Appendix O**

**Industry News and Updates – Appendix P**

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

**Future Business**

**Adjournment**

# Oklahoma Health Care Authority

Drug Utilization Review Board  
(DUR Board)

Meeting – November 14, 2018 @ 4:00pm

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

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## AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Muchmore, Chairman:

**1. Call to Order**

A. Roll Call – Dr. Cothran

Items to be presented by Dr. Muchmore, Chairman:

**2. Public Comment Forum**

A. Acknowledgment of Speakers for Public Comment

Items to be presented by Dr. Muchmore, Chairman:

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

A. October 10, 2018 DUR Minutes – Vote

B. October 10, 2018 DUR Recommendations Memorandum

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

**4. Update on Medication Coverage Authorization Unit/2018 Fall Pipeline Update  
– See Appendix B**

A. Medication Coverage Activity for October 2018

B. Pharmacy Helpdesk Activity for October 2018

C. 2018 Fall Pipeline Update

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

**5. Action Item – Vote to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib)  
– See Appendix C**

A. Introduction

B. College of Pharmacy Recommendations

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

**6. Action Item – Vote to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix)  
– See Appendix D**

A. Introduction

B. College of Pharmacy Recommendations

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

**7. Action Item – Vote to Prior Authorize Yescarta® (Axicabtagene) and to Update the Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications Approval Criteria – See Appendix E**

A. Introduction

B. Recommendations

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

**8. Action Item – Vote to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc) – See Appendix F**

A. Introduction

B. Recommendations

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

**9. Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Hemlibra<sup>®</sup> (Emicizumab-kxwh), Feiba<sup>®</sup> (Anti-Inhibitor Coagulant Complex), Novoseven<sup>®</sup> RT [Coagulation Factor VIIa (Recombinant)], and Jivi<sup>®</sup> [Antihemophilic Factor (Recombinant), PEGylated-aucl] – See Appendix G**

- A. Current Prior Authorization Criteria
- B. Utilization of Factor Replacement Products
- C. Prior Authorization of Factor Replacement Products
- D. Market News and Updates
- E. Inhibitors and Treatment
- F. Hemlibra<sup>®</sup> (Emicizumab-kxwh) Product Summary
- G. Jivi<sup>®</sup> [Antihemophilic Factor (Recombinant), PEGylated-aucl] Product Summary
- H. Recommendations
- I. Utilization Details of Factor Replacement Products

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

**10. Action Item – Vote to Prior Authorize Nocdurna<sup>®</sup> (Desmopressin Acetate Sublingual Tablet) – See Appendix H**

- A. Introduction
- B. College of Pharmacy Recommendations

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

**11. Action Item – Vote to Prior Authorize Krystexxa<sup>®</sup> (Pegloticase) – See Appendix I**

- A. Introduction
- B. College of Pharmacy Recommendations

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

**12. Action Item – Vote to Prior Authorize Impoysz<sup>™</sup> (Clobetasol Propionate 0.025% Cream) – See Appendix J**

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

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

**13. Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Symdeko<sup>®</sup> (Tezacaftor/Ivacaftor) and Orkambi<sup>®</sup> (Lumacaftor/Ivacaftor Oral Granules) – See Appendix K**

- A. Current Prior Authorization Criteria
- B. Utilization of CFTR Modulators
- C. Prior Authorization of CFTR Modulators
- D. Market News and Updates
- E. Symdeko<sup>®</sup> (Tezacaftor/Ivacaftor) Product Summary
- F. College of Pharmacy Recommendations
- G. Utilization Details of CFTR Modulators

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

**14. 30-Day Notice to Prior Authorize Onpattro<sup>™</sup> (Patisiran) and Tegsedi<sup>™</sup> (Inotersen) – See Appendix L**

- A. Introduction
- B. Onpattro<sup>™</sup> (Patisiran) Product Summary
- C. Tegsedi<sup>™</sup> (Inotersen) Product Summary
- D. Market News and Updates
- E. College of Pharmacy Recommendations

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

**15. Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Zemdri™ (Plazomicin), Xerava™ (Eravacycline), Nuzyra™ (Omadacycline), Seysara™ (Sarecycline), and Ximino™ (Minocycline Extended-Release) – See Appendix M**

- A. Current Prior Authorization Criteria
- B. Utilization of Various Systemic Antibiotics
- C. Prior Authorization of Various Systemic Antibiotics
- D. Market News and Updates
- E. Product Summaries
- F. Cost Comparison
- G. College of Pharmacy Recommendations
- H. Utilization Details of Various Systemic Antibiotics

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

**16. Annual Review of Hepatitis C Medications – See Appendix N**

- A. Introduction
- B. Current Prior Authorization Criteria
- C. Hepatitis C Summary Statistics for Treated Members
- D. Trends of Hepatitis C Medication Utilization
- E. Utilization of Hepatitis C Medications
- F. Prior Authorization of Hepatitis C Medications
- G. Market News and Updates
- H. Regimen Comparison
- I. College of Pharmacy Recommendations
- J. Utilization Details of Hepatitis C Medications

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

**17. 30-Day Notice to Prior Authorize Signifor® LAR (Pasireotide) – See Appendix O**

- A. Acromegaly Summary
- B. Cushing's Disease Summary
- C. Market News and Updates
- D. Signifor® LAR (Pasireotide) Product Summary
- E. College of Pharmacy Recommendations

Non-Presentation; Questions Only:

**18. Industry News and Updates – See Appendix P**

- A. Introduction
- B. News and Updates

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

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

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

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

- A. Maintenance Asthma and Chronic Obstructive Pulmonary Disease (COPD) Medications
- B. Thrombocytopenia Medications
- C. Inhaled Anti-infective Medications
- D. Muscular Dystrophy Medications

*\*Future business subject to change.*

**21. Adjournment**







# Appendix A





**OKLAHOMA HEALTH CARE AUTHORITY  
DRUG UTILIZATION REVIEW BOARD MEETING  
MINUTES OF MEETING OF OCTOBER 10, 2018**

<b>BOARD MEMBERS:</b>	<b>PRESENT</b>	<b>ABSENT</b>
Stephen Anderson, Pharm.D.	x	
Markita Broyles, DPh, MBA	x	
Darlla D. Duniphin, MHS, PA-C		x
Theresa Garton, M.D.	x	
Carla Hardzog-Britt, M.D.	x	
Ashley Huddleston, Pharm.D., BCOP		x
John Muchmore, M.D., Ph.D.; Chairman	x	
Lee Munoz, D.Ph.	x	
James Osborne, Pharm.D.		x
Paul Louis Preslar, D.O., MBA; Vice Chairman	x	
<b>COLLEGE OF PHARMACY STAFF:</b>	<b>PRESENT</b>	<b>ABSENT</b>
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	
Sarai Connell, Pharm.D.; MBA; Resident	x	
Karen Egesdal, D.Ph.; SMAC-ProDUR Coordinator/OHCA Liaison		x
Thomas Ha, Pharm.D.; Clinical Pharmacist	x	
Bethany Holderread, Pharm.D.; Clinical Coordinator	x	
Shellie Keast, Ph.D.; Assistant Professor	x	
Brandy Nawaz, Pharm.D.; Clinical Pharmacist	x	
Timothy Pham, Ph.D.; Postdoctoral Research Fellow		x
Regan Smith, Pharm.D.; Clinical Pharmacist		x
Ashley Teel, Pharm.D.; Clinical Pharmacist		x
Jacquelyn Travers, Pharm.D.; Practice Facilitating Pharmacist	x	
Graduate Students: Philip Looper, Pharm.D.	x	
Michael Nguyen, Pharm.D.		x
Corby Thompson, Pharm.D.	x	
Laura Tidmore, Pharm.D.		x
Reagan Williams, Pharm.D.	x	
Visiting Pharmacy Student(s): Melissa Karner, John Schibi	x	
<b>OKLAHOMA HEALTH CARE AUTHORITY STAFF:</b>	<b>PRESENT</b>	<b>ABSENT</b>
Melody Anthony, Deputy State Medicaid Director		x
Marlene Asmussen, R.N.; Population Care Management Director		x
Burl Beasley, D.Ph.; M.P.H.; M.S. Pharm.; Sr. Director of Pharmacy	x	
Kelli Brodersen, Marketing Coordinator		x
Robert Evans, M.D.; Sr. Medical Director		x
Michael Herndon, D.O.; Chief Medical Officer		x
Maria Maule, J.D.; Senior Director Legal Services	x	
Nancy Nesser, Pharm.D.; J.D.; Pharmacy Director	x	
Thomas Nunn, D.O.; Medical Director	x	
Rebecca Pasternik-Ikard, J.D.; M.S.; R.N.; State Medicaid Director; CEO		x
Jill Ratterman, D.Ph.; Clinical Pharmacist	x	
Kerri Wade, Pharmacy Operations Manager	x	

<b>OTHERS PRESENT:</b>		
Jim Dunlap, PhRMA	Jesse Lewis, Bristol Myers Squibb	Frank Alvarado, Actelion
Chris Stanfield, Supernus	Jane Stephen, Amgen	Trebla Grant, Kite Pharma
Toby Thompson, Pfizer	Roger Grotzinger, Bristol Myers Squibb	Matt Forney, Merck
Roxann Domingez, AbbVie	Tony Molchan, AbbVie	Jim Chapman, AbbVie
Cris Valladares, Celgene	Brian Maves, Pfizer	Ahmad Nessar, Amgen
Krystin Lorg, Avadel	Christopher Holtzer, AbbVie	Gia McLean, Celgene

<b>PRESENT FOR PUBLIC COMMENT:</b>	
Ahmad Nessar	Amgen
Krystin Lorg	Avadel
Christopher Holtzer	AbbVie
Gia McLean	Celgene

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

**1A: ROLL CALL**

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

**ACTION: NONE REQUIRED**

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

**2A: AGENDA ITEM NO. 14 AHMAD NESSER**

**2B: AGENDA ITEM NO. 14 CHRISTOPHER HOLTZER**

**2C: AGENDA ITEM NO. 14 GIA MCLEAN**

**2D: AGENDA ITEM NO. 15 CHRISTOPHER HOLTZER**

**2E: AGENDA ITEM NO. 16 KRYSTIN LORG**

**ACTION: NONE REQUIRED**

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

**3A: SEPTEMBER 12, 2018 DUR MINUTES – VOTE**

**3B: SEPTEMBER 12, 2018 DUR RECOMMENDATIONS MEMORANDUM**

Materials included in agenda packet; presented by Dr. Cothran

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 4: 2019 DRUG UTILIZATION REVIEW (DUR) BOARD MEETING DATES**

**4A: 2019 DUR BOARD MEETING DATES**

Materials included in agenda packet; presented by Dr. Holderread

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 5: UPDATES ON MEDICATION COVERAGE AUTHORIZATION**

**UNIT/SOONERPSYCH PROGRAM UPDATE**

**5A: MEDICATION COVERAGE ACTIVITY FOR SEPTEMBER 2018**

**5B: PHARMACY HELPDESK ACTIVITY FOR SEPTEMBER 2018**

**5C: SOONERPSYCH PROGRAM UPDATE**

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 6: VOTE TO PRIOR AUTHORIZE NUTRESTORE® (L-GLUTAMINE) AND SIKLOS® (HYDROXYUREA)**

**6A: INTRODUCTION**

**6B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Abbott

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 7: VOTE TO PRIOR AUTHORIZE PALYNZIQ™ (PEGVALIASE-PQPZ)**

**7A: PHENYLKETONURIA PHARMACOTHERAPY**

**7B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Nawaz

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 8: VOTE TO PRIOR AUTHORIZE GALAFOLD™ (MIGALASTAT)**

**8A: INTRODUCTION**

**8B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 9: VOTE TO PRIOR AUTHORIZE QBREXZA™ (GLYCOPYRRONIUM)**

**9A: INTRODUCTION**

**9B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Chandler

Dr. Anderson moved to approve; seconded by Dr. Broyles

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 10: VOTE TO PRIOR AUTHORIZE FLOLIPID® (SIMVASTATIN ORAL SUSPENSION) AND UPDATE THE PRIOR AUTHORIZATION CRITERIA FOR ANTIHYPERLIPIDEMICS**

**10A: INTRODUCTION**

**10B: COLLEGE OF PHARMACY RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Adams

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 11: VOTE TO PRIOR AUTHORIZE VERZENIO™ (ABEMACICLIB), OGIVRI™ (TRASTUZUMAB-DKST), AND LYNPARZA® (OLAPARIB)**

**11A: INTRODUCTION**

**11B: PRODUCT SUMMARIES**

**11C: RECOMMENDATIONS**

Materials included in agenda packet; presented by Dr. Borders

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

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 12: ANNUAL REVIEW OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) AND CHRONIC MYELOID LEUKEMIA (CML) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE YESCARTA® (AXICABTAGENE)**

**12A: INTRODUCTION**

**12B: CURRENT PRIOR AUTHORIZATION CRITERIA**

**12C: UTILIZATION OF ALL/CML MEDICATIONS**

**12D: PRIOR AUTHORIZATION OF ALL/CML MEDICATIONS**

**12E: MARKET NEWS AND UPDATES**

**12F: YESCARTA® (AXICABTAGENE) PRODUCT SUMMARY**

**12G: RECOMMENDATIONS**

**12H: UTILIZATION DETAILS OF ALL/CML MEDICATIONS**

Materials included in agenda packet; presented by Dr. Borders

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 13: ANNUAL REVIEW OF SKIN CANCER MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE BRAFTOVI™ (ENCORAFENIB), MEKTOVI® (BINIMETINIB), AND LIBTAYO® (CEMIPLIMAB-RWLC)**

- 13A: INTRODUCTION**
- 13B: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 13C: UTILIZATION OF SKIN CANCER MEDICATIONS**
- 13D: PRIOR AUTHORIZATION OF SKIN CANCER MEDICATIONS**
- 13E: MARKET NEWS AND UPDATES**
- 13F: PRODUCT SUMMARIES**
- 13G: RECOMMENDATIONS**
- 13H: UTILIZATION DETAILS OF SKIN CANCER MEDICATIONS**

Materials included in agenda packet; presented by Dr. Borders

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 14: ANNUAL REVIEW OF TARGETED IMMUNOMODULATOR AGENTS AND 30-DAY NOTICE TO PRIOR AUTHORIZE ILUMYA™ (TILDRAKIZUMAB-ASMN) AND OLUMIANT® (BARICITINIB)**

- 14A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 14B: UTILIZATION OF TARGETED IMMUNOMODULATOR AGENTS**
- 14C: PRIOR AUTHORIZATION OF TARGETED IMMUNOMODULATOR AGENTS**
- 14D: MARKET NEWS AND UPDATES**
- 14E: ILUMYA™ (TILDRAKIZUMAB-ASMN) PRODUCT SUMMARY**
- 14F: OLUMIANT® (BARICITINIB) PRODUCT SUMMARY**
- 14G: PEMPHIGUS VULGARIS (PV) SUMMARY**
- 14H: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 14I: UTILIZATION DETAILS OF TARGETED IMMUNOMODULATOR AGENTS**

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 15: ANNUAL REVIEW OF GONADOTROPIN-RELEASING HORMONE (GnRH) MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE TRIPTODUR® (TRIPTORELIN) AND ORLISSA™ (ELAGOLIX)**

- 15A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 15B: UTILIZATION OF GnRH MEDICATIONS**
- 15C: PRIOR AUTHORIZATION OF GnRH MEDICATIONS**
- 15D: MARKET NEWS AND UPDATES**
- 15E: TRIPTODUR® (TRIPTORELIN) PRODUCT SUMMARY**
- 15F: ORLISSA™ (ELAGOLIX) PRODUCT SUMMARY**
- 15G: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 15H: UTILIZATION DETAILS OF GnRH MEDICATIONS**

Materials included in agenda packet; presented by Dr. Abbott

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 16: ANNUAL REVIEW OF BLADDER CONTROL MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE NOCDURNA® (DESMOPRESSIN ACETATE SUBLINGUAL TABLETS)**

- 16A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 16B: UTILIZATION OF BLADDER CONTROL MEDICATIONS**
- 16C: PRIOR AUTHORIZATION OF BLADDER CONTROL MEDICATIONS**
- 16D: MARKET NEWS AND UPDATES**
- 16E: NOCDURNA® (DESMOPRESSIN ACETATE SUBLINGUAL TABLETS) PRODUCT SUMMARY**
- 16F: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 16G: UTILIZATION DETAILS OF BLADDER CONTROL MEDICATIONS**

Materials included in agenda packet; presented by Dr. Chandler

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 17: ANNUAL REVIEW OF CONSTIPATION AND DIARRHEA MEDICATIONS**

- 17A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 17B: UTILIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS**
- 17C: PRIOR AUTHORIZATION OF CONSTIPATION AND DIARRHEA MEDICATIONS**
- 17D: MARKET NEWS AND UPDATES**
- 17E: COST COMPARISON: CONSTIPATION MEDICATIONS**
- 17F: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 17G: UTILIZATION DETAILS OF CONSTIPATION AND DIARRHEA MEDICATIONS**

Materials included in agenda packet; presented by Dr. Adams  
Dr. Hardzog-Britt moved to approve; seconded by Dr. Munoz

**ACTION: MOTION CARRIED**

**AGENDA ITEM NO. 18: ANNUAL REVIEW OF TOPICAL CORTICOSTEROIDS AND 30-DAY NOTICE TO PRIOR AUTHORIZE IMPOYZ™ (CLOBETASOL PROPIONATE 0.025% CREAM)**

- 18A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 18B: UTILIZATION OF TOPICAL CORTICOSTEROIDS**
- 18C: PRIOR AUTHORIZATION OF TOPICAL CORTICOSTEROIDS**
- 18D: MARKET NEWS AND UPDATES**
- 18E: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 18F: UTILIZATION DETAILS OF TOPICAL CORTICOSTEROIDS**

Materials included in agenda packet; presented by Dr. Nawaz

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 19: ANNUAL REVIEW OF GOUT MEDICATIONS AND 30-DAY NOTICE TO PRIOR AUTHORIZE KRYSTEXXA® (PEGLOTICASE)**

- 19A: CURRENT PRIOR AUTHORIZATION CRITERIA**
- 19B: UTILIZATION OF GOUT MEDICATIONS**
- 19C: PRIOR AUTHORIZATION OF GOUT MEDICATIONS**
- 19D: MARKET NEWS AND UPDATES**
- 19E: KRYSTEXXA® (PEGLOTICASE) PRODUCT SUMMARY**
- 19F: COLLEGE OF PHARMACY RECOMMENDATIONS**
- 19G: UTILIZATION DETAILS OF GOUT MEDICATIONS**

Materials included in agenda packet; presented by Dr. Connell

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 20: INDUSTRY NEWS AND UPDATES**

- 20A: INTRODUCTION**
- 20B: NEWS AND UPDATES**

Materials included in agenda packet; non-presentation; questions only

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 21: U.S. FOOD AND DRUG ADMINISTRATION (FDA) AND DRUG ENFORCEMENT ADMINISTRATION (DEA) UPDATES**

Materials included in agenda packet; presented by Dr. Cothran

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 22: FUTURE BUSINESS\* (UPCOMING PRODUCT AND CLASS REVIEWS)**

- 22A: HEPATITIS C MEDICATIONS**
- 22B: HEMOPHILIA MEDICATIONS**
- 22C: ONPATTRO™ (PATISIRAN)**
- 22D: SYSTEMIC ANTIBIOTICS**
- 22E: CYSTIC FIBROSIS MEDICATIONS**

*\*Future business subject to change.*

Materials included in agenda packet; presented by Dr. Holderread

**ACTION: NONE REQUIRED**

**AGENDA ITEM NO. 23:            ADJOURNMENT**

The meeting was adjourned at 5:40 pm





# *The University of Oklahoma*

*Health Sciences Center*

**COLLEGE OF PHARMACY**

**PHARMACY MANAGEMENT CONSULTANTS**

## **Memorandum**

**Date:** October 11, 2018

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

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

**Subject:** Drug Utilization Review (DUR) Board Recommendations from Meeting of October 10, 2018

### **Recommendation 1: 2019 Drug Utilization Review Board Meeting Dates**

MOTION CARRIED by unanimous approval.

- January 9, 2019
- February 13, 2019
- March 13, 2019
- April 10, 2019
- May 8, 2019
- June 12, 2019
- July 10, 2019
- August 14, 2019
- September 11, 2019
- October 9, 2019
- November 13, 2019
- December 11, 2019

### **Recommendation 2: SoonerPsych Program Update**

NO ACTION REQUIRED.

### **Recommendation 3: Vote to Prior Authorize NutreStore® (L-Glutamine) and Siklos® (Hydroxyurea)**

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Siklos® (hydroxyurea) and NutreStore® (L-glutamine) with the following criteria:

**Siklos® (Hydroxyurea Tablets) Approval Criteria:**

1. An FDA approved indication of sickle cell anemia; and
2. Member must be 2 years of age or older; and
3. Member must have a history of moderate-to-severe, painful crises; and
4. A trial of hydroxyurea capsules or a patient-specific, clinically significant reason why hydroxyurea capsules are not appropriate for the member; and
5. Prescriber must agree to monitor blood counts every 2 weeks throughout therapy; and
6. Prescriber must agree to monitor the member for the development of secondary malignancies; and
7. Female members must not be pregnant and must have a negative pregnancy test prior to therapy initiation; and
8. Male and female members of reproductive potential must be willing to use effective contraception during and after treatment with Siklos® for at least 6 months after therapy; and
9. Member must not be given live vaccines while on Siklos® therapy; and
10. Initial approvals will be for the duration of 12 months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

**NutreStore® (L-Glutamine) Approval Criteria [Short Bowel Syndrome (SBS) Diagnosis]:**

1. An FDA approved diagnosis of SBS; and
2. NutreStore® must be used in conjunction with a recombinant human growth hormone product that is approved for this indication; and
3. Member must be receiving optimal management of SBS (e.g., specialized oral diet, enteral feedings, parenteral nutrition, fluid and micronutrient supplements); and
4. Approvals will be for up to 16 weeks.

**NutreStore® (L-Glutamine) Approval Criteria [Sickle Cell Disease (SCD) Diagnosis]:**

1. A diagnosis of SCD; and
2. Member must be 5 years of age or older; and
3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. NutreStore® must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate amount of drug required.
6. Initial approvals will be for a duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

Additionally, the College of Pharmacy recommends updating the prior authorization criteria for Endari™ (L-glutamine) with the changes noted in red:

**Endari™ (L-Glutamine) Approval Criteria:**

1. An FDA approved diagnosis of sickle cell disease (SCD); and
2. Member must be 5 years of age or older; and

3. A trial of hydroxyurea or documentation why hydroxyurea is not appropriate for the member; and
4. Endari™ must be prescribed by, or in consultation with, a hematologist or a specialist with expertise in treatment of SCD (or in consultation with an advanced care practitioner with a supervising physician who is a hematologist or specialist with expertise in treating SCD); and
5. A patient-specific, clinically significant reason why NutreStore® (L-glutamine powder for oral solution) cannot be used must be provided; and
6. 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.
7. Initial approvals will be for a duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

#### **Recommendation 4: Vote to Prior Authorize Palynziq™ (Pegvaliase-pqpz)**

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Palynziq™ (pegvaliase-pqpz) and updating the current prior authorization criteria for Kuvan® (sapropterin). The following criteria would apply (changes noted in red):

##### **Palynziq™ (Pegvaliase-pqpz) Approval Criteria:**

1. An FDA approved diagnosis to reduce blood phenylalanine concentrations in patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations >600µmol/L on existing management; and
2. Documentation of active management with a phenylalanine restricted diet; and
3. Baseline phenylalanine concentration must be documented on the prior authorization request and must be drawn within the last 30 days; and
4. Documentation the member's average blood phenylalanine concentration over the last 6 months is >600µmol/L on existing management; and
5. Concomitant use with Kuvan® (sapropterin) will not be approved; and
6. Prescriber, pharmacy, and member must be enrolled in the Palynziq™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
7. Initial dose must be administered under the supervision of a health care provider equipped to manage anaphylaxis and observe the member for at least 60 minutes following injection; and
8. Member must be prescribed auto-injectable epinephrine and be counseled on its appropriate use; and
9. Initial approvals will be for the duration of 33 weeks to allow for initial titration and for 24 weeks of maintenance treatment with 20mg once daily dosing. Patients should then be assessed for a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L.
  - a. If member has not achieved a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤600µmol/L,

- approvals may be granted for the 40mg once daily dosing for a duration of 16 weeks; or
- b. If member has achieved a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration  $\leq 600\mu\text{mol/L}$ , subsequent approvals will be for the duration of one year; and
10. Members who do not achieve at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration  $\leq 600\mu\text{mol/L}$  after 16 weeks of continuous treatment with the maximum dosage of 40mg once daily will not be approved for subsequent approvals; and
  11. Subsequent approvals will be for the duration of one year.
  12. Reauthorization will require the following:
    - a. Documentation of active management with a phenylalanine restricted diet; and
    - b. Verification from the prescriber of continued response to therapy.

**Kuvan® (Sapropterin) Approval Criteria:**

1. An FDA approved diagnosis of phenylketonuria; and
2. Documentation of active management with a phenylalanine restricted diet; and
3. Member must not have two null mutations in *trans*; and
4. Baseline phenylalanine concentration must be documented on the prior authorization request and must be drawn within the last 30 days; and
5. Concomitant use with Palynziq™ (pegvaliase-pqpz) will not be approved; and
6. Initial approvals will be for the duration of 30 days. After which time, the prescriber must verify that the member responded to treatment as defined by laboratory documentation of  $\geq 30\%$  decrease in blood phenylalanine levels from baseline.
  - a. If the member was initiated at 10mg/kg/day dose, then a subsequent trial of 20mg/kg/day for a duration of 30 days can be approved. After which time, the prescriber must verify that the member responded to treatment as defined by laboratory documentation of  $\geq 30\%$  decrease in blood phenylalanine levels from baseline.
  - b. If the member was initiated at 20mg/kg/day dose, then no additional approvals will be granted after a trial period of 30 days if the member did not respond to treatment as defined by laboratory documentation of  $\geq 30\%$  decrease in blood phenylalanine levels from baseline.
7. Subsequent approvals will be for the duration of one year.
8. Reauthorization will require the following:
  - a. Documentation of active management with a phenylalanine restricted diet; and
  - b. Verification from the prescriber of continued response to therapy.

**Recommendation 5: Vote to Prior Authorize Galafold™ (Migalastat)**

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Galafold™ (migalastat) with the following criteria [the criteria shown in red on criteria 4 has been added due to current lack of evidence for efficacy using Galafold™ (migalastat) with enzyme replacement therapy]:

### **Galafold™ (Migalastat) Approval Criteria:**

1. An FDA approved diagnosis of Fabry disease with a confirmed amenable *GLA* gene variant based on in vitro assay data; and
2. Galafold™ must be prescribed in consultation with a geneticist or an advanced care practitioner with a supervising physician who is a geneticist; and
3. Member must have an estimated glomerular filtration rate (eGFR) of at least 30mL/min/1.73m<sup>2</sup>; and
4. Galafold™ will not be approved for concomitant use with enzyme replacement therapy (ERT); and
5. Galafold™ will initially be approved for six months. After that time, compliance will be required for continued authorization; and
6. A quantity limit of 14 capsules per 28 days will apply.

### **Recommendation 6: Vote to Prior Authorize Qbrexza™ (Glycopyrronium)**

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the prior authorization of Qbrexza™ (glycopyrronium) with the following criteria [the criteria shown in red on line 2 has been updated based on the DUR Board recommendation, and additional criteria has been added on line 4 to ensure safe product use]:

### **Qbrexza™ (Glycopyrronium) Approval Criteria:**

1. An FDA approved diagnosis of primary axillary hyperhidrosis in pediatric patients 9 years of age to 20 years of age; and
2. Documentation of assessment by a licensed behavior specialist **or the prescribing physician** indicating the member's hyperhidrosis is causing social anxiety, depression, or similar mental health-related issues that impact the member's ability to function in day-to-day living must be provided; and
3. Member must have failed a trial of Drysol™ (20% aluminum chloride) at least three weeks in duration; and
4. **Prescriber must verify that the member has received counseling on the safe and proper use of Qbrexza™; and**
5. A quantity limit of one box (30 cloths) per 30 days will apply.

### **Recommendation 7: Vote to Prior Authorize FloLipid® (Simvastatin Oral Suspension) and Update the Prior Authorization Criteria for Antihyperlipidemics**

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends the following changes to the Statin Medications and Ezetimibe Product Based Prior Authorization (PBPA) category (changes noted in red):

1. Placement of FloLipid® (simvastatin oral suspension) into the Special Prior Authorization (PA) Tier:
  - a. Use of FloLipid® will require a patient-specific, clinically significant reason why the member cannot use simvastatin oral tablets, even when the tablets are crushed.

- Moving ezetimibe to Tier-1 based on generic availability and low net cost.

Statin Medications and Ezetimibe*	
Tier-1	Special PA
atorvastatin (Lipitor®)	fluvastatin (Lescol® & Lescol® XL)
<b>ezetimibe (Zetia®)</b>	lovastatin (Altoprev®)
lovastatin (Mevacor®)	pitavastatin calcium (Livalo®)
pravastatin (Pravachol®)	pitavastatin magnesium (Zypitamag™)
rosuvastatin (Crestor®)	pitavastatin sodium (Nikita™)
simvastatin (Zocor®)	<b>simvastatin suspension (FloLipid®)</b>
	simvastatin/ezetimibe (Vytorin®)

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

### Statin Medications and Ezetimibe Special Prior Authorization (PA) Approval Criteria:

- Use of any Special PA medication will require a patient-specific, clinically significant reason why lower tiered medications with similar or higher LDL reduction cannot be used; and
- Use of FloLipid® (simvastatin oral suspension) will require a patient specific, clinically significant reason why the member cannot use simvastatin oral tablets, even when the tablets are crushed.

Additionally, the College of Pharmacy recommends removing the prior authorization from omega-3-acid ethyl esters (generic Lovaza®), based on low net cost, as well as removing the nicotinic acid trial requirement from the current omega-3 fatty acids approval criteria, based on recommendations from the Drug Utilization Review (DUR) Board (changes noted in red):

### Omega-3 Fatty Acids Approval Criteria:

- Laboratory documentation of severe hypertriglyceridemia (fasting triglycerides  $\geq 500\text{mg/dL}$ ) and controlled diabetes (fasting glucose  $< 150\text{mg/dL}$  at the time of triglycerides measurement and HgA1c  $< 7.5\%$ ); and
- Previous failure with ~~both nicotinic acid and~~ fibric acid medications; and
- Use of Vascepa® or Epanova® requires a **previous failure of** or a patient-specific, clinically significant reason why the member cannot use omega-3-acid ethyl esters (generic Lovaza®), **which is available without prior authorization**; and
- Use of Vascepa® 0.5 gram requires a patient-specific, clinically significant reason why the member cannot use Vascepa® 1 gram.

Furthermore, the College of Pharmacy recommends the following updates to the current Juxtapid® and Kynamro® Approval Criteria, based on net costs (changes noted in red):

### Juxtapid® (Lomitapide) and Kynamro® (Mipomersen) Approval Criteria:

- An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following criteria:
  - A documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
  - An untreated total cholesterol  $> 500\text{mg/dL}$  and triglycerides  $< 300\text{mg/dL}$  and at least one of the following:

- i. Documentation that both parents have untreated total cholesterol >250mg/dL; or
  - ii. Presence of tendinous/cutaneous xanthoma prior to age 10 years; and
- 2. Documented ~~failure trial~~ of high dose statin therapy (LDL reduction capability equivalent to ~~atorvastatin 80mg or higher~~ rosuvastatin 40mg) or maximally tolerated statin therapy at least 12 weeks in duration; and
- 3. Documented trial of Repatha® (evolocumab) at least 12 weeks in duration; and
- 4. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
- 5. Prescriber must be certified with Juxtapid® or Kynamro® REMS program.

Lastly, the College of Pharmacy recommends the following updates to the current PCSK9 Inhibitors Approval Criteria, based on the new FDA approved indications for Repatha® (changes noted in red):

**PCSK9 Inhibitors Approval Criteria:**

**1. For Repatha® (evolocumab):**

- a. An FDA approved diagnosis of homozygous familial hypercholesterolemia (HoFH) defined by the presence of at least one of the following:
  - i. Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality via genetic testing; or
  - ii. An untreated total cholesterol >500mg/dL and at least one of the following:
    - 1. Documented evidence of definite heterozygous familial hypercholesterolemia (HeFH) in both parents; or
    - 2. Presence of tendinous/cutaneous xanthoma prior to age 10 years; or
- b. An FDA approved diagnosis of primary hyperlipidemia; or
- c. An FDA approved indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease (CVD); and
  - i. Documentation of established CVD; and
    - 1. Supporting diagnoses/conditions and dates of occurrence signifying established CVD; or

**2. For Praluent® (alirocumab):**

- d. An FDA approved diagnosis of HeFH defined by the presence of one of the following criteria:
  - i. Documented functional mutation(s) in the LDL receptor (LDLR) gene or other HeFH-related genes via genetic testing; or
  - ii. Definite HeFH using either the Simon Broome Register criteria or the Dutch Lipid Network criteria; or
- e. An FDA approved diagnosis of clinical atherosclerotic cardiovascular disease defined by the presence of one of the following criteria:
  - i. High cardiovascular risk confirmed by Framingham risk score; and
    - 1. Supporting diagnoses/conditions signifying this risk level; or
  - ii. Documented history of Coronary Heart Disease (CHD); and
    - 1. Supporting diagnoses/conditions and dates of occurrence signifying history of CHD; and

3. Member must be 13 years of age or older for the diagnosis of HoFH or must be 18 years of age or older for all other FDA-approved diagnoses or indications; and
4. Member must be on high dose statin therapy (LDL reduction capability equivalent to rosuvastatin 40mg) or on maximally tolerated statin therapy; and
  - a. Statin trials must be at least 12 weeks in duration (dosing, dates, duration of treatment, and reason for discontinuation must be provided); and
  - b. LDL-cholesterol (LDL-C) levels should be included following at least 12 weeks of treatment with each statin medication; and
  - c. For statin intolerance due to myalgia, creatine kinase (CK) labs verifying rhabdomyolysis must be provided; and
  - d. Tier structure rules still apply; and
5. Member requires additional lowering of LDL-C (baseline, current, and goal LDL-C levels must be provided); and
6. Prescriber must verify that member has been counseled on appropriate use, storage of the medication, and administration technique; and
7. A quantity limit of two syringes or pens per 28 days will apply for Praluent®. A quantity limit of two syringes or autoinjectors per 28 days will apply for Repatha® 140mg and a quantity limit of one autoinjector per 28 days for Repatha® 420mg. Patients requesting Repatha® 420mg strength will not be approved for multiple 140mg syringes or autoinjectors but instead should use one 420mg autoinjector.
8. Initial approvals will be for the duration of three months. Continued authorization at that time will require the prescriber to provide recent LDL-C levels to demonstrate the effectiveness of this medication, and compliance will be checked at that time and every six months thereafter for continued approval.

**Recommendation 8: Vote to Prior Authorize Verzenio™ (Abemaciclib), Ogivri™ (Trastuzumab-dkst), and Lynparza® (Olaparib)**

MOTION CARRIED by unanimous approval.

**Afinitor® (Everolimus) Approval Criteria [Breast Cancer Diagnosis]:**

1. Diagnosis of advanced breast cancer; and
2. Negative expression of human epidermal receptor type 2 (HER2); and
3. Hormone receptor positive; and
4. Used in combination with exemestane, fulvestrant, or tamoxifen; and
5. Member must have failed treatment with, have a contraindication to, or be intolerant to letrozole or anastrozole.

**Afinitor® (Everolimus) Approval Criteria [Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures Diagnosis]:**

1. An FDA approved diagnosis of TSC-associated partial-onset seizures; and
2. Initial prescription must be written by a neurologist or neuro-oncologist; and
3. Member must have failed therapy with at least three other medications commonly used for seizures; and
4. Afinitor® must be used as adjunctive treatment; and



5. The member must not be taking any P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin) concurrently with Afinitor®; and
6. The member must not be taking St. John's wort concurrently with Afinitor®; and
7. The prescriber must verify that Afinitor® trough levels and adverse reactions (e.g., non-infectious pneumonitis, stomatitis, hyperglycemia, dyslipidemia, thrombocytopenia, neutropenia, febrile neutropenia) will be monitored, and dosing changes or discontinuations will correspond with recommendations in the drug labeling; and
8. Verification from the prescriber that female members will use contraception while receiving Afinitor® therapy and for eight weeks after the last dose of Afinitor® and that male members with female partners of reproductive potential will use contraception while receiving Afinitor® therapy and for four weeks after the last dose of Afinitor®; and
9. The member's recent body surface area (BSA) must be provided on the prior authorization request in order to authorize the appropriate amount of drug required according to package labeling.
10. Initial approvals will be for the duration of three months. For continuation, the prescriber must include information regarding improved response/effectiveness of the medication.

**Kisqali® (Ribociclib) Approval Criteria [Breast Cancer Diagnosis]:**

- ~~1. A patient-specific, clinically significant reason why the member cannot use the co-packaged formulation with letrozole; and~~
- ~~2. A diagnosis of advanced or metastatic breast cancer, initial therapy; and~~
3. Member must be hormone receptor positive; and
4. Member must be human epidermal receptor type 2 (HER2)-negative; and
5. If used in combination with an aromatase inhibitor:
  - a. Diagnosis of advanced or metastatic breast cancer, initial therapy; or
6. If used in combination with fulvestrant:
  - a. Diagnosis of advanced or metastatic breast cancer, as initial endocrine based therapy or following disease progression on endocrine therapy; and
  - b. Must be used in postmenopausal women only.
- ~~7. Ribociclib must be given in combination with an aromatase inhibitor; and~~
- ~~8. Ribociclib must be used in postmenopausal women only.~~

**Kisqali® Femara® Co-Pack (Ribociclib/Letrozole) Approval Criteria [Breast Cancer Diagnosis]:**

1. Diagnosis of advanced or metastatic breast cancer, initial therapy; and
2. Member must be hormone receptor positive; and
3. Member must be human epidermal receptor type 2 (HER2)-negative.;~~and~~
- ~~4. Ribociclib must be used in postmenopausal women only.~~

**Lynparza® (Olaparib) Approval Criteria [Ovarian Cancer Diagnosis]:**

1. Diagnosis of deleterious or suspected deleterious germline BRCA mutated (gBRCAm), advanced ovarian cancer; and
2. The member must have been treated with three or more prior lines of chemotherapy. Prior chemotherapy regimens should be documented on the prior authorization request; and
3. A quantity limit based on FDA approved dosing will apply.

**Lynparza® (Olaparib) Approval Criteria [Breast Cancer Diagnosis]:**

1. Diagnosis of metastatic breast cancer; and
2. Member must have shown progression on previous chemotherapy in any setting; and
3. Human epidermal receptor 2 (HER2)-negative; and
4. Positive test for a germline BRCA-mutation (gBRCAm); and
5. Members with hormone receptor positive disease must have failed prior endocrine therapy or are considered to not be a candidate for endocrine therapy.

**Lynparza® (Olaparib) Approval Criteria [Maintenance Treatment Diagnosis]:**

1. Used for maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy; and
2. The member must have been completed therapy with the platinum agent in the prior 8 weeks; and
3. A quantity limit based on FDA approved dosing will apply.

**Ogivri™ (Trastuzumab-dkst) Approval Criteria [Breast Cancer Diagnosis]:**

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing breast cancer; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab).

**Ogivri™ (Trastuzumab-dkst) Approval Criteria [Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Diagnosis]:**

1. Diagnosis of human epidermal receptor 2 (HER2)-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma; and
2. A patient-specific, clinically significant reason why the member cannot use Herceptin® (trastuzumab).

**Perjeta® (Pertuzumab) Approval Criteria [Breast Cancer Diagnosis]:**

1. Positive expression of human epidermal receptor type 2 (HER2); and
2. Used in one of the following settings:
  - a. Metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease:
    - i. Used in combination with trastuzumab and docetaxel; or
  - b. Neoadjuvant treatment of members with locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive):
    - i. Used in combination with trastuzumab and docetaxel (neoadjuvant treatment may also contain other agents in addition to trastuzumab and docetaxel); or
  - c. Adjuvant systemic therapy for patients with node positive, HER2-positive tumors or high-risk node negative members [tumor >1cm; tumor 0.5 to 1cm with histologic or nuclear grade 3; estrogen receptor (ER)/progesterone receptor (PR) negative; or age <35]:
    - i. Used in combination with trastuzumab and paclitaxel following AC (doxorubicin/cyclophosphamide); or
    - ii. Used in combination with trastuzumab and docetaxel following AC; or
    - iii. Used in combination with TCH (docetaxel/carboplatin/trastuzumab).

**Verzenio™ (Abemaciclib) Approval Criteria [Breast Cancer Diagnosis]:**

1. Used in one of the following settings:
  - a. In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women; or
  - b. In combination with fulvestrant with disease progression following endocrine therapy in advanced or metastatic breast cancer; or
  - c. As monotherapy for disease progression following endocrine therapy and prior chemotherapy in metastatic breast cancer; and
2. All the following criteria must be present:
  - a. Advanced or metastatic breast cancer; and
  - b. Progressed after endocrine therapy when used with fulvestrant or as initial therapy in combination with an aromatase inhibitor; and
  - c. Hormone receptor positive; and
  - d. Human epidermal receptor 2 (HER2)-negative.

**Recommendation 9: Annual Review of Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications and 30-Day Notice to Prior Authorize Yescarta® (Axicabtagene)**

NO ACTION REQUIRED.

**Recommendation 10: Annual Review of Skin Cancer Medications and 30-Day Notice to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc)**

NO ACTION REQUIRED.

**Recommendation 11: Annual Review of Targeted Immunomodulator Agents and 30-Day Notice to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib)**

NO ACTION REQUIRED.

**Recommendation 12: Annual Review of Gonadotropin-Releasing Hormone (GnRH) Medications and 30-Day Notice to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix)**

NO ACTION REQUIRED.

**Recommendation 13: Annual Review of Bladder Control Medications and 30-Day Notice to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablet)**

NO ACTION REQUIRED.

## **Recommendation 14: Annual Review of Constipation and Diarrhea Medications**

**MOTION CARRIED** by unanimous approval.

The College of Pharmacy recommends the following updates to the current prior authorization criteria for the constipation and diarrhea medications (changes noted in red):

1. Updating the approval criteria for Trulance® (plecanatide), based on the new FDA approved indication for the treatment of irritable bowel syndrome with constipation (IBS-C).
2. Removing the requirement of a reason why the member cannot use Amitiza® or Movantik® from the approval criteria for Symproic® (naldemedine), based on similar net costs for the treatment of opioid-induced constipation (OIC).
3. Adding a reason why the member cannot use Symproic® (naldemedine) to the approval criteria for Relistor® (methylnaltrexone) tablets and injection for the diagnosis of OIC in members with chronic, non-cancer pain, based on net costs.

### **Trulance® (Plecanatide) Approval Criteria:**

1. An FDA approved diagnosis of chronic idiopathic constipation (CIC) **or irritable bowel syndrome with constipation (IBS-C)** in members 18 years of age or older; and
2. Documentation that constipation-causing therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients); and
3. Documented and updated colon screening for members older than 50 years of age; and
4. 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
5. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
6. A quantity limit of 30 tablets for a 30 day supply will apply.

### **Symproic® (Naldemedine) 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, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; 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 older 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. Symproic® must be discontinued if treatment with the opioid pain medication is also discontinued.
9. A quantity limit of 30 tablets for a 30-day supply will apply.

**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, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; 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 older 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), Movantik® (naloxegol), or Symproic® (naldemedine) 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.

**Relistor® (Methylnaltrexone) Injection Approval Criteria [Opioid-Induced Constipation (OIC) in Chronic Non-Cancer Pain Diagnosis]:**

1. An FDA approved diagnosis of OIC in members 18 years of age or older with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation; and
2. Documentation of the underlying cause of chronic pain, or reason why member is on chronic opioid therapy; and
3. Member must have current use of opioid medications; and
4. Documented and updated colon screening for members older 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. Member must not have known or suspected gastrointestinal obstruction; and
  7. A patient-specific, clinically significant reason why member cannot use Amitiza® (lubiprostone), Movantik® (naloxegol), or Symproic® (naldemedine) must be provided; and
  8. A patient-specific, clinically significant reason why member cannot use the tablet formulation of Relistor® must be provided; and
  9. 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.
  10. Approval will initially be for 12 weeks of therapy. Further approval may be granted if prescriber documents member is responding well to treatment.
  11. Relistor® must be discontinued if treatment with the opioid pain medication is also discontinued.
  12. A quantity limit of 30 units per month will apply.

**Recommendation 15: Annual Review of Topical Corticosteroids and 30-Day Notice to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream)**

NO ACTION REQUIRED.

**Recommendation 16: Annual Review of Gout Medications and 30-Day Notice to Prior Authorize Krystexxa® (Pegloticase)**

NO ACTION REQUIRED.

**Recommendation 17: Industry News and Updates**

NO ACTION REQUIRED.

**Recommendation 18: U.S. Food and Drug Administration (FDA) and Drug Enforcement Administration (DEA) Updates**

NO ACTION REQUIRED.



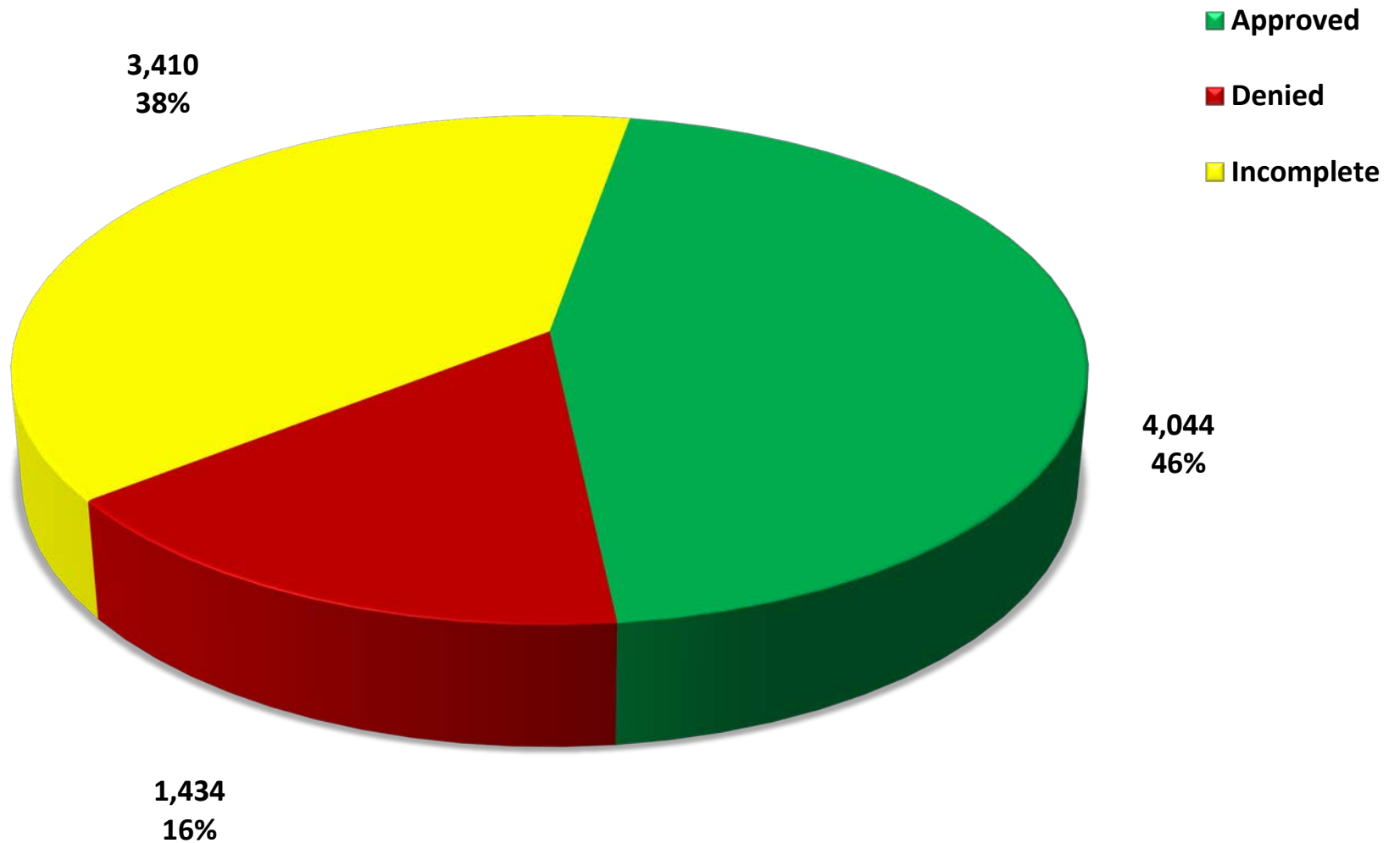
# Appendix B





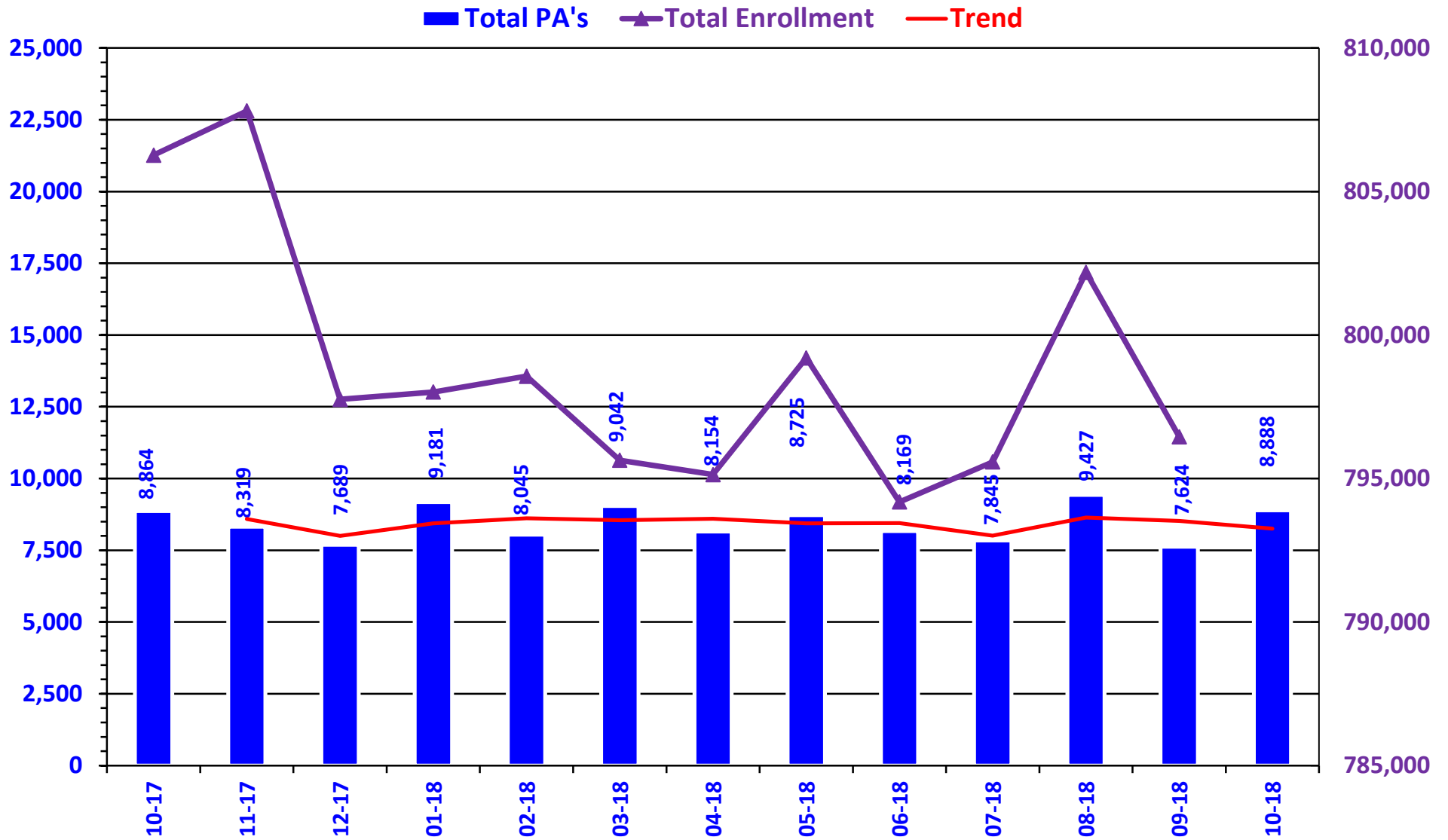


# PRIOR AUTHORIZATION ACTIVITY REPORT: OCTOBER 2018



*PA totals include approved/denied/incomplete/overrides*

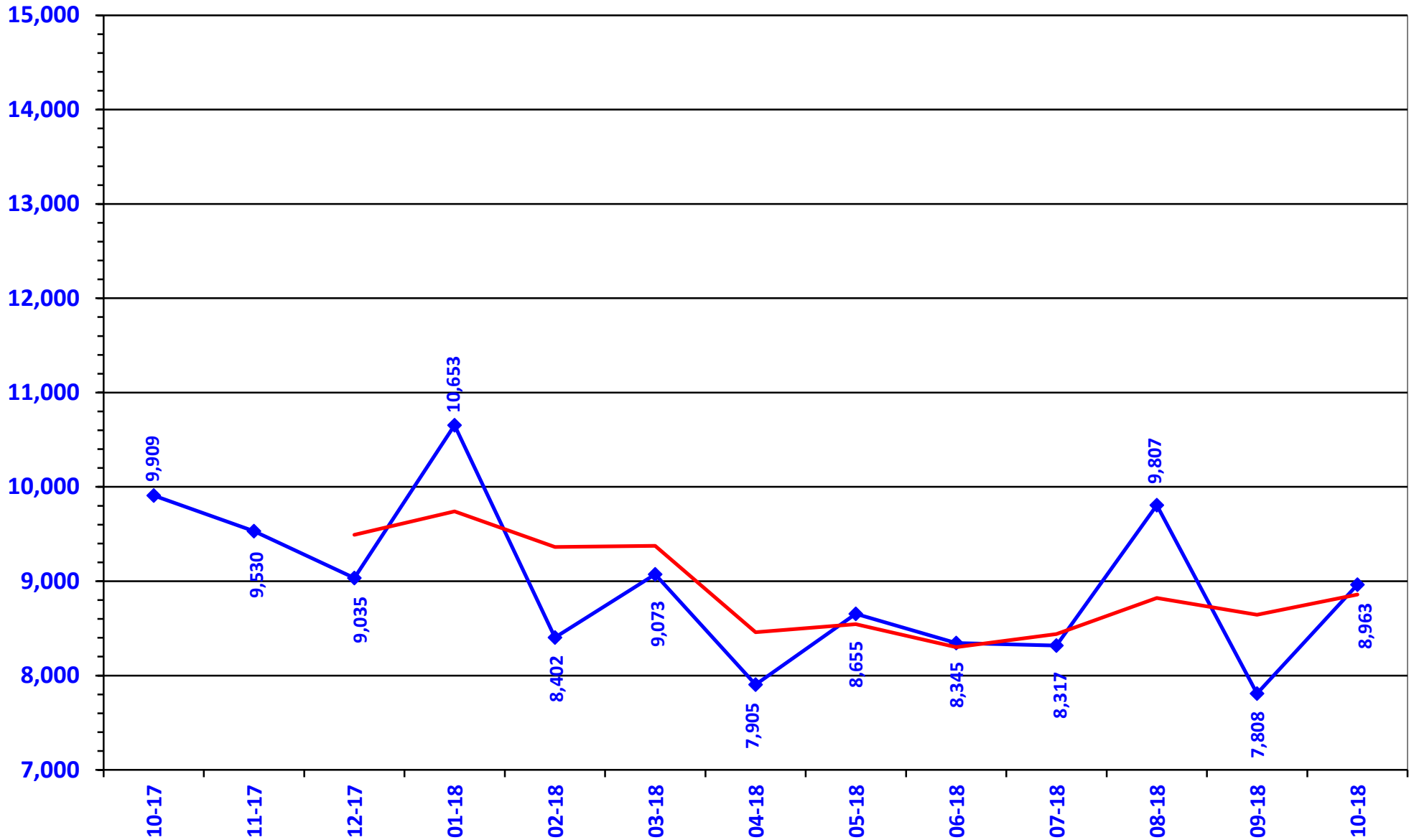
# PRIOR AUTHORIZATION REPORT: OCTOBER 2017 – OCTOBER 2018



PA totals include approved/denied/incomplete/overrides

# CALL VOLUME MONTHLY REPORT: OCTOBER 2017 – OCTOBER 2018

◆ Total Calls    — Trend



## Prior Authorization Activity 10/1/2018 Through 10/31/2018

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort/Dulera	226	24	69	133	307
Analgesic - NonNarcotic	15	0	3	12	0
Analgesic - Narcotic	372	176	30	166	164
Angiotensin Receptor Antagonist	27	6	9	12	318
Antiasthma	77	21	20	36	346
Antibiotic	42	21	4	17	266
Anticonvulsant	160	64	15	81	338
Antidepressant	201	62	42	97	322
Antidiabetic	224	62	33	129	347
Antifungal	13	0	8	5	0
Antihistamine	15	3	5	7	358
Antimigraine	61	3	21	37	247
Antineoplastic	89	57	7	25	177
Antiparasitic	15	3	0	12	8
Antiulcers	153	29	58	66	158
Anxiolytic	64	40	1	23	312
Atypical Antipsychotics	240	124	24	92	352
Biologics	145	83	15	47	293
Bladder Control	70	7	20	43	357
Blood Thinners	279	162	18	99	347
Botox	41	29	9	3	357
Buprenorphine Medications	410	287	16	107	82
Cardiovascular	105	45	11	49	335
Chronic Obstructive Pulmonary Disease	171	28	44	99	302
Constipation/Diarrhea Medications	166	21	76	69	248
Contraceptive	17	14	2	1	357
Dermatological	147	24	66	57	263
Diabetic Supplies	402	244	17	141	184
Diuretic	16	12	0	4	335
Endocrine & Metabolic Drugs	144	74	19	51	128
Erythropoietin Stimulating Agents	25	14	4	7	102
Fibromyalgia	204	29	96	79	304
Gastrointestinal Agents	122	24	31	67	167
Growth Hormones	102	72	9	21	148
Hepatitis C	189	123	7	59	8
HFA Rescue Inhalers	53	1	9	43	358
Insomnia	35	4	8	23	123
Insulin	125	39	18	68	313
Miscellaneous Antibiotics	20	1	2	17	12
Multiple Sclerosis	34	12	7	15	187
Muscle Relaxant	56	4	19	33	191
Nasal Allergy	57	13	18	26	152
Neurological Agents	104	34	33	37	229
NSAIDs	171	21	48	102	213
Ocular Allergy	31	2	10	19	100
Osteoporosis	23	12	4	7	331
Other*	321	63	71	187	256
Otic Antibiotic	17	1	4	12	7
Pediculicide	10	0	5	5	0
Respiratory Agents	25	17	0	8	191

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

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Statins	13	7	0	6	331
Stimulant	821	392	89	340	345
Synagis	365	115	126	124	149
Testosterone	44	15	11	18	326
Topical Antifungal	26	5	4	17	14
Topical Corticosteroids	71	0	45	26	0
Vitamin	87	26	32	29	168
Pharmacotherapy	65	62	0	3	330
Emergency PAs	0	0	0	0	
<b>Total</b>	<b>7,323</b>	<b>2,833</b>	<b>1,372</b>	<b>3,118</b>	

#### Overrides

Brand	22	15	1	6	306
Compound	13	12	0	1	84
Cumulative Early Refill	4	4	0	0	180
Diabetic Supplies	8	6	0	2	133
Dosage Change	339	318	3	18	12
High Dose	3	2	0	1	97
Ingredient Duplication	10	10	0	0	12
Lost/Broken Rx	74	71	1	2	11
NDC vs Age	294	196	22	76	267
Nursing Home Issue	102	89	0	13	13
Opioid Quantity	35	31	1	3	144
Other*	35	30	3	2	11
Quantity vs. Days Supply	545	371	28	146	252
STBS/STBSM	18	10	0	8	67
Stolen	11	9	0	2	12
Temporary Unlock	1	1	0	0	31
Third Brand Request	51	36	3	12	17
<b>Overrides Total</b>	<b>1,565</b>	<b>1,211</b>	<b>62</b>	<b>292</b>	
<b>Total Regular PAs + Overrides</b>	<b>8,888</b>	<b>4,044</b>	<b>1,434</b>	<b>3,410</b>	

#### Denial Reasons

Unable to verify required trials.	2,791
Does not meet established criteria.	1,453
Lack required information to process request.	585

#### Other PA Activity

Duplicate Requests	685
Letters	11,698
No Process	10
Changes to existing PAs	726
Helpdesk Initiated Prior Authorizations	649
PAs Missing Information	34

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

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# 2018 Fall Pipeline Update

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Oklahoma Health Care Authority  
November 2018

## Introduction

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The following report is a pipeline review compiled by the University of Oklahoma College of Pharmacy. Information in this report is focused on medications not yet approved by the U.S. Food and Drug Administration (FDA). The pipeline report is not an all-inclusive list, and medications expected to be highly utilized or have a particular impact in the SoonerCare population have been included for review. Pipeline data is collected from a variety of sources and is subject to change; dates listed are projections and all data presented are for informational purposes only. Costs listed in the following report do not reflect rebated prices or net costs.

## Baloxavir Marboxil<sup>1,2,3,4,5,6,7,8</sup>

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**Anticipated Indication(s):** Orally administered antiviral for the treatment of uncomplicated influenza in patients 12 years of age and older.

**Clinical Trial(s):** Baloxavir marboxil was evaluated in a Phase 3 multicenter, randomized, double-blind, placebo-controlled study including a total of 1,436 influenza patients in the United States and Japan. The primary efficacy endpoint was time to alleviation of symptoms (TTAS); secondary endpoints included time to resolution of fever and the time to cessation of viral shedding. Baloxavir marboxil reduced the duration of symptoms by more than one day (median time 53.7 hours vs. 80.2 hours;  $P < 0.0001$ ). Baloxavir marboxil also reduced the duration of fever (median time 24.5 hours vs. 42.0 hours;  $P < 0.0001$ ) and the time to cessation of viral shedding (median time 24.0 hours vs. 96.0 hours;  $P < 0.0001$ ) compared to placebo. Similar efficacy results were seen between baloxavir marboxil and oseltamivir in relation to duration of symptoms (median time 53.5 hours vs. 53.8 hours;  $P = 0.7560$ ) and fever reduction (median time 24.4 hours vs. 24.0 hours;  $P = 0.9225$ ), but significant differences were observed in time to cessation of viral shedding favoring baloxavir marboxil (24.0 hours vs. 72.0 hours;  $P < 0.0001$ ). Baloxavir marboxil was well-tolerated and had a numerically lower overall incidence of adverse events (20.7%) reported compared with placebo (24.6%) or oseltamivir (24.8%).

**Place in Therapy:** During the 2017 to 2018 influenza season, the Centers for Disease Control and Prevention (CDC) reported 1,210,053 specimens were tested for the influenza virus nationally, 224,113 (18.5%) of which tested positive. Currently there are three antiviral therapies recommended by the CDC for the acute treatment of influenza: oseltamivir (Tamiflu<sup>®</sup>), peramivir (Rapivab<sup>®</sup>), and zanamivir (Relenza<sup>®</sup>). Amantadine is also commonly used for the treatment of influenza. Oseltamivir and amantadine require multiple day therapy, but similar to baloxavir marboxil, are available as an oral formulation. Peramivir is administered as a

one-time intravenous (IV) infusion over 15 to 30 minutes, and zanamivir is an inhalation powder administered over five days.

**Projected FDA Decision:** December 24, 2018

**SoonerCare Impact:** During fiscal year 2018, a total of 75,689 members had paid pharmacy claims for CDC-recommended influenza antivirals, accounting for 80,230 claims totaling \$12,323,715.23 in drug spending and an average cost per claim of \$153.60.

## **Brexanolone**<sup>1,9,10,11</sup>

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**Anticipated Indication(s):** IV administered gamma aminobutyric acid-A (GABA-A) receptor modulator for the treatment of postpartum depression (PPD).

**Clinical Trial(s):** Brexanolone was evaluated in two Phase 3 studies: a randomized, placebo-controlled study of 120 severe PPD patients and a randomized, placebo-controlled study of 108 moderate PPD patients. The primary outcome of both studies was the reduction in the physician administered Hamilton Rating Scale for Depression (HAM-D) score before and after brexanolone treatment. A score of  $\geq 26$  indicates severe PPD and a score of 20 to 25 indicates moderate PPD. In the severe PPD study, a one-time IV infusion of brexanolone 90 $\mu$ g/kg/hour administered over 60 hours reduced the average HAM-D score by 17.7 points at hour 60, compared to placebo with an average reduction of 14.0 points from baseline. Brexanolone resulted in statistically significant reductions in the HAM-D scores beginning at 24 hours, and the effects at 60 hours were sustained at 30 days. In the moderate PPD study, a one-time IV infusion of brexanolone 90 $\mu$ g/kg/hour administered over 60 hours reduced the average HAM-D score at hour 60 by 15.0 points from baseline compared with an average reduction of 12.0 points for placebo.

**Place in Therapy:** An estimated 11.5% of new mothers will experience PPD, with a large number of cases going undiagnosed. If approved, brexanolone would be the first FDA approved therapy indicated for the treatment of PPD. Current PPD treatment guidelines recommend oral selective serotonin reuptake inhibitors (SSRIs) as the mainstay of moderate-to-severe PPD treatment; however, these can take several weeks to show efficacy. Brexanolone has shown efficacy as early as 48 hours, but administration requires a 60-hour infusion and a 7-day interruption from breastfeeding. Additionally, efficacy data beyond 30 days post-brexanolone treatment has not been established.

**Projected FDA Decision:** December 19, 2018

**SoonerCare Impact:** During fiscal year 2018, a total of 139 members had at least one submitted diagnosis of postpartum mood disturbance. A total of 37,366 female members 14 to 45 years of age had paid claims for antidepressants during fiscal year 2018, accounting for 180,731 claims totaling \$4,811,946.93 in drug spending and an average cost per claim of \$26.62.

## Pipeline Table<sup>1,2,12</sup>

Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
ulipristal acetate	Allergan	uterine fibroids	PO	Filed NDA	Pending
oliceridine	Trevena	acute pain	IV	Filed NDA	Pending
sufentanil	Acelrx	acute pain	SL	Filed NDA	Pending
salmon calcitonin	Tarsa/Unigene Laboratories	osteoporosis	PO	Filed NDA	4 <sup>th</sup> quarter 2018
primatene HFA	Amphastar	asthma	INH	Filed NDA	Late 2018
Otezla® (apremilast)	Celgene	PSO	PO	Files sNDA	Late 2018
tamsulosin DR	Female Health/Aspen	BPH	PO	Filed NDA	Late 2018
rizatriptan film	IntelGenx/Red Hill	acute migraines	SL	Filed NDA	Late 2018
astodimer	Starpharma	bacterial vaginosis	VG	Filed NDA	Late 2018
revefenacin	Theravance	COPD	INH	Filed NDA	11/13/2018
rifamycin	Cosmo	traveler's diarrhea	PO	Filed NDA	11/16/2018
emapalumab	NovImmune SA	primary hemophagocytic lymphohistiocytosis	IV	Filed BLA	11/20/2018
amifampridine	BioMarin/Catalyst	LEMS	PO	Filed NDA	11/28/2018
bupivacane collagen matrix	Innocoll	postsurgical pain	Implant	Filed NDA	11/30/2018
rituximab biosimilar	Teva/Celltrion	CLL/SLL; RA; NHL	IV	Filed BLA	11/30/2018
siponimod	Novartis	MS	PO	Filed NDA	December 2018
brexanolone	Sage/Ligand	PPD	IV	Filed NDA	12/19/2018
solriamfetol	Jazz Pharmaceuticals	narcolepsy/SA	PO	Filed NDA	12/20/2018
prucalopride	Shire	CIC	PO	Filed NDA	12/21/2018
buprenorphine	Braeburn	opioid dependence	SC	Filed NDA	12/26/2018
Ravicti® (glycerol phenylbutyrate)	Horizon	urea cycle disorder (<2 months of age)	PO	Filed sNDA	12/27/2018
dexamethasone implant	Ocular Therapeutics	ocular pain	IO	Filed NDA	12/28/2018
cladarabine	Merck/Teva	MS	PO	Filed NDA	1 <sup>st</sup> quarter 2019
Envarsus XR® (tacrolimus)	Veloxis	kidney transplant rejection	PO	Filed sNDA	01/07/2019
romosozumab	Amgen	osteoporosis (women)	SC	Filed sBLA	01/11/2019
apomorphine	Sunovion	Parkinson's Disease	SL	Filed NDA	01/29/2019
samidorphan/buprenorphine	Alkermes	MDD	SL	Filed NDA	01/31/2019
iclaprim	Motif Bio	ABSSSI	IV	Filed NDA	02/14/2019
ravulizumab	Alexion	PNH	IV	Filed BLA	02/19/2019
afamelanotide	Clinuvel	erythropoietic protoporphyria	SC	Filed NDA	02/25/2019
loteprednol etabonate 0.38%	Bausch & Lomb	ocular pain	IO	Filed NDA	02/25/2019
turoctocog alfa pegol	Novo Nordisk	hemophilia A	IV	Filed BLA	02/27/2019
Opsumit® (macitentan)	Janssen	chronic thromboembolic pulmonary HTN	PO	Filed sNDA	02/28/2019
netarsudil/latanoprost	Aerie	glaucoma	IO	Filed NDA	3/15/2019



Medication Name*	Manufacturer	Therapeutic Use	Route of Admin	Approval Status	Anticipated FDA Response
fosphenytoin/ sulfobutylether betacyclodextrin	Sedor	seizures	IV	Filed NDA	03/22/2019
olopatadine/ mometasone furoate	Glenmark	allergic rhinitis	IN	Filed NDA	03/22/2019
sotagliflozin	Sanofi	T1DM; T2DM	PO	Filed NDA	03/26/2019
glucagon	Eli Lilly/Locemia	DM	IN	Filed NDA	2 <sup>nd</sup> quarter 2019
Tudorza® Pressair® (aclidinium bromide)	Circassia	CV outcomes	INH	Filed sNDA	04/01/2019
aclidinium/formoterol	Circassia	COPD	INH	Filed NDA	04/01/2019
metoclopramide spray	Evoke	diabetic gastroparesis	IN	Filed NDA	04/01/2019
sumatriptan	Dr. Reddy's	migraine treatment	IN	Filed NDA	04/02/2019
risankizumab	AbbVie	PSO	SC	Filed BLA	04/25/2019
NKTR-181	Nektar	chronic low back pain	PO	Filed NDA	05/31/2019
lumateperone	Intra-Cellular Therapies/Bristol- Myers Squibb	schizophrenia/ bipolar disorder/AD	PO	Filed NDA	Mid-2019

NDA = New Drug Application; BLA = Biologic License Application; sBLA = supplemental Biologic License Application; sNDA = supplemental New Drug Application; Admin = administration; IV = intravenous; PO = oral; SL = sublingual; SC = subcutaneous; IM = intramuscular; IO = intraocular; VG = vaginal; INH = inhaled; IN = intranasal; HFA = hydrofluoroalkane; DR = delayed-release; PSO = psoriasis; BPH = benign prostatic hyperplasia; COPD = chronic obstructive pulmonary disease; LEMS = Lambert-Eaton myasthenic syndrome; CLL = chronic lymphocytic leukemia; SLL = small lymphocytic lymphoma; RA = rheumatoid arthritis; NHL = non-Hodgkin's lymphoma; MS = multiple sclerosis; PPD = postpartum depression; SA = sleep apnea; CIC = chronic idiopathic constipation; MDD = major depressive disorder; ABSSSI = acute bacterial skin and skin structure infection; PNH = paroxysmal nocturnal hemoglobinuria; HTN = hypertension; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus; DM = diabetes mellitus; CV = cardiovascular; AD = Alzheimer's disease

\*Most biosimilars and oncology medications excluded from table. Medications known to have received a Complete Response Letter from the FDA that have not resubmitted were also excluded.

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- <sup>1</sup> OptumRx. RxOutlook® 3<sup>rd</sup> Quarter 2018. Available online at: <https://professionals.optumrx.com/publications/library/rxoutlook-q3-2018.html>. Issued 08/15/2018. Last accessed 10/19/2018.
- <sup>2</sup> MagellanRx Management. MRx Pipeline. Available online at: [https://www1.magellanrx.com/media/773130/mrx-pipeline\\_july-2018.pdf](https://www1.magellanrx.com/media/773130/mrx-pipeline_july-2018.pdf). Issued 07/2018. Last accessed 10/19/2018.
- <sup>3</sup> Roche. FDA grants Priority Review to Roche's baloxavir marboxil for the treatment of influenza. Available online at: <https://www.roche.com/investors/updates/inv-update-2018-06-26.htm>. Issued 06/26/2018. Last accessed 10/19/2018.
- <sup>4</sup> Centers for Disease Control and Prevention (CDC). Update: Influenza Activity in the United States During the 2017–18 Season and Composition of the 2018–19 Influenza Vaccine. *Morbidity and Mortality Weekly Report (MMWR)*. Available online at: [https://www.cdc.gov/mmwr/volumes/67/wr/mm6722a4.htm?s\\_cid=mm6722a4\\_w](https://www.cdc.gov/mmwr/volumes/67/wr/mm6722a4.htm?s_cid=mm6722a4_w). Issued 06/08/2018. Last accessed 10/19/2018.
- <sup>5</sup> Tamiflu® Prescribing Information. Genentech. Available online at: [https://www.gene.com/download/pdf/tamiflu\\_prescribing.pdf](https://www.gene.com/download/pdf/tamiflu_prescribing.pdf). Last revised 04/2018. Last accessed 10/19/2018.
- <sup>6</sup> Rapivab® Prescribing Information. BioCryst Pharmaceuticals, Inc. Available online at: <http://labeling.seqirus.com/PI/US/Rapivab/EN/Rapivab-Prescribing-Information.pdf>. Last revised 04/2018. Last accessed 10/19/2018.
- <sup>7</sup> Relenza® Prescribing Information. GlaxoSmithKline. Available online at: [https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing\\_Information/Relenza/pdf/RELENZA-PI.PDF](https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Relenza/pdf/RELENZA-PI.PDF). Last revised 06/2018. Last accessed 10/19/2018.
- <sup>8</sup> Amantadine Prescribing Information. Alembic Pharmaceuticals, Inc. Available online at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4157d9a7-a53f-4dde-b051-fe3e9a674913>. Last revised 08/02/2018. Last accessed 10/19/2018.
- <sup>9</sup> Caffrey M. Results on Brexanolone IV for Postpartum Depression Shared at ACOG. *American Journal of Managed Care*. Available online at: <https://www.ajmc.com/conferences/acog-2018/results-on-brexanolone-iv-for-postpartum-depression-shared-at-acog>. Issued 04/28/2018. Last accessed 11/01/2018.
- <sup>10</sup> Sage Therapeutics. Sage Therapeutics Submits New Drug Application to U.S. FDA for Intravenous Brexanolone in the Treatment of Postpartum Depression. *Business Wire*. Available online at: <http://investor.sagerx.com/news-releases/news-release-details/sage-therapeutics-submits-new-drug-application-us-fda>. Issued 04/23/2018. Last accessed 11/01/2018.
- <sup>11</sup> Hirst KP, Moutier CY. Postpartum Major Depression. *Am Fam Physician*. 2010; 82(8):926-933.
- <sup>12</sup> OptumRx. RxOutlook® brand pipeline forecast. Available online at: [https://cdn-aem.optum.com/content/dam/optum3/professional-optumrx/news/outlook/2018q3\\_rxbrandpipelineforecast.pdf](https://cdn-aem.optum.com/content/dam/optum3/professional-optumrx/news/outlook/2018q3_rxbrandpipelineforecast.pdf). Issued 08/15/2018. Last accessed 11/01/2018.



# Appendix C





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# Vote to Prior Authorize Ilumya™ (Tildrakizumab-asmn) and Olumiant® (Baricitinib)

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Oklahoma Health Care Authority  
November 2018

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## Introduction<sup>1,2,3,4,5,6</sup>

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- **Ilumya™ (tildrakizumab-asmn):** In March 2018, the U.S. Food and Drug Administration (FDA) approved tildrakizumab-asmn, an interleukin (IL)-23 antagonist, for the treatment of adults with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic or phototherapy. Ilumya™ is supplied as 100mg/mL single-dose, pre-filled syringes. The recommended dose of tildrakizumab is 100mg via subcutaneous (sub-Q) injection at weeks 0, 4, and every 12 weeks thereafter. Tildrakizumab should only be administered by a health care provider.
- **Olumiant® (baricitinib):** In June 2018, the FDA approved baricitinib, a Janus kinase (JAK) inhibitor, for the treatment of adult patients with moderately-to-severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. Use of baricitinib in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended. Olumiant® is supplied as 2mg oral tablets. The recommended dose of baricitinib is 2mg by mouth once daily. Baricitinib initiation is not recommended in patients with an absolute lymphocyte count (ALC) <500cells/mm<sup>3</sup>, absolute neutrophil count (ANC) <1,000cells/mm<sup>3</sup>, or hemoglobin (Hgb) level <8g/dL. Baricitinib has a boxed warning for risk of serious infections, malignancy, and thrombosis.
- **Rituxan® (rituximab):** In June 2018, the FDA approved rituximab for the treatment of adults with moderate-to-severe pemphigus vulgaris (PV), an autoimmune blistering disease that affects the skin and mucous membranes. Rituximab was previously approved for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, RA, granulomatosis with polyangiitis (GPA), and microscopic polyangiitis.

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## Recommendations

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The College of Pharmacy recommends the addition of Ilumya™ (tildrakizumab-asmn) and Olumiant® (baricitinib) to Tier-3 of the Targeted Immunomodulator Agents Product Based Prior Authorization (PBPA) category. Current Tier-3 approval criteria for this category will apply. Additionally, the College of Pharmacy recommends the following criteria for Rituxan® (rituximab) for the treatment of adults with moderate-to-severe pemphigus vulgaris (PV):

### **Rituxan® (Rituximab) Approval Criteria [Pemphigus Vulgaris (PV) Diagnosis]:**

1. An FDA approved diagnosis of moderate-to-severe PV; and
2. Rituxan® must be used in combination with a tapering course of glucocorticoids; and
3. Initial approvals will be for two 1,000mg intravenous (IV) infusions separated by 2 weeks and a 500mg infusion at month 12. Subsequent approvals may be authorized based on

6-month evaluations or upon relapse. Subsequent infusions may be no sooner than 16 weeks after the previous infusion.

Targeted Immunomodulator Agents*±		
Tier-1 (DMARDs appropriate to disease state)	Tier-2*	Tier-3
6-mercaptopurine	adalimumab (Humira®) <sup>+</sup>	abatacept (Orencia®) <sup>Δ</sup>
azathioprine	etanercept (Enbrel®)	adalimumab-adbm (Cyltezo™)
hydroxychloroquine		adalimumab-atto (Amjevita™)
leflunomide		alefacept (Amevive®)
mesalamine		anakinra (Kineret®)
methotrexate		apremilast (Otezla®)
minocycline		<b>baricitinib (Olumiant®)</b>
NSAIDs		brodalumab (Siliq™)
oral corticosteroids		canakinumab (Ilaris®) <sup>¥</sup>
		certolizumab pegol (Cimzia®)
		etanercept-szsz (Erelzi™)
		golimumab (Simponi® & Simponi® Aria™)
		guselkumab (Tremfya™)
		infliximab (Remicade®)
		infliximab-abda (Renflexis™)
		infliximab-dyyb (Inflectra™)
		ixekizumab (Taltz®)
		rituximab (Rituxan®) <sup>~</sup>
		sarilumab (Kevzara®)
		secukinumab (Cosentyx®) <sup>Ω</sup>
		<b>tildrakizumab-asmn (Ilumya™)</b>
		tocilizumab (Actemra®) <sup>π</sup>
		tofacitinib (Xeljanz® & Xeljanz® XR) <sup>Δ</sup>
		ustekinumab (Stelara®)
		vedolizumab (Entyvio™)

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

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

<sup>±</sup>Biosimilars or reference products preferred based on lowest net cost product. Authorization of higher net cost biosimilars or reference products requires a patient-specific, clinically significant reason why the member could not use the preferred formulation.

<sup>+</sup>Unique criteria applies for a diagnosis of hidradenitis suppurativa (HS) or noninfectious intermediate and posterior uveitis and panuveitis.

<sup>Δ</sup>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® or the prefilled syringe formulation of Orencia® authorization would also require a patient-specific, clinically significant reason why the member could not use the immediate-release formulation of Xeljanz® or the prefilled syringe formulation of Orencia®.

<sup>¥</sup>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).

<sup>~</sup>Unique criteria applies for a diagnosis of pemphigus vulgaris (PV).

<sup>Ω</sup>For Cosentyx™ (secukinumab), only a trial of Humira® from the available Tier-2 medications will be required (based on supplemental rebate participation).

<sup>π</sup>Unique criteria applies for a diagnosis of giant cell arteritis (GCA) or chimeric antigen receptor T (CAR T) cell-induced cytokine release syndrome (CRS).

### **Targeted Immunomodulator 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.

### **Targeted Immunomodulator 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.

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<sup>1</sup> Sun Pharmaceutical Industries, Ltd. Sun Pharma Announces U.S. FDA Approval of Ilumya™ (tildrakizumab-asmn) for the Treatment of Moderate-to-Severe Plaque Psoriasis. *PR Newswire*. Available online at: <https://www.prnewswire.com/news-releases/sun-pharma-announces-us-fda-approval-of-ilumya-tildrakizumab-asmn-for-the-treatment-of-moderate-to-severe-plaque-psoriasis-300617454.html>. Issued 03/21/2018. Last accessed 10/18/2018.

<sup>2</sup> Ilumya™ Prescribing Information. Sun Pharmaceutical Industries, Ltd. Available online at: <https://www.sunpharma.com/sites/default/files/pressreleases/ILUMYA%20US%20Prescribing%20Information.pdf>. Last revised 03/2018. Last accessed 10/18/2018.

<sup>3</sup> Eli Lilly and Company. FDA Approves Olumiant® (baricitinib) 2-mg Tablets for the Treatment of Adults with Moderately-to-Severely Active Rheumatoid Arthritis. *PR Newswire*. Available online at: <https://www.prnewswire.com/news-releases/fda-approves-olumiant-baricitinib-2-mg-tablets-for-the-treatment-of-adults-with-moderately-to-severely-active-rheumatoid-arthritis-300658215.html>. Issued 06/01/2018. Last accessed 10/18/2018.

<sup>4</sup> Olumiant® Prescribing Information. Eli Lilly and Company. Available online at: <http://uspl.lilly.com/olumiant/olumiant.html#pi>. Last revised 05/2018. Last accessed 10/18/2018.

<sup>5</sup> Ernst D. Rituxan Approved for Moderate to Severe Pemphigus Vulgaris. *Monthly Prescribing Reference (MPR)*. Available online at: <https://www.empr.com/news/pemphigus-vulgaris-rituxan-rituximab-approved-autoimmune-blistering-disease/article/772092/>. Issued 06/08/2018. Last accessed 10/18/2018.

<sup>6</sup> Rituxan® Prescribing Information. Genentech, Inc. Available online at: [https://www.gene.com/download/pdf/rituxan\\_prescribing.pdf](https://www.gene.com/download/pdf/rituxan_prescribing.pdf). Last revised 06/2018. Last accessed 10/18/2018.







# Appendix D





# Vote to Prior Authorize Triptodur® (Triptorelin) and Orilissa™ (Elagolix)

Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2,3,4,5,6,7,8</sup>

**Triptodur® (triptorelin)** is a gonadotropin-releasing hormone (GnRH) agonist indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). Triptodur® is supplied as single-use kits containing one single-dose vial of triptorelin 22.5mg, one prefilled glass syringe of sterile water for injection, and two needles. It is recommended to administer triptorelin as a single 22.5mg intramuscular (IM) injection once every 24 weeks. It is the first GnRH agonist approved for dosing once every 6 months for CPP.

### Cost Comparison:

Product	Cost Per Unit	Cost Per Year
<b>Triptodur® (triptorelin) 22.5mg</b>	<b>\$16,400.00</b>	<b>\$32,800.00</b>
Lupron Depot-Ped® (leuprolide) 15mg	\$2,945.42*	\$35,345.04*
Supprelin® LA (histrelin) 50mg	\$30,441.90	\$30,441.90

Costs do not reflect rebated prices or net costs. Costs based on National Average Drug Acquisition Costs (NADAC), Wholesale Acquisition Costs (WAC), Specialty Pharmaceutical Allowable Cost (SPAC), or State Maximum Allowable Cost (SMAC) if NADAC unavailable.

Unit = vial or kit

\*Lupron Depot-Ped® was first approved by the U.S. Food and Drug Administration (FDA) in 1993 and has a significant federal rebate.

**Orilissa™ (elagolix)** is a GnRH receptor antagonist indicated for the management of moderate-to-severe pain associated with endometriosis. Elagolix is the first oral GnRH antagonist specifically developed for women with moderate-to-severe endometriosis pain. Orilissa™ is supplied as 150mg and 200mg oral tablets. The recommended dose for patients with normal liver function or mild hepatic impairment is 150mg once daily for up to 24 months or 200mg twice daily for up to 6 months. The recommended dose for patients with moderate hepatic impairment is 150mg once daily for up to 6 months.

### Cost Comparison:

Product	Cost Per Unit	Cost Per Month	Cost Per 6 Months
<b>Orilissa™ (elagolix) 150mg</b>	<b>\$30.17</b>	<b>\$844.76</b>	<b>\$5,068.56</b>
<b>Orilissa™ (elagolix) 200mg</b>	<b>\$15.09</b>	<b>\$845.04</b>	<b>\$5,070.24</b>
Lupron Depot® (leuprolide) 3.75mg	\$1,191.39*	\$1,191.39*	\$7,148.34*
Synarel® (nafarelin) 2mg/mL	\$354.57	\$2,836.56	\$17,019.36

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

Unit = tablet, kit, or mL

\*Lupron Depot® was first FDA approved in 1989 and has a significant federal rebate.

## Recommendations

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The College of Pharmacy recommends the prior authorization of Orilissa™ (elagolix) with the following criteria:

### **Orilissa™ (Elagolix) Approval Criteria:**

1. An FDA approved diagnosis of moderate-to-severe pain associated with endometriosis; and
2. Member must be 18 years of age or older; and
3. Member must not have known osteoporosis; and
4. Female members must not be pregnant and must have a negative pregnancy test prior to initiation of therapy; and
5. Female members of reproductive potential must be willing to use effective non-hormonal contraception during treatment with Orilissa™ and for at least one week after discontinuing treatment; and
6. Member must not have severe hepatic impairment (Child-Pugh C); and
7. Member must not be taking a strong organic anion transporting polypeptide (OATP) 1B1 inhibitor (e.g., cyclosporine, gemfibrozil); and
8. Orilissa™ must be prescribed by, or in consultation with, an obstetrician/gynecologist or a specialist with expertise in the treatment of endometriosis; and
9. A failed trial at least one month in duration with nonsteroidal anti-inflammatory drugs (NSAIDs) or a patient-specific, clinically significant reason why the member cannot use NSAIDs; and
10. A failed trial at least three months in duration of hormonal contraceptives or a patient-specific, clinically significant reason why the member cannot use hormonal contraceptives; and
11. A patient-specific, clinically significant reason why the member cannot use leuprolide depot formulations which are available without prior authorization; and
12. Dosing and lifetime approval duration will be limited based on the following:
  - a. Coexisting condition of moderate hepatic impairment (Child-Pugh B):
    - i. 150mg once daily for a maximum of 6 months; and
  - b. Normal liver function or mild hepatic impairment (Child-Pugh A):
    - i. 150mg once daily for a maximum of 24 months; or
    - ii. 200mg twice daily for a maximum of 6 months.

Additionally, the College of Pharmacy recommends the placement of Triptodur® (triptorelin) into Tier-3 of the Gonadotropin-Releasing Hormone (GnRH) Medications Product Based Prior Authorization (PBPA) category as shown in red:

### **Supprelin® LA (Histrelin), Synarel® (Nafarelin), and Triptodur® (Triptorelin) Approval Criteria:**

1. An FDA approved diagnosis of central precocious puberty confirmed by submitting the following:
  - a. Documentation of onset of symptoms <8 years of age in females and 9 years of age in males; and

- b. Documentation that bone age is advanced 1 year beyond the chronological age; and
  - c. Lab assessment:
    - i. Documentation of abnormal basal gonadotropin levels; or
    - ii. Documentation of pubertal response to a gonadotropin-releasing hormone analog stimulation test; and
2. Approvals may be granted with documentation of failed trials of lower tiered products or an FDA approved indication not covered by a lower tiered product.

<b>Gonadotropin-Releasing Hormone (GnRH) Medications</b>		
<b>Tier-1</b>	<b>Tier-2</b>	<b>Tier-3</b>
leuprolide (Lupron® Depot)	histrelin (Supprelin® LA)	nafarelin (Synarel®)
leuprolide (Lupron Depot-Ped®)		<b>triptorelin (Triptodur®)</b>

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

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<sup>1</sup> Triptodur® (triptorelin) Prescribing Information. Arbor Pharmaceuticals, LLC. Available online at: <http://triptodur.com/hcp/Triptodur%20PI%20Rev.%2009.2017.pdf>. Last revised 09/2017. Last accessed 10/15/2018.

<sup>2</sup> Triptorelin (Triptodur) for Central Precocious Puberty. *The Medical Letter* 2018; 60:7-8.

<sup>3</sup> Lupron Depot-Ped® Prescribing Information. AbbVie, Inc. Available online at: <https://www.rxabbvie.com/pdf/lupronpediatric.pdf>. Last revised 05/2017. Last accessed 10/15/2018.

<sup>4</sup> Han DH. FDA Approved Triptodur for Central Precocious Puberty. *Monthly Prescribing Reference (MPR)*. Available online at: <https://www.empr.com/news/triptodur-triptorelin-pediatric-precocious-puberty/article/672526/>. Issued 06/30/2017. Last accessed 10/15/2018.

<sup>5</sup> Orilissa™ (elagolix) Prescribing Information. AbbVie, Inc. Available online at: [https://www.rxabbvie.com/pdf/orilissa\\_pi.pdf](https://www.rxabbvie.com/pdf/orilissa_pi.pdf). Last revised 07/2018. Last accessed 10/15/2018.

<sup>6</sup> Elagolix (Orilissa) – An Oral GnRH Antagonist for Endometriosis Pain. *The Medical Letter* 2018; 60:158-160.

<sup>7</sup> AbbVie, Inc. AbbVie Receives U.S. FDA Approval of Orilissa™ (elagolix) for the Management of Moderate to Severe Pain Associated with Endometriosis. *PR Newswire*. Available online at: <https://news.abbvie.com/news/abbvie-receives-us-fda-approval-orilissa-elagolix-for-management-moderate-to-severe-pain-associated-with-endometriosis.htm>. Issued 07/24/2018. Last accessed 10/15/2018.

<sup>8</sup> Lupron Depot® Prescribing Information. AbbVie, Inc. Available online at: [https://www.rxabbvie.com/pdf/lupronuro\\_pi.pdf](https://www.rxabbvie.com/pdf/lupronuro_pi.pdf). Last revised 06/2016. Last accessed 10/15/2018.





# Appendix E





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# Vote to Prior Authorize Yescarta® (Axicabtagene) and to Update the Acute Lymphoblastic Leukemia (ALL) and Chronic Myeloid Leukemia (CML) Medications Approval Criteria

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Oklahoma Health Care Authority  
November 2018

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## Introduction<sup>1</sup>

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- **Yescarta® (axicabtagene):** In October 2017, the U.S. Food and Drug Administration (FDA) granted regular approval to axicabtagene for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL). Although axicabtagene is not an acute lymphoblastic leukemia (ALL) or chronic myeloid leukemia (CML) therapy, it will be reviewed with this class to allow for both chimeric antigen receptor (CAR) T-cell therapies to be reviewed together [i.e., Kymriah® (tisagenlecleucel), Yescarta® (axicabtagene)].
- **Bosulif® (bosutinib):** In December 2017, the FDA granted accelerated approval to bosutinib for the treatment of patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome positive (Ph+) CML. Bosutinib was previously approved for the treatment of chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy.
- **Kymriah® (tisagenlecleucel):** In May 2018, the FDA approved tisagenlecleucel, a CD19-directed genetically modified autologous T-cell immunotherapy, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including DLBCL not otherwise specified, high grade B-cell lymphoma, and DLBCL arising from FL. Tisagenlecleucel was previously approved for the treatment of B-cell precursor ALL that is refractory or in second or later relapse.

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## Recommendations

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- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations. Changes can be seen in the following criteria listed in red (only criteria with updates listed).
- The prior authorization of Yescarta® (axicabtagene) with the following criteria listed in red:

### Yescarta® (Axicabtagene) Approval Criteria [Lymphoma Diagnosis]:

1. Large B-cell lymphoma [including diffuse large B cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Member must be 18 years of age or older; and

3. Relapsed or refractory disease; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had two or more lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

**Bosulif® (Bosutinib) Approval Criteria [Chronic Myeloid Leukemia (CML) Diagnosis]:**

1. Members with chronic, accelerated, or blast phase CML; ~~and with resistance or intolerance after primary treatment with either: dasatinib, imatinib, or nilotinib with the following BCR-ABL1 transcript levels:~~
  - a. ~~0.01% to 1% at >12 months; or~~
  - b. ~~>1% to 10% at ≥12 months; or~~
  - c. ~~>10% at any milestone.~~
2. Newly diagnosed or resistant/intolerant to other tyrosine kinase inhibitors (TKIs).

**Kymriah® (Tisagenlecleucel) Approval Criteria [Lymphoma Diagnosis]:**

1. Large B-cell lymphoma [including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)]; and
2. Relapsed or refractory disease; and
3. Member must be 18 years of age or older; and
4. Member must not have primary central nervous system lymphoma; and
5. Member must have had two or more lines of therapy; and
6. Health care facilities must be on the certified list to administer chimeric antigen receptor (CAR) T-cells and must be trained in the management of cytokine release syndrome (CRS), neurologic toxicities, and comply with the REMS requirements.

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<sup>1</sup> U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm>. Last revised 10/16/2018. Last accessed 10/18/2018.



# Appendix F





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# Vote to Prior Authorize Braftovi™ (Encorafenib), Mektovi® (Binimetinib), and Libtayo® (Cemiplimab-rwlc)

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Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2,3,4,5</sup>

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- **Braftovi™ (encorafenib) and Mektovi® (binimetinib):** In June 2018, the U.S. Food and Drug Administration (FDA) approved encorafenib and binimetinib for use in combination in patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation.
- **Libtayo® (cemiplimab-rwlc):** In September 2018, the FDA approved cemiplimab-rwlc for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.
- **Zelboraf® (vemurafenib):** In November 2017, the FDA granted regular approval to vemurafenib for the treatment of patients with Erdheim-Chester Disease (ECD) with a BRAF V600 mutation. Vemurafenib was previously approved for the treatment of patients with hairy-cell leukemia, non-small cell lung cancer (NSCLC), and melanoma.
- **Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib):** In May 2018, the FDA approved dabrafenib in combination with trametinib for the treatment of anaplastic thyroid cancer (ATC) with a BRAF V600E mutation.
- **Yervoy® (ipilimumab) in combination with Opdivo® (nivolumab):** In July 2018, the FDA granted accelerated approval to ipilimumab for use in combination with nivolumab for the treatment of patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

## Recommendations

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- Update the prior authorization criteria to reflect new FDA approved indications and guideline recommendations. Changes can be seen in the following criteria listed in red (only criteria with updates listed).
- The prior authorization of Braftovi™ (encorafenib), Mektovi® (binimetinib), and Libtayo® (cemiplimab-rwlc) with the following criteria listed in red:

### **Braftovi™ (Encorafenib) Approval Criteria [Melanoma Diagnosis]:**

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and
3. Used in combination with binimetinib.

### **Mektovi® (Binimetinib) Approval Criteria [Melanoma Diagnosis]:**

1. Diagnosis of unresectable or metastatic melanoma; and
2. BRAF V600E or V600K mutation; and

3. Used in combination with encorafenib.

**Libtayo® (Cemiplimab-rwlc) Approval Criteria [Cutaneous Squamous Cell Carcinoma (CSCC) Diagnosis]:**

1. Diagnosis of metastatic or locally advanced CSCC; and
2. Member is not eligible for curative surgery or radiation; and
3. Member has not received prior immunotherapy agent(s) [e.g., Keytruda® (pembrolizumab), Opdivo® (nivolumab), Yervoy® (ipilimumab)].

**Opdivo® (Nivolumab) Approval Criteria [Metastatic Colorectal Cancer (mCRC) Diagnosis]:**

1. Diagnosis of mCRC; and
2. Disease has progressed on treatment with 5-FU, oxaliplatin, and irinotecan; and
3. Tumor possesses high microsatellite-instability or mismatch repair deficiency; and
4. Used as a single-agent or in combination with ipilimumab.

**Yervoy® (Ipilimumab) Approval Criteria [Metastatic Colorectal Cancer (mCRC) Diagnosis]:**

1. Diagnosis of mCRC; and
2. Disease has progressed on treatment with 5-FU, oxaliplatin, and irinotecan; and
3. Tumor possesses microsatellite instability-high or mismatch repair deficiency; and
4. Used in combination with nivolumab.

**Mekinist® (Trametinib) Approval Criteria [Anaplastic Thyroid Cancer (ATC) Diagnosis]:**

1. Diagnosis of ATC; and
2. Locally advanced or metastatic disease; and
3. BRAF V600E mutation; and
4. No satisfactory locoregional treatment options.

**Tafinlar® (Dabrafenib) Approval Criteria [Anaplastic Thyroid Cancer (ATC) Diagnosis]:**

1. Diagnosis of ATC; and
2. Locally advanced or metastatic disease; and
3. BRAF V600E mutation; and
4. No satisfactory locoregional treatment options.

**Zelboraf® (Vemurafenib) Approval Criteria [Erdheim-Chester Disease (ECD) Diagnosis]:**

1. Diagnosis of ECD; and
2. BRAF V600E or V600K mutation; and
3. Vemurafenib must be used as a single-agent.

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<sup>1</sup> U.S. Food and Drug Administration (FDA). Hematology/Oncology (Cancer) Approvals & Safety Notifications. Available online at: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm>. Last revised 10/16/2018. Last accessed 10/19/2018.

<sup>2</sup> Regeneron Pharmaceuticals, Inc. FDA Approves Libtayo<sup>®</sup> (cemiplimab-rwlc) as First and Only Treatment for Advanced Cutaneous Squamous Cell Carcinoma. Available online at: <https://newsroom.regeneron.com/news-releases/news-release-details/fda-approves-libtaylor-cemiplimab-rwlc-first-and-only-treatment>. Issued 09/28/2018. Last accessed 10/19/2018.

<sup>3</sup> Braftovi<sup>™</sup> Prescribing Information. Array Biopharma. Available online at: [http://www.arraybiopharma.com/documents/Braftovi\\_Prescribing\\_information.pdf](http://www.arraybiopharma.com/documents/Braftovi_Prescribing_information.pdf). Last revised 06/2018. Last accessed 10/19/2018.

<sup>4</sup> Mektovi<sup>®</sup> Prescribing Information. Array Biopharma. Available online at: [http://www.arraybiopharma.com/documents/Mektovi\\_Prescribing\\_information.pdf](http://www.arraybiopharma.com/documents/Mektovi_Prescribing_information.pdf). Last revised 06/2018. Last accessed 10/19/2018.

<sup>5</sup> Libtayo<sup>®</sup> (cemiplimab-rwlc) Prescribing Information. Regeneron Pharmaceuticals, Inc. Available online at: [https://www.regeneron.com/sites/default/files/Libtayo\\_FPI.pdf](https://www.regeneron.com/sites/default/files/Libtayo_FPI.pdf). Last revised 09/2018. Last accessed 10/19/2018.







# Appendix G





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# **Fiscal Year 2018 Annual Review of Factor Replacement Products and 30-Day Notice to Prior Authorize Hemlibra<sup>®</sup> (Emicizumab-kxwh), Feiba<sup>®</sup> (Anti-Inhibitor Coagulant Complex), Novoseven<sup>®</sup> RT [Coagulation Factor VIIa (Recombinant)], and Jivi<sup>®</sup> [Antihemophilic Factor (Recombinant), PEGylated-aucl]**

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**Oklahoma Health Care Authority  
November 2018**

## **Current Prior Authorization Criteria**

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### **Eloctate<sup>®</sup>, Adynovate<sup>®</sup>, Afstyla<sup>®</sup>, Alprolix<sup>®</sup>, Idelvion<sup>®</sup>, and Rebinyn<sup>®</sup> Approval Criteria:**

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
  - a. Hemophilia A: Advate<sup>®</sup> or current factor VIII replacement product; or
  - b. Hemophilia B: Benefix<sup>®</sup> or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of one year.

### **Obizur<sup>®</sup> [Antihemophilic Factor (Recombinant), Porcine Sequence] Approval Criteria:**

1. An FDA approved indication; and
2. Obizur<sup>®</sup> must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A patient-specific, clinically significant reason why the member cannot use Feiba<sup>®</sup> (anti-inhibitor coagulant complex) or NovoSeven<sup>®</sup> RT [coagulation factor VIIa (recombinant)]; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approval will be for the duration of the half-life study. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

### **Corifact<sup>®</sup> [Factor XIII Concentrate (Human)] and Tretten<sup>®</sup> [Coagulation Factor XIII A-Subunit (Recombinant)] Approval Criteria:**

1. An FDA approved indication; and

2. Corifact® or Tretten® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

**Coagadex® [Coagulation Factor X (Human)] Approval Criteria:**

1. An FDA approved indication; and
2. Coagadex® must be prescribed by a hematologist specializing in rare bleeding disorders, or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. A half-life study must be performed to determine the appropriate dose and dosing interval; and
4. Initial approval will be for the duration of the half-life study and immediate needs. After a half-life study is performed and appropriate dose and interval is determined, subsequent approvals will be for the duration of one year.

**Standards of Care for Pharmacies Providing Factor Replacement Products:**

1. The Provider/Pharmacy must be licensed as a pharmacy by the Oklahoma State Board of Pharmacy. The Pharmacist-in-Charge must be licensed as a pharmacist in Oklahoma.
2. The Provider/Pharmacy agrees that it will provide the following services:
  - a. The provider/pharmacy shall be capable to provide a full range of factor products including all available vial sizes.
  - b. The provider/pharmacy must have 24 hours per day, 7 days per week “24/7” support in the event of an after-hours emergency.
  - c. The provider/pharmacy shall deliver within 24 hours (with a delivery goal of 4 hours) of notification of a need due to current bleeding episode. If the patient is not having an emergency/current bleeding episode the provider/pharmacy must deliver factor within 3 days of notification of need.
  - d. The provider/pharmacy shall provide all necessary supplies for appropriate preparation and administration of the factor product as well as appropriate sharps and bio-hazardous disposal unit which includes retrieval and destruction of disposal unit. If the items are SoonerCare compensable, they must be billed as durable medical equipment (DME) via a DME contract.
  - e. The provider/pharmacy must provide access to multilingual interpreters for those patients and families where English is not the primary language. The interpreters must be available “24/7”, in order to assure availability in the event of an after-hours emergency.
  - f. Case Management:
    - i. Case Management can be performed by a pharmacist, nurse, social worker, or case manager.
    - ii. An in-home patient assessment must be performed upon initiation of services and at least yearly thereafter:

1. In-home assessments will include but not be limited to the following:
    - a. Verification of appropriate and adequate storage
    - b. A current inventory of factor product and supplies
    - c. Verification of access to a bio-hazardous waste disposal unit
    - d. A review of current treatment records/logs
    - e. An assessment of educational opportunities to be performed by appropriately trained staff (please refer to 3, b, ii below)
    - f. Identification of adverse events
  2. In the event a patient or caregiver refuses entry to the home, the pharmacy must re-attempt the in-home assessment within three months. If the patient or caregiver continues to deny access, the pharmacy must discuss this issue with the prescribing provider and develop an action plan to verify items set forth in subparagraph 2, f, ii, 1 above. Documentation must be kept of any refusal, re-attempt, and action plan.
  - iii. Regular follow up with the patient either via telephone, video call, or in-person. This contact should be quarterly and should include but not be limited to the following:
    1. All recent bleed episodes reported should be forwarded to the prescribing practitioner immediately.
    2. Current inventory
      - a. Number of factor doses on hand
      - b. Expiration dates of vials on hand
    3. Confirmation of factor storage
    4. Adverse events
      - a. If adverse events are reported to a non-clinical case manager, a clinician should become involved immediately.
  - iv. Coordination of care including nursing, DME, treating practitioner, and all medications, regardless of source.
3. Educational requirements:
- a. Staff Education:
    - i. Staff having contact with the patient via telephone, video calling, or in-person, must be knowledgeable about hemophilia and other bleeding disorders.
    - ii. Two hours of Continuing Education (CE) on hemophilia or other related bleeding disorders must be completed each year. Licensed staff must use accredited CE based on their license type. Non-licensed staff may use non-accredited CE performed by a licensed professional.
      1. Staff members, whether employed or contracted by the pharmacy, required to complete CE include but are not limited to the following:
        - a. Pharmacist in Charge
        - b. Nurse Manager
        - c. Nurse Performing Direct Patient Care
        - d. Social Worker
        - e. Case Manager (including customer service representatives)

2. Documentation of educational activity completed must be kept at the pharmacy and must include the CE certificate or date of activity, staff in attendance, and name and license of professional providing activity.
- b. Member and Caregiver Education:
- i. Pharmacy staff must encourage engagement with the Oklahoma Comprehensive Hemophilia Treatment Center. Studies have shown better clinical outcomes for those patients engaged with a comprehensive hemophilia treatment center.
  - ii. Pharmacy staff must discuss educational needs of the patient with the treating practitioner. Once educational opportunities are identified, the pharmacy staff must provide training for the patients and family members in accordance with the treating physician or mid-level practitioner. All patient efforts must be documented. Areas of education may include but are not limited to the following:
    1. Proper storage for factor products and ancillary supplies
    2. Proper disposal of bio-hazardous waste
    3. Preparation of factor and supplies
    4. Training on self-infusion:
      - a. Prescriber to provide order.
        - i. Professional licensed nurse (LPN or RN) to train patients or caregivers for peripheral venous access.
        - ii. Licensed RN to train patients or caregivers on central line care (e.g., PICC line, InfusaPort, etc.) which includes but is not limited to access, flushing, infusions, and dressing changes.
      - b. Training must be in accordance with the Medical and Scientific Advisory Council (MASAC) guidelines.
    5. Treatment record keeping
    6. Factor and supply management
4. Factor Product Dispensing and Delivery:
- a. Prescriptions cannot be filled without an expressed need from the patient, caregiver, or prescribing practitioner. Auto-filling is not allowed.
  - b. Factor products must be packaged in such a way that a patient or caregiver can easily determine what is to be used for each dose.
    - i. If the factor dose to be infused only consists of one vial/box then the vial/box should be labeled as such.
    - ii. If the factor dose to be infused consists of two or more vials/boxes then each dose should be packaged as a group of appropriate vials/boxes and labeled as an individual dose.
  - c. Factor dose must be within 5% of the prescribed dose.
    - i. If unable to provide factor dosing within 5% of prescribed dose, then pharmacy must provide proof of all available vial sizes from the manufacturer at the time dispensing occurred.
    - ii. Any dose requiring more than 3 vials/boxes to be used must be approved by the prescribing practitioner and documented.

- iii. Pharmacy staff must, by the 10th of every month, fax or email to the Oklahoma Health Care Authority (OHCA) a record of dispensing for the previous month, to include but not limited to the member's name, SoonerCare ID, date dispensed, prescriber name, product, prescribed dose, units per vial dispensed, quantity of each vial size, how the doses were packaged if more than one vial was to be used per dose, type of treatment (prophylaxis, episodic, or breakthrough), and delivery confirmation with member or caregivers' signature.
    - d. Any factor product which is short-dated (expiring within six months) may only be dispensed after approval from the prescribing practitioner and must be documented.
    - e. The pharmacy staff must assure appropriate storage of the factor products and supplies including cold chain supply shipping and delivery. The pharmacy must be able to trace the supply chain from manufacturer to patient delivery.
    - f. The pharmacy must keep records of all lots of factor products dispensed to each patient and notify patient and treating practitioner of any recalls of dispensed factor products. The pharmacy must participate in the National Patient Notification System for clotting factor recalls.
    - g. The pharmacy provider must have a plan in place for delivery of factor products to the patient in the event of a natural disaster.
  5. The Provider/Pharmacy must originally attest to the OHCA these standards of care will be followed and must re-attest yearly.
  6. The OHCA Auditing:
    - a. The OHCA has the right to audit records of the blood clotting factor providers to assure all requirements are being met. The OHCA will audit these records which include but is not limited to the following:
      - i. In-home assessment records
      - ii. Educational information and training provided
      - iii. Adverse event records including reports to other state and federal agencies
      - iv. Sharps and bio-hazardous waste disposal units delivery proof and education on proper disposal in patient record
      - v. Patient records
        1. Original prescriptions
        2. Dispensing records (including lot numbers and expiration dates)
    - b. The pharmacy will be excluded from providing blood factor products if the OHCA finds that the pharmacy is out of compliance with the requirements as outlined.

## Utilization of Factor Replacement Products: Fiscal Year 2018

### Factor Replacement Product Fiscal Year Comparison: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units	Cost Per Utilizer Per Year
2017	74	667	\$14,680,721.41	\$22,010.08	\$1,125.13	\$10,512,402
2018	85	697	\$18,748,696.44	\$26,899.13	\$1,381.32	\$12,131,607
% Change	14.90%	4.50%	27.70%	22.20%	22.80%	15.40%
Change	11	30	\$4,067,975.03	\$4,889.05	\$256.19	\$1,619,205

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

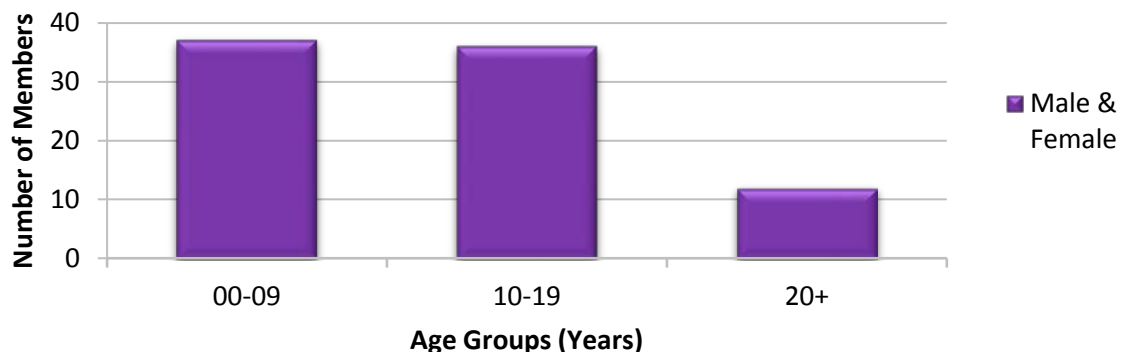
### Factor Replacement Product Fiscal Year Comparison: Medical Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Total Units	Cost Per Utilizer Per Year
2017	9	36	\$1,430,098.34	\$39,724.95	762,469	\$158,899.82
2018	11	25	\$1,213,298.95	\$48,537.95	614,176	\$110,299.91
% Change	22%	-30.5%	-15.1%	22.1%	-19.4%	-30.6%
Change	3	-11	-\$216,766.39	\$8,813.00	-148,293	-\$48,599.91

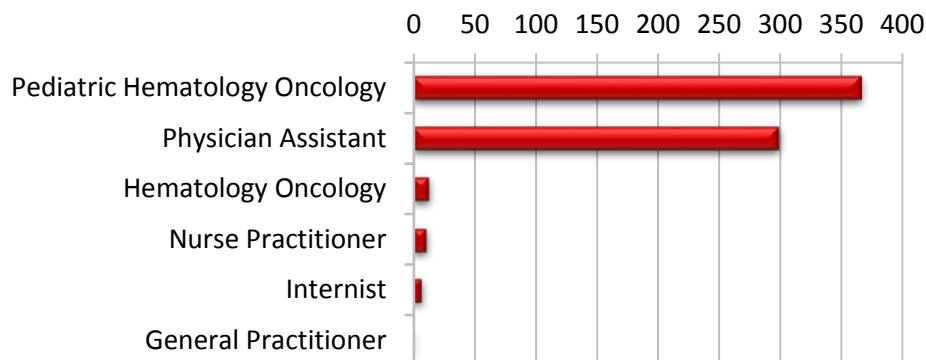
\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

### Demographics of Members Utilizing Factor Replacement Products: Pharmacy Claims



### Top Prescriber Specialties of Factor Replacement Products by Number of Claims: Pharmacy Claims

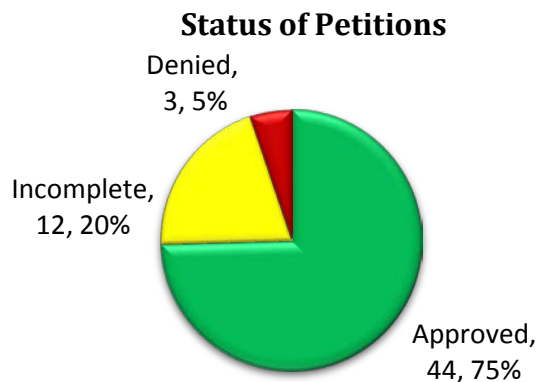




## Prior Authorization of Factor Replacement Products

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There were 59 prior authorization requests for 20 unique members submitted for factor replacement products during state fiscal year (SFY) 2018. The following chart shows the status of the submitted petitions for SFY 2018.



- There were 19 pharmacies with attestations for the Standards of Care (SOC) signed for SFY 2018. There are currently 18 pharmacies with attestations for the SOC signed for SFY 2019.

## Market News and Updates<sup>1,2,3,4,5,6,7,8,9,10,11,12</sup>

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

- **November 2017:** Hemlibra® (emicizumab-kxwh)
- **August 2018:** Jivi® [antihemophilic factor (recombinant) PEGylated-aucl]

### New Indication Approval(s):

- **April 2018:** Vonvendi® [von Willebrand factor (recombinant)] received an expanded indication to include the perioperative management of bleeding in adults with von Willebrand disease.
- **October 2018:** The FDA approved an expanded indication for Hemlibra® (emicizumab-kxwh) to allow for prophylactic treatment for patients with hemophilia A without inhibitors.

### Pipeline Update(s):

- **Fitusiran:** In December 2017, the FDA lifted a hold on clinical trials with fitusiran, a ribonucleic acid interfering (RNAi) therapeutic agent targeting antithrombin. Alnylam and Sanofi began enrolling patients in Phase 3 studies in 2018. Fitusiran is a subcutaneous (sub-Q) treatment being studied in patients with hemophilia A and B with and without inhibitors.
- **Marzeptacog alfa (MarzAA):** In January 2018, Catalyst Biosciences announced the beginning of patient enrollment in their Phase 2/3 clinical trial of marzeptacog alfa which is a sub-Q factor VIIa treatment for patient with hemophilia A or B with inhibitors. Positive interim study data was reported in August 2018. Three patients with annualized bleeding rates (ABR) of 15.9 to 26.7 all had zero bleeding episodes during the treatment period ranging from 44 to 50 days.

- **N8-GP:** In February 2018, Novo Nordisk filed a Biologics License Application (BLA) with the FDA for N8-GP, an extended half-life factor VIII for treatment of patients with hemophilia A. In the pathfinder clinical trials, which included more than 250 patients with hemophilia A, adults using N8-GP prophylactically had an ABR of 1.3 episodes per year, whereas pediatric patients on prophylactic treatment had an ABR of 1.95 episodes. A decision is expected by the FDA in the first quarter of 2019.
- **Factor IX Gene Therapy:**
  - In July 2018, Spark Therapeutics and Pfizer announced Pfizer has initiated a Phase 3 clinical study of fidanacogene elaparvovec (formerly known as SPK-9001) in patients with hemophilia B.
  - UniQure is currently enrolling patients in a Phase 3 trial with their hemophilia B gene therapy, AMT-061, with dosing expected to begin in the first quarter of 2019.
- **Factor VIII Gene Therapy:**
  - In October 2017, BioMarin was granted Breakthrough Therapy designation by the FDA for its gene therapy, valoctocogene roxaparvovec (formerly known as BMN270). In late 2017 and early 2018, BioMarin began Phase 3 clinical studies of valoctocogene roxaparvovec in patients with hemophilia A.

## **Inhibitors and Treatment**<sup>13,14,15,16</sup>

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Approximately 1 in 5 patients with hemophilia A and 1 in 100 patients with hemophilia B will develop an antibody to factor replacement products. These antibodies are called inhibitors. Inhibitor development is a major complication for people living with hemophilia. Certain risk factors have been identified for the development of inhibitors:

- Certain gene mutations
- Number of times factor replacement has been used in a lifetime
- Increased frequency and dose of treatment
- Black race or Hispanic ethnicity
- Family history of inhibitors

Diagnosis occurs via a blood test. The test measures for the presence of an inhibitor as well as the amount of inhibitor. The inhibitor titers are measured in Nijmegen-Bethesda units (NBU) or Bethesda units (BU) depending on the type of assay the laboratory uses. Low titer inhibitors are defined as <5.0 NBU/BU while high titers are >5.0 NBU/BU.

Treatment becomes very costly and carries a large burden for the patient and caregivers. There are few options for patients with inhibitors. If there is a low titer, then using large doses of clotting factor to overcome the inhibitor is an option. Another treatment option for inhibitors is immune tolerance induction (ITI). ITI attempts to teach the body that factor is a normal part of the blood. ITI requires large doses of factor everyday for weeks to months and possibly years. There is no standard protocol for ITI. In patients with hemophilia A, ITI is successful approximately 70% of the time while patients with hemophilia B see a success rate around 30%. Bypassing agents (BPAs) are used to treat patients with high titer inhibitors. BPAs are used prophylactically to prevent bleeding and are also used to treat bleeding episodes. There are currently two BPAs on the market, Feiba<sup>®</sup> and Novoseven<sup>®</sup> RT. Feiba<sup>®</sup> is an anti-inhibitor coagulant complex or activated prothrombin complex concentrate (aPCC) indicated for use in patients with hemophilia A and B with inhibitors. Feiba<sup>®</sup> contains non-activated factor II, IX, and

X and mainly activated factor VII. Novoseven® RT is a recombinant activated factor VII indicated for the treatment of bleeding episodes in patients with hemophilia A and B with inhibitors, congenital factor VII deficiency, acquired hemophilia, and Glanzmann's thrombasthenia with refractoriness to platelet transfusions with or without antibodies to platelets. Recently, the FDA approved a new treatment for patients with hemophilia A with inhibitors, Hemlibra® (emicizumab-kxwh).

## **Hemlibra® (Emicizumab-kxwh) Product Summary**<sup>17,18,19,20,21,22,23</sup>

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**FDA Approval(s):** November 2017 and October 2018

**Indication(s):** Hemlibra® (emicizumab-kxwh) is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

**Mechanism of Action:** Emicizumab is a bispecific monoclonal antibody which bridges activated factor IX and factor X to restore the function of the missing activated factor VIII that is needed for effective hemostasis.

### **Dosing:**

- The recommended initial dosing for emicizumab is 3mg/kg sub-Q once weekly for the first 4 weeks, followed by a maintenance dose of:
  - 1.5mg/kg once weekly; or
  - 3mg/kg every two weeks; or
  - 6mg/kg once every four weeks.

### **Special Considerations:**

- Thromboembolism and Thrombotic Microangiopathy Associated with Emicizumab and aPCC: Concomitant use with aPCC such as Feiba® for breakthrough bleeding episodes at doses of aPCC >100 IU/kg/24 hours was associated with reports of thromboembolism and thrombotic microangiopathy.
- Laboratory Coagulation Test Interference: Due to the mechanism of action of emicizumab, the intrinsic pathway clotting-based lab tests are affected. The altered tests include activated clotting time (ACT), activated partial thromboplastin time (aPTT), and all assays based on aPTT such as one-stage factor VIII activity. Clinicians cannot use these tests to monitor emicizumab activity, determine dosing for factor replacement or anti-coagulation, or measure factor VIII inhibitor titers.
- Neutralizing Antibodies: At least four patients have developed neutralizing antibodies to emicizumab which equated to <1% in the clinical studies.

**Clinical Studies:** The safety and efficacy of emicizumab were established in four (HAVEN 1, 2, 3, and 4) clinical studies in patients with hemophilia A with or without factor VIII inhibitors.

- HAVEN 1 was a randomized, multicenter, open-label, clinical trial in adult and adolescent males with hemophilia A with an inhibitor to factor VIII who had previously received on-demand or prophylactic treatment with BPAs. A total of 109 participants 12 years of age or older were included in the study. At 24 weeks, the ABR in patients receiving emicizumab was 2.9 versus 23.3 in the group receiving no prophylaxis, accounting for an 87% difference in the ABR between the two groups. In a third group,

participants who had previously received prophylactic treatment with BPAs were then treated with emicizumab prophylactically. There was a 79% lower ABR in patients receiving emicizumab compared to the ABR in patients receiving prophylaxis with BPAs.

- **HAVEN 2** was a single-arm, multicenter, open-label clinical trial in pediatric males with hemophilia A with an inhibitor to factor VIII who were previously treated with BPAs. In the interim analysis of 60 patients, 57 of whom were younger than 12 years of age, there was a 99% reduction in the ABR with emicizumab versus prior BPA treatment in an intra-individual comparison.
- **HAVEN 3** was a randomized, multicenter, open-label clinical trial in adult and adolescent males with hemophilia A without inhibitors to factor VIII who previously received on-demand or prophylactic treatment with factor VIII. There were 152 males participating in the four group study. Groups A and B were given prophylactic treatment with emicizumab 1.5mg/kg/week and 3mg/kg every two weeks, respectively. Group C received no prophylaxis. Group D allowed an intra-individual comparison due to those participants previously receiving factor VIII prophylaxis then switching to emicizumab 1.5mg/kg/week during the study. At week 24, there was a 96% and 97% reduction in the ABRs in groups A and B, respectively, when compared to group C. Group D saw 68% reduction in the ABR in the intra-individual comparison.
- **HAVEN 4** was a single-arm, multicenter, open-label, clinical trial in adult and adolescent males with hemophilia A with and without factor VIII inhibitors. The 41 patients included in the trial had previously received factor VIII on demand, prophylactically, or a BPA. The trial evaluated the efficacy of emicizumab dosed at 3mg/kg sub-Q once weekly for four weeks followed by 6mg/kg every four weeks thereafter. The ABR was 2.4 during the trial period (median observation time: 26.1 weeks).

**Institute for Clinical and Economic Review (ICER) Report:** In April 2018, ICER published a report looking at emicizumab for hemophilia A with inhibitors focusing on patients that will not be treated with ITI or for whom ITI has failed. ICER concluded that emicizumab improves patient outcomes as well as lowers treatment costs when compared to either prophylaxis with BPAs or no prophylaxis (on-demand treatment only) with BPAs for patients with hemophilia A with inhibitors. The report also noted there are no long-term outcomes or safety studies at the current time.

**Medical and Scientific Advisory Council (MASAC) Recommendations:** In November 2017, the MASAC issued interim guidance on acute bleeding management and use of laboratory assays for patients using emicizumab. The recommendations include having a plan in place for how to treat any breakthrough bleeding. The patient needs to use caution with all BPAs and use recombinant factor VIIa when possible. If aPCC is necessary, the initial dose should be at 50 IU/kg but not exceed 100 IU/kg/day. Any repeated doses of either recombinant factor VIIa or aPCC should be under medical supervision. If the patient required BPA for longer than 24 hours, the patient should be evaluated for thromboembolic events. For lab assay recommendations while a patient is on emicizumab, routine monitoring of emicizumab is not required. While on emicizumab, aPTT-based assays should not be used since the results will be inaccurate. Only chromogenic assays using a bovine reagent can be used to assay factor VIII activity or inhibitor levels.

## Cost Comparison:

Factor Replacement Product	Cost*	Cost for 4 Weeks of Prophylaxis Therapy
Hemlibra® (emicizumab-kxwh) <sup>‡</sup>	\$97.72 per mg	\$29,316.00 - \$35,179.20
Feiba® (anti-inhibitor coagulant complex) <sup>+</sup>	\$2.08 per unit	\$123,879.00
Advate® [antihemophilic factor (recombinant)] <sup>¥</sup>	\$1.32 per unit	\$18,480.00 - \$36,960.00

\*Costs based on Specialty Pharmaceutical Allowable Cost (SPAC). Costs do not reflect rebated prices or net costs.

<sup>‡</sup>Hemlibra® (emicizumab-kxwh) dosing 1.5mg/kg weekly to 6mg/kg every 4 weeks for a 50kg patient.

<sup>+</sup>Feiba® dosing 85 u/kg every other day for a 50kg patient.

<sup>¥</sup>Advate® dosing 20 to 40 u/kg every other day for a 50kg patient.

## Jivi® [Antihemophilic Factor (Recombinant) PEGylated-aucl] Product Summary<sup>24,25</sup>

**FDA Approval:** August 2018

**Indication(s):** Jivi® [antihemophilic factor (recombinant) PEGylated-aucl] is indicated for use in previously treated adults and adolescents (12 years of age and older) with hemophilia A (congenital factor VIII deficiency) for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding
- Routine prophylaxis to reduce the frequency of bleeding episodes

**Dosing:** One unit of Jivi® per kg of body weight will raise the factor VIII level by 2 international units per deciliter [IU/dL]; therefore, the recommended dose would be calculated by using the following equation:

- $\text{Dose (IU)} = \text{body weight (kg)} \times \text{desired factor VIII rise (IU/dL or \% of normal)} \times 0.5 \text{ (IU/kg per IU/dL)}$ 
  - Example: 50kg x 40 IU/dL (%) x 0.5 IU/kg per IU/dL = 1,000 IU per dose
- **Bleeding Episodes/On-Demand Treatment:**
  - Minor bleeding episodes should be treated with 20 to 40% of normal or 10 to 20 IU/kg. Dosing should be repeated every 24 to 48 hours until bleeding is resolved.
  - Moderate bleeding episodes should be treated with 30 to 60% of normal or 15 to 30 IU/kg. Dosing should be repeated every 24 to 48 hours until bleeding is resolved.
  - Major bleeding episodes should be treated with 60 to 100% of normal or 30 to 50 IU/kg. Dosing should be repeated every 8 to 24 hours until bleeding is resolved.
- **Perioperative Bleeding Management:**
  - Minor procedures (e.g., skin biopsies, tooth extraction) should be treated with 30 to 60% of normal or 15 to 30 IU/kg. Dosing should be repeated every 24 hours for at least one day until healing is achieved.
  - Major procedures (e.g., organ removal, joint replacement) should be treated with 80 to 100% of normal or 40 to 50 IU/kg. Dosing should be repeated every 12 to 24 hours until adequate wound healing is complete, then continued for at least another seven days to maintain factor VIII activity of 30 to 60% of normal.
- **Routine Prophylaxis:**
  - Initial recommended regimen: 30 to 40 IU/kg twice per week
  - Based on bleeding episodes:
    - The regimen may be adjusted to 45 to 60 IU/kg every five days

- The regimen may require further adjustments in dosing frequency

**Prolonged Half-Life:** Jivi® is a recombinant B-domain deleted human coagulation factor VIII (BDD-rFVIII) with polyethylene-glycol (PEG) conjugated to the protein, which slows down removal from the blood. Jivi® has a half-life ranging from 17.4 to 18.6 hours. Factor VIII has an average half-life of 12 hours.

**Clinical Study:** The safety and efficacy of Jivi® was established in the PROTECT VIII clinical study in adolescent and adult males with severe hemophilia A.

- **PROTECT VIII** was a multinational, Phase 2/3, partially randomized, open-label clinical trial which evaluated the safety and efficacy of Jivi®. The primary endpoint was ABR. After a 10-week run-in period of participants receiving Jivi® at 25 IU/kg twice per week, 13 patients who had more than one bleeding episode during the run-in period had a dose change to 30 to 40 IU/kg twice per week. A total of 97 participants had one or fewer bleeding episodes during the run-in period; the 97 were subsequently randomized to receive either 45 to 60 IU/kg every five days or 60 IU/kg every seven days prophylactically. For the 13 patients not eligible for randomization, the ABR went from 17.2 during the run-in period (weeks 1 to 10) to 4.1 after the dose was increased to 30 to 40 IU/kg (weeks 11 to 36). The ABR for this group was 12 in the previous 12 months. The group randomized to receive 45 to 60 IU/kg every five days had an ABR of 1.9, while ABR for patients in the 60 IU/kg every seven days treatment group was 3.9. No inhibitors were detected during the study period.

### Cost Comparison:

Factor Replacement Product	Cost Per Unit	Cost for 4 Weeks of Prophylaxis Therapy
Jivi® [antihemophilic factor (recombinant) PEGylated-aucl] <sup>‡</sup>	\$2.19*	\$26,280 - \$35,040
Advate® [antihemophilic factor (recombinant)] <sup>+</sup>	\$1.32**	\$18,480 - \$36,960

Costs do not reflect rebated prices or net costs.

\*Wholesale Acquisition Cost (WAC)

\*\*Specialty Pharmaceutical Allowable Cost (SPAC)

<sup>‡</sup>Jivi® [antihemophilic factor (recombinant) PEGylated-aucl] dosing 30 to 40 u/kg twice weekly for a 50kg patient.

<sup>+</sup>Advate® dosing 20 to 40 u/kg every other day for a 50kg patient.

### Recommendations

The Oklahoma Health Care Authority recommends the prior authorization of Jivi® [antihemophilic factor (recombinant) PEGylated-aucl ], Hemlibra® (emicizumab-kxwh), Feiba® (anti-inhibitor coagulant complex), Novoseven® RT [coagulation factor VIIa (recombinant)] with the following criteria:

#### Adynovate®, Afstyla®, Alprolix®, Eloctate®, Idelvion®, Jivi®, and Rebinyn® Approval Criteria:

1. An FDA approved indication; and
2. Requested medication must be prescribed by a hematologist specializing in hemophilia, or a mid-level practitioner with a supervising physician that is a hematologist specializing in hemophilia; and
3. A patient-specific, clinically significant reason why the member cannot use the following:
  - a. Hemophilia A: Advate® or current factor VIII replacement product; or

- b. Hemophilia B: Benefix® or current factor IX replacement product; and
4. A half-life study must be performed to determine the appropriate dose and dosing interval; and
5. Initial approvals will be for the duration of the half-life study. If the half-life study shows significant benefit in prolonged half-life, subsequent approvals will be for the duration of one year.

**Hemlibra® (Emicizumab-kxwh) Approval Criteria:**

1. Member must have a diagnosis of hemophilia A; and
2. Hemlibra® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders; and
3. Prescriber must be able to monitor appropriate blood clotting tests and levels utilizing testing which accounts for the interaction of Hemlibra® and blood factors by following the Medical and Scientific Advisory Council (MASAC) guidance; and
4. For members with hemophilia A an inhibitor to factor VIII:
  - a. Member must have failed immune tolerance induction (ITI) or is not a good candidate for ITI; and
  - b. Member's hemophilia cannot be managed without the use of bypassing agent(s) (e.g., Feiba® or Novoseven® RT) as prophylaxis for prevention of bleeding episodes, or the member is unable to maintain venous access for daily infusions; and
  - c. Member's hemophilia is not currently controlled with the use of bypassing agent(s); and
  - d. Prescriber must counsel member and/or caregiver on the risks of utilizing Feiba® for breakthrough bleeding while on Hemlibra®, and member should be monitored closely if any bypassing agent is given; or
5. For members with hemophilia A without an inhibitor:
  - a. Member's current prophylaxis therapy is not adequate to prevent spontaneous bleeding episodes; or
  - b. Member is unable to maintain venous access for prophylactic infusions; and
  - c. Treatment plan must be made to address breakthrough bleeds and procedures; and
  - d. Routine lab screening must occur for factor VIII inhibitor while using Hemlibra® since this would change the treatment plan for bleeds and procedures; and
6. First dose must be given in a health care facility; and
7. In order to calculate appropriate dosing, the member's recent weight must be provided and have been taken within the last 3 months.
8. Initial approvals will be for 3 months of therapy. Subsequent approvals will be the duration of 1 year if there has been a decrease in the member's spontaneous bleeding episodes since beginning Hemlibra® treatment.

**Feiba® (Anti-Inhibitor Coagulation Complex) Approval Criteria:**

1. Member must be diagnosed with hemophilia A or B with an inhibitor; and
2. Feiba® must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

**Novoseven® RT [Coagulation Factor VIIa (Recombinant)] Approval Criteria:**

1. An FDA approved diagnosis of one of the following:
  - a. Hemophilia A or B with inhibitors; or
  - b. Congenital factor VII deficiency; or
  - c. Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets; or
  - d. Acquired hemophilia; and
2. Novoseven® RT must be prescribed by a hematologist specializing in rare bleeding disorders or a mid-level practitioner with a supervising physician that is a hematologist specializing in rare bleeding disorders.

At this time the Oklahoma Health Care Authority does not recommend any changes to the current Standards of Care for pharmacies providing factor replacement products.

**Utilization Details of Factor Replacement Products: Fiscal Year 2018****Pharmacy Claims: Fiscal Year 2018**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM
<b>ADVATE PRODUCTS</b>					
ADVATE INJ 1500 UNIT	42	11	\$848,922.75	\$982.55	\$20,212.45
ADVATE INJ 500 UNIT	33	8	\$342,138.55	\$585.85	\$10,367.83
ADVATE INJ 1000 UNIT	29	8	\$376,872.81	\$744.81	\$12,995.61
ADVATE INJ 2000 UNIT	18	4	\$558,954.47	\$1,678.54	\$31,053.03
ADVATE INJ 250 UNIT	3	1	\$9,241.37	\$154.02	\$3,080.46
ADVATE INJ 3000 UNIT	1	1	\$3,929.41	\$1,964.70	\$3,929.41
<b>SUBTOTAL</b>	<b>126</b>	<b>20</b>	<b>\$2,140,059.36</b>	<b>\$911.05</b>	<b>\$16,984.60</b>
<b>KOGENATE PRODUCTS</b>					
KOGENATE FS INJ 1000 UNIT	54	14	\$945,243.94	\$873.61	\$17,504.52
KOGENATE FS INJ 500 UNIT	38	11	\$356,532.35	\$450.17	\$9,382.43
KOGENATE FS INJ 2000 UNIT	36	8	\$1,197,371.15	\$1,330.41	\$33,260.31
KOGENATE FS INJ 500 UNIT	14	2	\$87,905.27	\$211.31	\$6,278.95
KOGENATE FS INJ 2000 UNIT	13	2	\$364,686.00	\$954.68	\$28,052.77
KOGENATE FS INJ 1000 UNIT	7	1	\$117,224.10	\$580.32	\$16,746.30
KOGENATE FS INJ 250 UNIT	7	4	\$25,903.49	\$171.55	\$3,700.50
KOGENATE FS INJ 2000 UNIT	6	4	\$196,126.01	\$1,281.87	\$32,687.67
KOGENATE FS INJ 3000 UNIT	2	1	\$61,208.46	\$1,093.01	\$30,604.23
KOGENATE FS INJ 500 UNIT	1	1	\$3,554.23	\$118.47	\$3,554.23
<b>SUBTOTAL</b>	<b>178</b>	<b>18</b>	<b>\$3,355,755.00</b>	<b>\$805.90</b>	<b>\$18,852.56</b>
<b>FEIBA PRODUCTS</b>					
FEIBA INJ 1750-3250 UNIT	29	4	\$5,780,915.33	\$8,017.91	\$199,341.91
<b>SUBTOTAL</b>	<b>29</b>	<b>4</b>	<b>\$5,780,915.33</b>	<b>\$8,017.91</b>	<b>\$199,341.91</b>
<b>ELOCTATE PRODUCTS</b>					
ELOCTATE INJ 1500 UNIT	14	3	\$436,132.08	\$1,260.50	\$31,152.29
ELOCTATE INJ 1000 UNIT	13	3	\$232,212.93	\$863.25	\$17,862.53
ELOCTATE INJ 500 UNIT	12	4	\$77,921.89	\$962.00	\$6,493.49
ELOCTATE INJ 2000 UNIT	10	1	\$240,827.90	\$4,816.56	\$24,082.79
ELOCTATE INJ 750 UNIT	5	3	\$99,793.49	\$712.81	\$19,958.70
ELOCTATE INJ 3000 UNIT	5	1	\$259,127.80	\$10,365.11	\$51,825.56
ELOCTATE INJ 4000 UNIT	4	1	\$167,864.60	\$8,393.23	\$41,966.15



PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM
ELOCTATE INJ 250 UNIT	1	1	\$4,897.26	\$174.90	\$4,897.26
<b>SUBTOTAL</b>	<b>64</b>	<b>6</b>	<b>\$1,518,777.95</b>	<b>\$1,583.71</b>	<b>\$23,730.91</b>
<b>WILATE PRODUCTS</b>					
WILATE 1000-1000 UNIT	39	7	\$726,482.67	\$1,036.35	\$18,627.76
WILATE 500-500 UNIT	21	6	\$130,281.54	\$301.58	\$6,203.88
<b>SUBTOTAL</b>	<b>60</b>	<b>8</b>	<b>\$856,764.21</b>	<b>\$756.19</b>	<b>\$14,279.40</b>
<b>ALPROLIX PRODUCTS</b>					
ALPROLIX INJ 500 UNIT	14	2	\$92,259.12	\$234.16	\$6,589.94
ALPROLIX INJ 2000 UNIT	7	2	\$20,295.21	\$120.80	\$2,899.32
ALPROLIX INJ 4000 UNIT	7	1	\$435,135.90	\$2,197.66	\$62,162.27
ALPROLIX INJ 1000 UNIT	5	1	\$36,218.85	\$258.71	\$7,243.77
ALPROLIX INJ 250 UNIT	3	1	\$8,834.20	\$105.17	\$2,944.73
ALPROLIX INJ 3000 UNIT	1	1	\$27,412.15	\$979.01	\$27,412.15
<b>SUBTOTAL</b>	<b>37</b>	<b>3</b>	<b>\$620,155.43</b>	<b>\$612.80</b>	<b>\$16,760.96</b>
<b>HELIXATE PRODUCTS</b>					
HELIXATE FS INJ 500 UNIT	1	1	\$4,456.80	\$1,485.60	\$4,456.80
HELIXATE FS INJ 1000 UNIT	1	1	\$1,264.80	\$421.60	\$1,264.80
<b>SUBTOTAL</b>	<b>2</b>	<b>1</b>	<b>\$5,721.60</b>	<b>\$953.60</b>	<b>\$2,860.80</b>
<b>ALPHANATE PRODUCTS</b>					
ALPHANATE INJ VWF/HUM 1000 UNIT	6	2	\$64,358.35	\$514.87	\$10,726.39
ALPHANATE INJ VWF/HUM 500 UNIT	1	1	\$546.35	\$546.35	\$546.35
<b>SUBTOTAL</b>	<b>7</b>	<b>3</b>	<b>\$64,904.70</b>	<b>\$515.12</b>	<b>\$9,272.10</b>
<b>XYNTHA PRODUCTS</b>					
XYNTHA SOLOF INJ 2000 UNIT	10	1	\$379,357.95	\$1,273.01	\$37,935.80
<b>SUBTOTAL</b>	<b>10</b>	<b>1</b>	<b>\$379,357.95</b>	<b>\$1,273.01</b>	<b>\$37,935.80</b>
<b>ADYNOVATE PRODUCTS</b>					
ADYNOVATE INJ 1000 UNIT	13	3	\$241,663.21	\$1,064.60	\$18,589.48
ADYNOVATE INJ 2000 UNIT	11	3	\$277,583.35	\$1,119.29	\$25,234.85
ADYNOVATE INJ 500 UNIT	8	1	\$52,131.44	\$251.84	\$6,516.43
ADYNOVATE INJ 3000 UNIT	6	1	\$384,213.78	\$2,286.99	\$64,035.63
ADYNOVATE INJ 1500 UNIT	6	1	\$127,494.52	\$708.30	\$21,249.09
<b>SUBTOTAL</b>	<b>44</b>	<b>4</b>	<b>\$1,083,086.30</b>	<b>\$1,051.54</b>	<b>\$24,615.60</b>
<b>NUWIQ PRODUCTS</b>					
NUWIQ KIT 1000 UNIT	18	3	\$359,242.69	\$1,053.50	\$19,957.93
NUWIQ KIT 500 UNIT	12	3	\$143,262.91	\$758.00	\$11,938.58
NUWIQ KIT 2500 UNIT	7	1	\$274,299.31	\$2,031.85	\$39,185.62
NUWIQ KIT 2000 UNIT	4	1	\$215,930.38	\$4,318.61	\$53,982.60
NUWIQ KIT 250 UNIT	4	2	\$13,097.25	\$195.48	\$3,274.31
NUWIQ KIT 3000 UNIT	3	1	\$172,743.24	\$2,303.24	\$57,581.08
<b>SUBTOTAL</b>	<b>48</b>	<b>5</b>	<b>\$1,178,575.78</b>	<b>\$1,375.23</b>	<b>\$24,553.66</b>
<b>MONOCLATE PRODUCTS</b>					
MONOCLATE-P INJ 1500 UNIT	6	1	\$95,898.75	\$1,917.97	\$15,983.13
MONOCLATE-P INJ 1000 UNIT	2	1	\$38,170.00	\$1,908.50	\$19,085.00
<b>SUBTOTAL</b>	<b>8</b>	<b>2</b>	<b>\$134,068.75</b>	<b>\$1,915.27</b>	<b>\$16,758.59</b>
<b>HUMATE PRODUCTS</b>					
HUMATE-P SOL 250-600 UNIT	9	6	\$7,139.49	\$475.97	\$793.28
HUMATE-P SOL 500-1200 UNIT	1	1	\$3,270.32	\$1,090.11	\$3,270.32
<b>SUBTOTAL</b>	<b>10</b>	<b>6</b>	<b>\$10,409.81</b>	<b>\$578.32</b>	<b>\$1,040.98</b>
<b>RIXUBIS PRODUCTS</b>					

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/DAY	COST/CLAIM
RIXUBIS INJ 1000 UNIT	4	3	\$8,279.05	\$1,379.84	\$2,069.76
RIXUBIS INJ 2000 UNIT	2	2	\$7,846.54	\$2,615.51	\$3,923.27
RIXUBIS INJ 500 UNIT	1	1	\$692.79	\$692.79	\$692.79
<b>SUBTOTAL</b>	<b>7</b>	<b>4</b>	<b>\$16,818.38</b>	<b>\$1,681.84</b>	<b>\$2,402.63</b>
<b>NOVOSEVEN PRODUCTS</b>					
NOVOSEVEN RT INJ 2MG	6	3	\$133,100.20	\$6,338.10	\$22,183.37
NOVOSEVEN RT INJ 8MG	3	1	\$728,119.65	\$104,017.09	\$242,706.55
<b>SUBTOTAL</b>	<b>9</b>	<b>4</b>	<b>\$861,219.85</b>	<b>\$30,757.85</b>	<b>\$95,691.09</b>
<b>BENEFIX PRODUCTS</b>					
BENEFIX INJ 2000 UNIT	5	2	\$25,498.97	\$3,187.37	\$5,099.79
BENEFIX INJ 1000 UNIT	3	2	\$6,944.58	\$992.08	\$2,314.86
<b>SUBTOTAL</b>	<b>8</b>	<b>3</b>	<b>\$32,443.55</b>	<b>\$2,162.90</b>	<b>\$4,055.44</b>
<b>KOVALTRY PRODUCTS</b>					
KOVALTRY INJ 1000 UNIT	16	2	\$245,000.00	\$1,103.60	\$15,312.50
KOVALTRY INJ 250 UNIT	4	1	\$19,172.00	\$342.36	\$4,793.00
KOVALTRY INJ 500 UNIT	1	1	\$2,582.60	\$1,291.30	\$2,582.60
<b>SUBTOTAL</b>	<b>21</b>	<b>2</b>	<b>\$266,754.60</b>	<b>\$952.70</b>	<b>\$12,702.60</b>
<b>IDELVION PRODUCTS</b>					
IDELVION SOL 500 UNIT	7	1	\$45,369.75	\$477.58	\$6,481.39
<b>SUBTOTAL</b>	<b>7</b>	<b>1</b>	<b>\$45,369.75</b>	<b>\$477.58</b>	<b>\$6,481.39</b>
<b>VONVENDI PRODUCTS</b>					
VONVENDI INJ 1300 UNIT	1	1	\$2,430.07	\$2,430.07	\$2,430.07
<b>SUBTOTAL</b>	<b>1</b>	<b>1</b>	<b>\$2,430.07</b>	<b>\$2,430.07</b>	<b>\$2,430.07</b>
<b>HEMLIBRA PRODUCTS</b>					
HEMLIBRA INJ 30MG/ML	8	2	\$95,314.64	\$972.60	\$11,914.33
HEMLIBRA INJ 60MG/0.4ML	6	2	\$166,703.22	\$1,389.19	\$27,783.87
<b>SUBTOTAL</b>	<b>14</b>	<b>2</b>	<b>\$262,017.86</b>	<b>\$1,201.92</b>	<b>\$18,715.56</b>
<b>TOTAL</b>	<b>697</b>	<b>85*</b>	<b>\$18,748,696.44</b>	<b>\$1,381.32</b>	<b>\$26,899.13</b>

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

### Medical Claims: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/CLAIM
J7187 VON WILLEBRAND FACTOR COMPLEX	2	2	\$1,213.30	\$606.65
J7189 FACTOR VIIA RECOMBINANT	14	2	\$1,195,450.07	\$85,389.29
J7192 FACTOR VII RECOMBINANT	8	6	\$15,075.58	\$1,884.39
J7195 FACTOR IX RECOMBINANT	1	1	\$1,560.00	\$1,560.00
<b>TOTAL</b>	<b>25<sup>+</sup></b>	<b>11*</b>	<b>\$1,213,298.95</b>	<b>\$89,440.33</b>

\*Total number of unduplicated claims.

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

<sup>1</sup> U.S. Food and Drug Administration (FDA). FDA approves new treatment to prevent bleeding in certain patients with hemophilia A. Available online at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585567.htm>. Issued 11/16/2017. Last accessed 10/23/2018.

<sup>2</sup> Bayer News Release. Bayer Receives FDA Approval for Jivi®, New Hemophilia A Treatment With Step-Wise Prophylaxis Dosing Regimen. Available online at: [https://www.jivi.com/static/documents/Press\\_Release.pdf](https://www.jivi.com/static/documents/Press_Release.pdf). Issued 08/30/2018. Last accessed 10/23/2018.

- <sup>3</sup> FDA Supplement Approval Letter. Available online at: <https://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM605039.pdf>. Issued 04/13/2018. Last accessed 10/23/2018.
- <sup>4</sup> FDA News Release. FDA approves emicizumab-kxwh for hemophilia A with or without factor VIII inhibitors. Available online at: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm622564.htm>. Issued 10/04/2018. Last accessed 10/23/2018.
- <sup>5</sup> Novo Nordisk News Release. Novo Nordisk files for regulatory approval of long-acting factor VIII (N8-GP) in the US and the EU for treatment of haemophilia A. Available online at: [https://www.novonordisk.com/en\\_gb/home/media/news-details.2171860.html](https://www.novonordisk.com/en_gb/home/media/news-details.2171860.html). Issued 02/27/2018. Last accessed 10/23/2018.
- <sup>6</sup> Inacio P. Fitusiran Clinical Development Among 2018 Corporate Goals, Alnylam Pharmaceuticals Says. *Hemophilia News Today*. Available online at: <https://hemophilianewstoday.com/2018/01/12/hemophilia-clinical-program-fitusiran-among-2018-goals-alnylam-pharmaceuticals-announces/>. Issued 01/12/2018. Last accessed 10/23/2018.
- <sup>7</sup> Catalyst Biosciences. Factor VIIa marzeptacog alfa (activated). Available online at: <https://www.catalystbiosciences.com/pipeline/hemostasis/factor-viia/>. Last accessed 10/23/2018.
- <sup>8</sup> Catalyst Biosciences. Catalyst Updates on Phase 2/3 Trial of Subcutaneous Therapy. *National Hemophilia Foundation*. Available online at: <https://www.hemophilia.org/Newsroom/Industry-News/Catalyst-Updates-on-Phase-2-3-Trial-of-Subcutaneous-Therapy>. Issued 08/17/2018. Last accessed 10/23/2018.
- <sup>9</sup> Pfizer, Inc. Pfizer Initiates Pivotal Phase 3 Program for Investigational Hemophilia B Gene Therapy. *Business Wire*. Available online at: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-initiates-pivotal-phase-3-program-for-investigational-hemophilia-b-gene-therapy-0>. Issued 04/16/2018. Last accessed 10/23/2018.
- <sup>10</sup> UniQure. UniQure Enrolls First Patient in Phase III HOPE-B Pivotal Study of AMT-061 in Patients with Hemophilia B. Available online at: [http://uniqure.com/PR\\_Initiation\\_Phase%20III\\_HOPE-B\\_trial\\_FINAL\\_6\\_28\\_2018\\_2\\_FINAL\\_PDF.pdf](http://uniqure.com/PR_Initiation_Phase%20III_HOPE-B_trial_FINAL_6_28_2018_2_FINAL_PDF.pdf). Issued 06/28/2018. Last accessed 10/23/2018.
- <sup>11</sup> BioMarin Pharmaceutical, Inc. FDA Grants Breakthrough Therapy Designation for BioMarin's Investigative Hemophilia A Gene Therapy. *National Hemophilia Foundation*. Available online at: <https://www.hemophilia.org/Newsroom/Industry-News/FDA-Grants-Breakthrough-Therapy-Designation-for-BioMarin-s-Investigative-Hemophilia-A-Gene-Therapy>. Issued 10/30/2017. Last accessed 10/23/2018.
- <sup>12</sup> BioMarin Pharmaceutical, Inc. BioMarin Doses First Patient in Global GENE8-1 Phase 3 Study of Valoctocogene Roxaparovec Gene Therapy for Severe Hemophilia A. *PR Newswire*. Available online at: <https://www.prnewswire.com/news-releases/biomarin-doses-first-patient-in-global-gener8-1-phase-3-study-of-valoctocogene-roxaparovec-gene-therapy-for-severe-hemophilia-a-300573456.html>. Issued 12/19/2017. Last accessed 10/23/2018.
- <sup>13</sup> Centers for Disease Control and Prevention (CDC). Inhibitors. Available online at: <https://www.cdc.gov/ncbddd/hemophilia/inhibitors.html>. Last revised 08/17/2018. Last accessed 11/05/2018.
- <sup>14</sup> Kempton CL, Meeks SL. Toward optimal therapy for inhibitors in hemophilia. *Blood* 2014; 124:3365-3372.
- <sup>15</sup> Feiba® Prescribing Information. Shire. Available online at: [https://www.shirecontent.com/PI/PDFs/FEIBA\\_USA\\_ENG.pdf](https://www.shirecontent.com/PI/PDFs/FEIBA_USA_ENG.pdf). Last revised 04/2018. Last accessed 11/05/2018.
- <sup>16</sup> Novoseven® Prescribing Information. Novo Nordisk USA. Available online at: <https://www.novosevent.com/>. Last revised 10/2018. Last accessed 11/05/2018
- <sup>17</sup> Hemlibra® Prescribing Information. Genentech USA, Inc. Available online at: [https://www.gene.com/download/pdf/hemlibra\\_prescribing.pdf](https://www.gene.com/download/pdf/hemlibra_prescribing.pdf). Last revised 10/2018. Last accessed 10/23/2018.
- <sup>18</sup> Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors. *N Engl J Med* 2017; 377:809-818.
- <sup>19</sup> Young G, Sidonio RF, Oldenburg J, et al. HAVEN 2 Updated Analysis: Multicenter, Open-Label, Phase 3 Study to Evaluate Efficacy, Safety and Pharmacokinetics of Subcutaneous Administration of Emicizumab Prophylaxis in Pediatric Patients with Hemophilia A with Inhibitors. *Blood* 2017; 130:85.
- <sup>20</sup> Mahlangu J, Oldenburg J, Paz-Priel I, et al. Emicizumab Prophylaxis in Patients Who Have Hemophilia A without Inhibitors. *N Engl J Med* 2018; 379:811-822.
- <sup>21</sup> Ingram I. Trials support Emicizumab as Standard TX in Hemophilia A. *MedPage Today*. Available online at: <https://www.medpagetoday.com/hematologyoncology/hemophilia/73018>. Issued 05/21/2018. Last accessed 10/10/2018.
- <sup>22</sup> Institute for Clinical and Economic Review. Emicizumab for Hemophilia A with Inhibitors: Effectiveness and Value. Available online at: [https://icer-review.org/wp-content/uploads/2017/08/ICER\\_Hemophilia\\_Final\\_Evidence\\_Report\\_041618.pdf](https://icer-review.org/wp-content/uploads/2017/08/ICER_Hemophilia_Final_Evidence_Report_041618.pdf). Issued 04/16/2018. Last accessed 10/23/2018.
- <sup>23</sup> National Hemophilia Foundation. MASAC Update on the Approval and Availability of the New Treatment: Emicizumab (Hemlibra), for Persons with Hemophilia A with Inhibitors to Factor VIII: Interim Guidance on Acute Bleed Management and Use of Laboratory Assays. Available online at: <https://www.hemophilia.org/sites/default/files/MASAC-Update-on-the-Approval-and-Availability-of-the-New-Treatment.pdf>. Issued 11/24/2017. Last accessed 10/24/2018.
- <sup>24</sup> Jivi® Prescribing information. Bayer HealthCare LLC. Available online at: [https://labeling.bayerhealthcare.com/html/products/pi/Jivi\\_PI.pdf](https://labeling.bayerhealthcare.com/html/products/pi/Jivi_PI.pdf). Last revised 08/2018. Last accessed 10/23/2018.
- <sup>25</sup> Reding MT, Ng HJ, Poulsen LH, et al. Safety and efficacy of BAY 94-9027, a prolonged-half-life factor VIII. *J Thromb Haemost* 2017; 15:411-419.





# Appendix H





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# Vote to Prior Authorize Nocdurna® (Desmopressin Acetate Sublingual Tablet)

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Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2,3</sup>

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- **Nocdurna® [desmopressin acetate sublingual (SL) tablet]:** Nocdurna® is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void. The antidiuretic effects are mediated by stimulation of vasopressin 2 (V2) receptors, thereby increasing water re-absorption in the kidneys and reducing urine production. Nocdurna® is supplied as SL tablets in two strengths: 27.7mcg and 55.3mcg. The recommended dosing is 27.7mcg once daily for women and 55.3mcg once daily for men. Nocdurna® has a boxed warning for the risk of hyponatremia, which may be life-threatening if severe. For this reason, prescribers should ensure serum sodium concentrations are normal before patients start or resume Nocdurna®. Additionally, serum sodium should be measured within one week and approximately one month after initiating therapy and periodically during treatment. The Wholesale Acquisition Cost (WAC) of one SL tablet of Nocdurna® is \$14.00, resulting in a monthly cost of \$420.00. For comparison, the monthly National Average Drug Acquisition Cost (NADAC) of desmopressin 0.1mg oral tablets is \$23.10 when dosed as 100mcg at bedtime.
- **Myrbetriq® (mirabegron) in combination with VESicare® (solifenacin):** In May 2018, Astellas Pharma, Inc. announced the U.S. Food and Drug Administration (FDA) approval of a supplemental New Drug Application (sNDA) for the use of Myrbetriq® (mirabegron) in combination with VESicare® (solifenacin) for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence (UUI), urgency, and urinary frequency. Both medications are products of Astellas Pharma and were previously FDA approved individually as monotherapy for OAB.

## Recommendations

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The College of Pharmacy recommends placement of Nocdurna® (desmopressin acetate SL tablets) into the Special Prior Authorization (PA) Tier of the Bladder Control Medications Product Based Prior Authorization (PBPA) category with criteria similar to Noctiva™ (desmopressin acetate nasal spray):

### **Nocdurna® (Desmopressin Acetate Sublingual Tablets) Approval Criteria:**

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and

3. The prescriber must confirm the member has a 6-month history of at least two nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and
5. Member must have failed a trial of DDAVP® (desmopressin acetate tablets) or have a patient-specific, clinically significant reason why the standard tablet formulation cannot be used; and
6. The prescriber must be willing to measure serum sodium levels prior to starting treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within the first week and approximately one month after starting treatment, and periodically during treatment; and
8. The prescriber must confirm the member is not taking loop diuretics; and
9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) <50mL/min/1.73m<sup>2</sup>; and
10. Initial approvals will be for the duration of 3 months; for continued authorization the prescriber must provide the following:
  - a. Documentation that serum sodium levels are acceptable to the prescriber; and
  - b. Documentation that the member is responding to treatment; and
11. Approvals will be limited to the 27.7mcg dose for female members; and
12. A quantity limit of 30 tablets per 30 days will apply.

The College of Pharmacy also recommends updating the Noctiva™ (desmopressin acetate nasal spray) criteria as shown in red to be consistent with Nocurna® (desmopressin acetate SL tablets) criteria and clarify the quantity limit to ensure appropriate use:

**Noctiva™ (Desmopressin Acetate Nasal Spray) Approval Criteria:**

1. An FDA approved diagnosis of nocturia due to nocturnal polyuria in adults ~~50 years of age and older~~; and
2. All other causes of nocturia have been ruled out or adequately treated [e.g., benign prostatic hyperplasia (BPH), overactive bladder (OAB), obstructive sleep apnea (OSA)]; and
3. The prescriber must confirm the member has a 6-month history of at least two nocturic episodes per night; and
4. Member has failed behavior modifications including reducing caffeine intake, alcohol intake, and nighttime fluid intake; and
5. Member must have failed a trial of DDAVP® (desmopressin tablets) or have a patient-specific, clinically significant reason why the tablet formulation cannot be used; and
6. The prescriber must be willing to measure serum sodium levels within seven days of anticipated start of treatment and document levels are acceptable; and
7. The prescriber must agree to monitor serum sodium levels within one month of starting treatment or increasing the dose; and
8. The prescriber must confirm the member is not taking any of the following:
  - a. Other medications via the nasal route; or



- b. Loop diuretics; and
- 9. The prescriber must confirm the member does not have renal impairment with an estimated glomerular filtration rate (eGFR) below 50mL/min/1.73m<sup>2</sup>; and
- 10. Initial approvals will be for the duration of 3 months; for continued authorization the prescriber must provide the following:
  - a. Documentation that serum sodium levels are acceptable to the prescriber; and
  - b. Documentation that the member is responding to treatment; and
- 11. A quantity limit of one bottle (3.8g) per 30 days will apply.

Additionally, the College of Pharmacy recommends updating the Bladder Control Medications PBPA Tier-3 criteria to include the use of Myrbetriq® in combination with VESicare® (changes noted in red).

**Bladder Control Medications Tier-3 Approval Criteria:**

- 1. A trial of all Tier-1 and Tier-2 medications that yielded inadequate clinical response or adverse effects; or
- 2. A unique indication which the Tier-1 and Tier-2 medications lack.
- 3. For use of Myrbetriq® (mirabegron) in combination with VESicare® (solifenacin), the member must have failed monotherapy with either mirabegron or solifenacin (minimum 4-week trial) defined by continued symptoms of urge urinary incontinence, urgency, and urinary frequency. Current tier structure rules will also apply.

Finally, the College of Pharmacy recommends the following:

- 1. Move trospium (Sanctura®) from Tier-2 to Tier-1 based on National Average Drug Acquisition Cost (NADAC).
- 2. Move tolterodine ER (Detrol LA®) from Tier-3 to Tier-2 based on NADAC. Current Tier-2 criteria will apply.

Bladder Control Medications			
Tier-1	Tier-2	Tier-3	Special PA
fesoterodine (Toviaz®)	tolterodine (Detrol®)	darifenacin (Enblex®)	desmopressin acetate nasal spray (Noctiva™) <sup>+</sup>
oxybutynin (Ditropan®)	<b>tolterodine ER (Detrol LA®)</b>	mirabegron (Myrbetriq®) <sup>Δ</sup>	<b>desmopressin acetate sublingual tablets (Nocdurna®)<sup>+</sup></b>
oxybutynin ER (Ditropan XL®)		oxybutynin gel (Gelnique®)	oxybutynin patch (Oxytrol®) <sup>+</sup>
<b>trospium (Sanctura®)</b>		solifenacin (VESicare®) <sup>Δ</sup>	
		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; PA = prior authorization

<sup>+</sup>Unique criteria specific to Oxytrol® (oxybutynin patch), Noctiva™ (desmopressin acetate nasal spray), and Nocdurna® (desmopressin acetate sublingual tablet) applies.

<sup>Δ</sup>Unique criteria specific to use of Myrbetriq® (mirabegron) in combination with VESicare® (solifenacin) applies.

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<sup>1</sup> Nocdurna® Prescribing Information. Ferring Pharmaceuticals, Inc. Available online at: <http://www.ferringusa.com/wp-content/uploads/2018/06/NOCDURNA-Prescribing-Information.pdf>. Last revised 06/2018. Last accessed 10/15/2018.

<sup>2</sup> Sand PK, Dmochowski RR, Reddy J, et al. Efficacy and Safety of Low Dose Desmopressin Orally Disintegrating Tablet in Women with Nocturia: Results of a Multicenter, Randomized, Double-Blind, Placebo Controlled, Parallel Group Study. *J Urol* 2013; 190:958-964.

<sup>3</sup> Weiss JP, Herschorn S, Albei CD, et al. Efficacy and Safety of Low Dose Desmopressin Orally Disintegrating Tablet in Men with Nocturia: Results of a Multicenter, Randomized, Double-Blind, Placebo Controlled, Parallel Group Study. *J Urol* 2013; 190:965-972.



# Appendix I





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# Vote to Prior Authorize Krystexxa® (Pegloticase)

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Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1</sup>

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**Krystexxa® (pegloticase)** is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Krystexxa® is supplied as a 1mL sterile concentrate for dilution containing 8mg of pegloticase protein. The recommended dose for adult patients is 8mg given as an intravenous (IV) infusion over 120 minutes every two weeks. Patients should be pre-medicated with antihistamines and corticosteroids. Patients should also discontinue oral urate-lowering agents prior to starting therapy with pegloticase, and serum uric acid (sUA) levels should be monitored prior to each infusion. Pegloticase has a boxed warning for anaphylaxis, infusion related reactions, and glucose-6-phosphate dehydrogenase (G6PD) deficiency-associated hemolysis and methemoglobinemia. The frequency of anaphylaxis in clinical trials was approximately 6%, despite all patients being treated with at least one dose of oral antihistamine(s), plus a corticosteroid and/or acetaminophen. Pre-medication is used to mitigate the risk for anaphylaxis, and patients should be monitored throughout the infusion process by a health care provider. Prior to infusion, sUA levels should be monitored and consideration should be given to discontinuing pegloticase if the patient has two consecutive levels >6mg/dL. Patients should also be screened for G6PD deficiency when appropriate, and pegloticase should not be administered to patients with G6PD deficiency.

## Cost Comparison:

Medication	Cost Per Unit	Cost Per 28 Days
<b>Krystexxa® (pegloticase) 8mg/mL vial</b>	<b>\$20,422.96</b>	<b>\$40,845.92</b>
Zurampic® (lesinurad) 200mg tablet	\$12.37	\$346.36
Uloric® (febuxostat) 40mg tablet	\$10.25	\$287.00
allopurinol 300mg tablet	\$0.15	\$4.20

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

Unit = mL or tablet

## Recommendations

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The College of Pharmacy recommends the prior authorization of Krystexxa® (pegloticase) with the following criteria:

### Krystexxa® (Pegloticase) Approval Criteria:

1. An FDA approved diagnosis of gout; and
2. Member must have symptomatic gout with:
  - a. ≥3 gout flares in the previous 18 months; or
  - b. ≥1 gout tophus; or
  - c. Gouty arthritis; and

3. Failure of the following urate lowering therapies: allopurinol, febuxostat, lesinurad, and probenecid titrated to the maximum tolerable dose for at least 3 months; and
4. Pegloticase must be administered in a health care setting by a health care provider prepared to manage anaphylaxis; and
5. Prescriber must attest that the member will be pre-medicated with antihistamines and corticosteroids to reduce the risk of anaphylaxis; and
6. Prescriber must document that member does not have glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting pegloticase; and
7. Member must discontinue oral urate-lowering agents prior to starting pegloticase; and
8. Member must receive gout flare prophylaxis with non-steroidal anti-inflammatory drug(s) (NSAIDs) or colchicine at least 1 week before initiation of pegloticase therapy and continue for at least 6 months unless medically contraindicated or member is unable to tolerate therapy.
9. Approvals will be for the duration of 6 months. Reauthorizations may be granted if the prescriber documents the member is responding well to treatment, and member has not exceeded >4 consecutive weeks without therapy.

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<sup>1</sup> Krystexxa® Prescribing Information. Horizon Pharma PLC. Available online at: [https://hzn.azureedge.net/public/KRYSTEXXA\\_Prescribing\\_Information.pdf](https://hzn.azureedge.net/public/KRYSTEXXA_Prescribing_Information.pdf). Last revised 07/2018. Last accessed 09/20/2018.



# Appendix J







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# Vote to Prior Authorize Impoyz™ (Clobetasol Propionate 0.025% Cream)

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Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2,3</sup>

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In November 2017, the U.S. Food and Drug Administration (FDA) approved **Impoyz™ (clobetasol propionate 0.025% cream)**, a new lower strength topical formulation of clobetasol. Impoyz™ cream is a topical corticosteroid indicated for the treatment of moderate-to-severe plaque psoriasis in patients 18 years of age and older. Impoyz™ 0.025% cream is available in a 60g tube and the recommended administration is a thin layer applied to the affected skin areas twice daily. Impoyz™ cream can be used for up to two consecutive weeks of treatment. The total dosage of Impoyz™ cream should not exceed 50g per week and use should be discontinued when control is achieved. The active ingredient, clobetasol propionate, is currently available in the 0.05% strength in several formulations including cream, foam, gel, lotion, ointment, liquid spray, topical solution, and shampoo. Impoyz™ cream recently became available on the market as of May 2018 and the Wholesale Acquisition Cost (WAC) of Impoyz™ cream is \$7.50 per gram, resulting in a cost of \$450.00 per 60g tube. Impoyz™ cream currently does not currently have a drug rebate agreement and is not a covered SoonerCare product at this time.

## Market News and Updates<sup>4</sup>

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### Pipeline:

- **October 2018:** BRYHALI™ (halobetasol propionate 0.01% lotion) received tentative approval from the FDA for the topical treatment of plaque psoriasis in adult patients. BRYHALI™ lotion is a new, potent-to-superpotent corticosteroid that contains 0.01% halobetasol propionate in a novel vehicle lotion. The safety of BRYHALI™ has been established in clinical trials with dosing for up to eight weeks with no increase in epidermal atrophy. The final FDA approval for BRYHALI™ lotion is pending the expiration of exclusivity for a related product, Ultravate® (halobetasol 0.05% lotion), which is expected in early November 2018. The company plans to launch BRYHALI™ lotion shortly thereafter, as scheduled, in November 2018. Halobetasol is currently available in the 0.05% strength in several formulations including cream, ointment, and lotion.

## Recommendations

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The College of Pharmacy recommends the placement of Impoyz™ (clobetasol propionate 0.025% cream) into Tier-3 of the Ultra-High to High Potency category of the Topical Corticosteroids Product Based Prior Authorization (PBPA) Tier Chart. Current Tier-3 criteria would apply.

Additionally, the College of Pharmacy recommends the following changes to the Topical Corticosteroids PBPA category:

1. Move Synalar® (fluocinolone acetonide 0.01% cream) from Tier-1 to Tier-2 of the Low Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.
2. Move desonide 0.05% lotion and desonide emollient 0.05% cream and ointment from Tier-2 to Tier-3 of the Low Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.
3. Move mometasone furoate 0.1% ointment from Tier-2 to Tier-1 of the Medium/High to Medium Potency category of the Topical Corticosteroid PBPA Tier Chart based on net cost.

**Tier-1 products are covered with no prior authorization necessary.**

**Tier-2 Topical Corticosteroid Approval Criteria:**

1. Documented trials of all Tier-1 topical corticosteroids of similar potency in the past 30 days that did not yield adequate relief; and
2. If Tier-1 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-2 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1, a patient-specific, clinically significant reason must be provided for use of a special dosage formulation of the requested medication in Tier-2 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

**Tier-3 Topical Corticosteroid Approval Criteria:**

1. Documented trials of all Tier-1 and Tier-2 topical corticosteroids of similar potency in the past 90 days that did not yield adequate relief; and
2. If Tier-1 and Tier-2 trials are completed and do not yield adequate relief, a patient-specific, clinically significant reason for requesting a Tier-3 in the same potency instead of trying a higher potency medication must be provided; and
3. When the same medication is available in Tier-1 or Tier-2, a patient-specific, clinically significant reason must be provided for use of a special dosage form of the requested medication in Tier-3 (e.g., foams, shampoos, sprays, kits); and
4. Topical corticosteroid kits require tier trials and a patient-specific, clinically significant reason for use of the kit over other standard formulations.

Topical Corticosteroids					
Tier-1		Tier-2		Tier-3	
Ultra-High to High Potency					
augmented betamethasone dipropionate 0.05% ( <b>Diprolene AF®</b> )	C,G	amcinonide 0.1%	C,O,L	<b>clobetasol propionate 0.025% (Impoyz™)</b>	<b>C</b>
betamethasone dipropionate 0.05% ( <b>Diprosone®</b> )	<b>O</b>	augmented betamethasone dipropionate 0.05% ( <b>Diprolene®</b> )	<b>O,L</b>	clobetasol propionate 0.05% ( <b>Clobex®</b> )	<b>Sh,Spr</b>

Topical Corticosteroids					
Tier-1		Tier-2		Tier-3	
clobetasol propionate 0.05% ( <b>Temovate</b> <sup>®</sup> )	<b>C,So</b>	betamethasone dipropionate 0.05% ( <b>Diprosone</b> <sup>®</sup> )	<b>C</b>	clobetasol propionate 0.05% ( <b>Olux</b> <sup>®</sup> , <b>Olux-E</b> <sup>®</sup> )	<b>F</b>
fluocinonide 0.05%	<b>C,O,So</b>	clobetasol propionate 0.05% ( <b>Clobex</b> <sup>®</sup> )	<b>L</b>	clobetasol propionate 0.05% ( <b>Temovate</b> <sup>®</sup> )	<b>O</b>
halobetasol propionate 0.05% ( <b>Ultravate</b> <sup>®</sup> )	<b>C</b>	clobetasol propionate 0.05% ( <b>Temovate</b> <sup>®</sup> )	<b>G</b>	desoximetasone 0.25% ( <b>Topicort</b> <sup>®</sup> )	<b>C,O,Spr</b>
		desoximetasone 0.05% ( <b>Topicort</b> <sup>®</sup> )	<b>G</b>		
		diflorasone diacetate 0.05% ( <b>Apexicon</b> <sup>®</sup> )	<b>C</b>		
		diflorasone diacetate 0.05% ( <b>Apexicon E</b> <sup>®</sup> )	<b>C,O</b>		
		fluocinonide 0.05%	<b>G</b>		
		fluocinonide 0.1% ( <b>Vanos</b> <sup>®</sup> )	<b>C</b>		
		flurandrenolide tape 0.05% ( <b>Cordran</b> <sup>®</sup> )	<b>Tape</b>		
		halcinonide 0.1% ( <b>Halog</b> <sup>®</sup> )	<b>C,O</b>		
		halobetasol propionate 0.05% ( <b>Ultravate</b> <sup>®</sup> )	<b>L,O</b>		
		halobetasol propionate/lactic acid 0.05%/10% ( <b>Ultravate X</b> <sup>®</sup> )	<b>C</b>		
Medium/High to Medium Potency					
betamethasone dipropionate 0.05%	<b>L</b>	betamethasone dipropionate/calcipotriene 0.064%/0.005% ( <b>Taclonex</b> <sup>®</sup> )	<b>O,Sus,Spr</b>	betamethasone dipropionate 0.05% ( <b>Sernivo</b> <sup>®</sup> )	<b>Spr</b>
betamethasone valerate 0.1% ( <b>Beta-Val</b> <sup>®</sup> )	<b>C,O,L</b>	betamethasone valerate 0.12% ( <b>Luxiq</b> <sup>®</sup> )	<b>F</b>	hydrocortisone valerate 0.2% ( <b>Westcort</b> <sup>®</sup> )	<b>C,O</b>
fluticasone propionate 0.05% ( <b>Cutivate</b> <sup>®</sup> )	<b>C,O</b>	calcipotriene/betamethasone dipropionate 0.064%/0.005% ( <b>Enstilar</b> <sup>®</sup> )	<b>F</b>		
mometasone furoate 0.1% ( <b>Elocon</b> <sup>®</sup> )	<b>C,L,S,O</b>	clocortolone pivalate 0.1% ( <b>Cloderm</b> <sup>®</sup> )	<b>C</b>		
triamcinolone acetonide 0.025%	<b>O</b>	desoximetasone 0.05% ( <b>Topicort LP</b> <sup>®</sup> )	<b>C,O</b>		
triamcinolone acetonide 0.1%	<b>C,O,L</b>	fluocinolone acetonide 0.025% ( <b>Synalar</b> <sup>®</sup> )	<b>C,O</b>		
triamcinolone acetonide 0.5%	<b>C,O</b>	fluocinonide emollient 0.05% ( <b>Lidex E</b> <sup>®</sup> )	<b>C</b>		
		flurandrenolide 0.05%	<b>C,L,O</b>		
		fluticasone propionate 0.05% ( <b>Cutivate</b> <sup>®</sup> )	<b>L</b>		
		hydrocortisone butyrate 0.1%	<b>C,O,L,S</b>		
		hydrocortisone probutate 0.1% ( <b>Pandel</b> <sup>®</sup> )	<b>C</b>		

Topical Corticosteroids					
Tier-1		Tier-2		Tier-3	
		prednicarbate 0.1% ( <b>Dermatop</b> <sup>®</sup> )	O,C		
		triamcinolone acetonide 0.147mg/g ( <b>Kenalog</b> <sup>®</sup> )	Spr		
Low Potency					
desonide 0.05% ( <b>Desonate</b> <sup>®</sup> )	G	alclometasone dipropionate 0.05% ( <b>Aclovate</b> <sup>®</sup> )	C,O	fluocinolone acetonide 0.01% ( <b>Derma-Smoothe</b> <sup>®</sup> ; <b>Derma-Smoothe FS</b> <sup>®</sup> )	Oil
fluocinolone acetonide 0.01% ( <b>Capex</b> <sup>®</sup> )	Sh	desonide 0.05% ( <b>Verdeso</b> <sup>®</sup> )	F	<b>desonide 0.05%</b>	L
hydrocortisone acetate 1%	C,O	fluocinolone acetonide 0.01% ( <b>Synalar</b> <sup>®</sup> )	So,C	<b>desonide emollient 0.05%</b>	C,O
hydrocortisone acetate 2.5%	C,O, L	hydrocortisone 2.5% ( <b>Texacort</b> <sup>®</sup> )	So		
hydrocortisone/urea 1%/10% ( <b>U-Cort</b> <sup>®</sup> )	C	hydrocortisone/pramoxine 1%/1% ( <b>Pramosone</b> <sup>®</sup> )	C,L		
triamcinolone acetonide 0.025%	C,L				

C= Cream; O = Ointment; L = Lotion; G = Gel, Sh = Shampoo; So = Solution; Spr = Spray; Sus = Suspension; F = Foam  
Tier structure based on supplemental rebate participation and/or National Average Drug Acquisition Costs (NADAC) or Wholesale Acquisition Costs (WAC) if NADAC unavailable.

<sup>1</sup> U.S. Food and Drug Administration (FDA) Drug Approvals. Impozyz<sup>™</sup> (clobetasol propionate) cream. Available online at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2017/209483Orig1s000TOC.cfm](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209483Orig1s000TOC.cfm). Issued 03/14/2017. Last accessed 10/11/2018.

<sup>2</sup> Encore Dermatology, Inc. Encore Dermatology Inc. Announces the Launch of Impozyz<sup>™</sup> (Clobetasol Propionate) Cream 0.025%, a newly formulated high-potency topical corticosteroid. Available online at: <http://www.encorederm.com/news/item/news-article-1-copy-3>. Issued 05/01/2018. Last accessed 10/11/2018.

<sup>3</sup> Impozyz<sup>™</sup> (Clobetasol Propionate) Cream 0.025% Prescribing Information. Encore Dermatology, Inc. Available online at: <http://www.encorederm.com/images/documents/Impozyz-Package-Insert--Patient-Information.pdf>. Last revised 11/2017. Last accessed 10/11/2018.

<sup>4</sup> Bausch Health Companies, Inc. Bausch Health's BRYHALI<sup>™</sup> (halobetasol propionate) Lotion, 0.01%, Receives Tentative FDA Approval for Plaque Psoriasis in Adults. *PR Newswire*. Available online at: [https://www.bauschhealth.com/news-room/news-releases/news-details/201810080700pr\\_news\\_uspr\\_ny31622](https://www.bauschhealth.com/news-room/news-releases/news-details/201810080700pr_news_uspr_ny31622). Issued 10/08/2018. Last accessed 10/11/2018.



# Appendix K





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# Fiscal Year 2018 Annual Review of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators and 30-Day Notice to Prior Authorize Symdeko® (Tezacaftor/Ivacaftor) and Orkambi® (Lumacaftor/Ivacaftor Oral Granules)

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Oklahoma Health Care Authority  
November 2018

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## Current Prior Authorization Criteria

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### Kalydeco® (Ivacaftor) Approval Criteria:

1. An FDA approved diagnosis of cystic fibrosis (CF) with a mutation in the *CFTR* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
2. Documentation must be submitted with results of *CFTR* genetic testing; and
3. Member must be 2 years of age or older; and
4. A quantity limit of two tablets or two granule packets per day (56 per 28 days) will apply.
5. 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 FEV<sub>1</sub>, will be required for continued approval.

### 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 member'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 FEV<sub>1</sub>, will be required for continued approval.

## Utilization of CFTR Modulators: Fiscal Year 2018

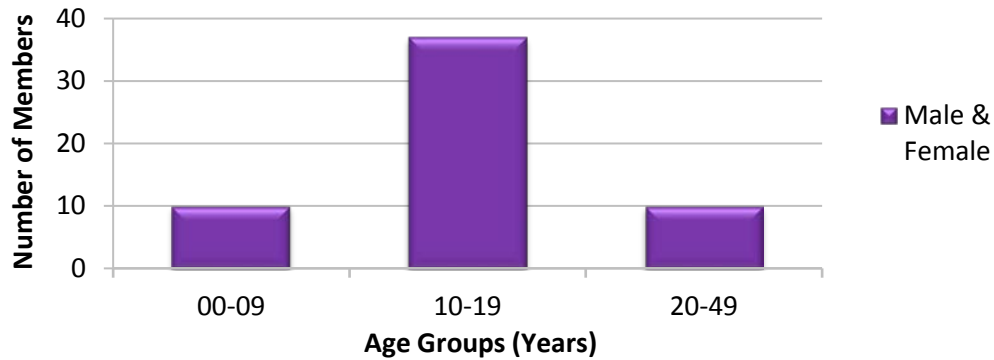
### Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2017	58	387	\$7,983,972.96	\$20,630.42	\$735.85	39,816	10,850
2018	57	472	\$10,081,544.76	\$21,359.21	\$762.83	44,968	13,216
% Change	-1.70%	22.00%	26.30%	3.50%	3.70%	12.90%	21.80%
Change	-1	85	\$2,097,571.80	\$728.79	\$26.98	5,152	2,366

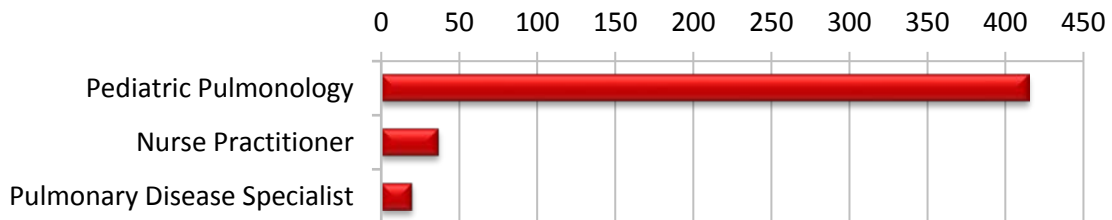
\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

### Demographics of Members Utilizing CFTR Modulators



### Top Prescriber Specialties of CFTR Modulators by Number of Claims

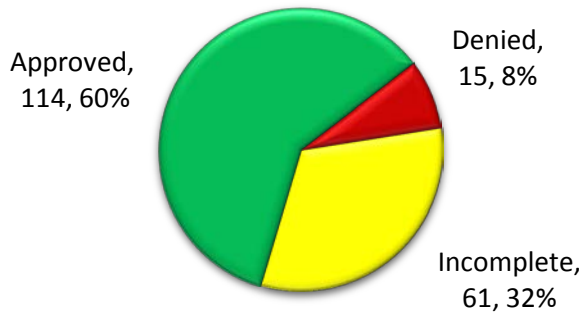


## Prior Authorization of CFTR Modulators

There were 190 prior authorization requests submitted for CFTR modulators during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



### Status of Petitions



### Market News and Updates<sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18</sup>

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#### Anticipated Patent Expiration(s):

- Kalydeco<sup>®</sup> (ivacaftor tablets): August 2027
- Orkambi<sup>®</sup> (lumacaftor/ivacaftor tablets and granules): December 2030
- Kalydeco<sup>®</sup> (ivacaftor granules): February 2033
- Symdeko<sup>®</sup> (tezacaftor/ivacaftor and ivacaftor tablets): July 2033

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

- **February 2018:** The FDA approved Symdeko<sup>®</sup> (tezacaftor/ivacaftor and ivacaftor tablets) to treat cystic fibrosis (CF) in patients 12 years of age and older who have two copies of the *F508del* mutation or one mutation that is responsive to Symdeko<sup>®</sup>.
- **August 2018:** The FDA approved an expanded age range for Orkambi<sup>®</sup> (lumacaftor/ivacaftor) to include treatment in children ages 2 through 5 years with CF who have two copies of the *F508del-CFTR* mutation, and approved a new oral granule formulation of Orkambi<sup>®</sup> in two dosage strengths (lumacaftor 100mg/ivacaftor 125mg and lumacaftor 150mg/ivacaftor 188mg) for weight-based dosing. Orkambi<sup>®</sup> was first approved in ages 12 years and older in July of 2015 and in September 2016 was approved for expanded use in children 6 to 11 years of age.
- **August 2018:** The FDA approved Kalydeco<sup>®</sup> (ivacaftor) to include use in children with CF ages 12 months and older who have at least one mutation in their *CFTR* gene that is responsive to Kalydeco<sup>®</sup> based on clinical and/or *in vitro* assay data. This FDA approval is based on data from an ongoing Phase 3 open-label safety study (ARRIVAL) of 25 children with CF aged 12 to <24 months who have one of 10 mutations in the *CFTR* gene (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P*, *G1349D*, or *R117H*). The study is ongoing in infants younger than one year of age. Kalydeco<sup>®</sup> was previously FDA approved for the treatment of CF in patients 2 years of age and older who have one of 38 ivacaftor-responsive mutations in the *CFTR* gene based on clinical and/or *in vitro* assay data.

#### News:

- **June 2018:** The Institute for Clinical and Economic Review (ICER) released its Final Evidence Report and Report-at-a-Glance on CFTR modulators for CF. The report was reviewed at a May 2018 public meeting of The Midwest Comparative Effectiveness

Public Advisory Council (CEPAC), one of ICER's three independent evidence appraisal committees. A majority of the CEPAC voted that, in their specified indications, Kalydeco<sup>®</sup>, Orkambi<sup>®</sup>, and Symdeko<sup>®</sup>, in combination with best supportive care, all offer a net health benefit compared to best supportive care alone, and voted that the therapies represent a low long-term value for money, due in large part to the high price of the drugs. ICER stated the price of Kalydeco<sup>®</sup>, Orkambi<sup>®</sup>, and Symdeko<sup>®</sup> would need to decrease by 71 to 77% to meet common cost-effectiveness thresholds. Among populations with different types of genetic mutations, the cost of the drugs was far greater than the common threshold for cost-effectiveness, \$100,000-\$150,000 per quality-adjusted life year (QALY) gained. The Vertex drug prices run from \$272,000 to \$311,000 annually. To be cost-effective, the analysis found Kalydeco<sup>®</sup> would have to cost between \$72,500 and \$86,450, while Orkambi<sup>®</sup> would need to cost between \$67,800 and \$80,000, and Symdeko<sup>®</sup>, the newest of the drugs, would need to run from \$68,200 to \$81,200. Many members of the Midwest CEPAC noted that the therapies offer other benefits beyond those looked at in clinical trials, such as reduced caregiver burden, a treatment option for patients in whom other therapies have not been effective, and improved ability for patients to return to work, school, or other activities. ICER stresses the manufacturer of these products bears a social responsibility to provide a transparent justification for prices based on the treatments' abilities to improve the length and quality of patients' lives.

- **October 2018:** The Canadian Agency for Drugs and Technologies in Health rejected Vertex's CF drug Orkambi<sup>®</sup> (lumacaftor/ivacaftor). The independent advisory group based its decision on uncertainty over clinical trials measuring the drug's effect on patient health and also cited lack of data on how the drug impacts survival or the necessity of lung transplants. The agency claimed Vertex Pharmaceuticals would have to lower its nearly \$249,000 price tag by up to 98.5%, depending on the patient population, to meet the QALY threshold. The recommendation is non-binding but federal, provincial, and territorial governments frequently follow the group's advice.

#### **Pipeline:**

- **January 2018:** Corbus Pharmaceuticals Holdings, Inc. announced that it has reached an agreement with the FDA on the design of a Phase 2b clinical trial for lenabasum (formerly known as anabasum, resunab, and JBT-101) a novel, oral, synthetic, investigational compound being developed to resolve chronic inflammation in patients with CF, systemic sclerosis, dermatomyositis, and systemic lupus erythematosus (SLE). Lenabasum is an oral compound that mimics the effects of endocannabinoids. Endocannabinoids are naturally-occurring chemicals in the body that are involved in regulating appetite, metabolism, mood, pain, and inflammation. Lenabasum preferentially binds to cannabinoid receptor type 2 (CB2), which is found primarily on the surfaces of activated immune cells. Upon binding to the CB2 receptors, lenabasum triggers the production of pro-inflammatory mediators, which reduce inflammation. Ultimately, lenabasum acts to "turn off" chronic inflammation and halt tissue thickening and scarring (fibrosis) without suppressing the activity of the immune system. It is thought that reducing inflammation could help prevent permanent tissue damage in the

lungs of people with CF. The Phase 2b CF study will include adolescents 12 to 17 years of age and the primary endpoint will be the occurrence of lung exacerbations. The FDA agreed that the event rate of pulmonary exacerbation is an acceptable sole primary efficacy endpoint for the clinical development program to support registration of lenabasum for the treatment of CF. Event rate of pulmonary exacerbation is the average number of pulmonary exacerbations per subject per time period. The Phase 2b multicenter, double-blinded, randomized, placebo-controlled study will enroll approximately 415 subjects with CF who are  $\geq 12$  years of age and at an increased risk for pulmonary exacerbations. Secondary efficacy outcomes include other measures of pulmonary exacerbations, change in CF Questionnaire-Revised (CFQ-R) respiratory domain score, and change in the percent predicted forced expiratory volume in 1 second (ppFEV<sub>1</sub>). The study will be conducted in approximately 100 sites across North America, Europe, Israel, and Australia. Subjects will be centrally randomized to one of three cohorts to receive lenabasum 20mg twice per day, lenabasum 5mg twice per day, or placebo twice per day for 28 weeks, with 4 weeks follow-up off active treatment. This Phase 2b CF study was designed with input from the Therapeutic Development Network of the CF Foundation and the European CF Society Clinical Trials Network. The planned Phase 2b clinical trial also has received a \$25 million Development Award from the CF Foundation in the United States.

- **April 2018:** Vertex Pharmaceuticals announced plans to conduct additional dose-ranging studies with VX-561 to support potential late-stage development of the novel agent used in an oral, triple-drug combination with tezacaftor/ivacaftor following the FDA's request for additional dose-ranging studies and monotherapy studies for VX-561.
- **June 2018:** Galapagos, a clinical-stage biotechnology company, announced topline results for the PELICAN study, the first Phase 2 trial for a novel C2 corrector, GLPG2737, in adult CF patients who are homozygous for the Class II *F508del* mutation. Participating patients were on stable treatment with Orkambi® for at least 12 weeks prior to the first study drug administration and were required to continue Orkambi® for the duration of the trial. Eligible patients were randomized to receive GLPG2737 (N=14) or placebo (N=8) over a period of 4 weeks, with up to 3 weeks follow-up. The primary endpoint was the change from baseline in sweat chloride concentration compared to placebo at day 28. The mean change from baseline in sweat chloride for the GLPG2737 treatment arm on day 28 versus placebo was a significant decrease of 19.6mmol/L (P=0.02). A positive trend in ppFEV<sub>1</sub> changes was also observed. The mean absolute change from baseline in ppFEV<sub>1</sub> for the GLPG2737 treatment arm versus placebo through day 28 was 3.4% (P=0.08). Further details will be presented at a future conference.
- **June 2018:** Galapagos announced an update on their triple combination therapy development plans. FALCON, a clinical trial with an investigational triple combination therapy comprising potentiator GLPG2451, C1 corrector GLPG2222, and C2 corrector GLPG2737 is currently underway. The first interim data from this trial are expected in the third quarter of 2018. AbbVie has decided not to proceed with the previously contemplated second triple combination therapy, consisting of the same C1 and C2 components combined with potentiator GLPG3067. Galapagos is reviewing the future of its CF collaboration with AbbVie.

- September 2018:** Vertex Pharmaceuticals announced that enrollment is complete for two Phase 3 studies of the next-generation corrector VX-659 in triple combination with tezacaftor/ivacaftor in patients with CF with one *F508del* mutation and one minimal function mutation and in patients with CF with two *F508del* mutations. Based on the completion of enrollment, Vertex expects to report data from both Phase 3 studies of the VX-659 triple combination regimen in late 2018. Vertex expects to complete enrollment of the two Phase 3 studies of the next-generation corrector VX-445 in triple combination with tezacaftor/ivacaftor in the fourth quarter of 2018 and to report data from these studies in the first quarter of 2019. Vertex plans to evaluate data from both the VX-659 and VX-445 Phase 3 triple combination programs to choose the best regimen to submit for potential regulatory approval. The data anticipated in late 2018 for VX-659 and in the first quarter of 2019 for VX-445 are expected to provide the basis for submission of a New Drug Application (NDA) to the FDA for CF patients with one *F508del* mutation and one minimal function mutation no later than mid-2019.
- October 2018:** Celtaxys, Inc. announced results of the Phase 2 EMPIRE-CF trial evaluating their once-daily anti-inflammatory molecule, acebilustat, for the treatment of CF, irrespective of the causative genotype. In the 200 patient, double-blind, placebo-controlled study, acebilustat demonstrated clinically meaningful improvements in pulmonary exacerbations, both reducing the frequency of pulmonary exacerbations and increasing time to next exacerbation over 48 weeks of therapy. These results showed that acebilustat-treated patients (N=133) exhibited a 19% reduction in pulmonary exacerbations and a 22% reduced risk in progressing to first pulmonary exacerbations versus placebo on a per protocol basis. Patients with less severe impairment of lung function (ppFEV<sub>1</sub> >75; N=47) achieved the largest benefit from acebilustat treatment, achieving a 35% reduction in pulmonary exacerbation rate, a 43% reduction in risk of experiencing their first exacerbation, and a 96% increased likelihood of being free of exacerbations after 48 weeks of treatment versus placebo. Furthermore, patients concomitantly treated with CFTR modulator therapy (N=43) exhibited a clinically meaningful 20% reduction in pulmonary exacerbations, a 29% increased time to first exacerbation, and a 47% higher likelihood of no exacerbations compared to patients treated with CFTR modulators and placebo. Celtaxys, with continued support from the CF Foundation, has commenced preparations for designing and executing the Phase 3 clinical program of acebilustat.

## **Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor Tablets) Product Summary<sup>19</sup>**

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**Indication(s):** Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets) is a combination of tezacaftor and ivacaftor, indicated for the treatment of patients with CF 12 years of age and older who are homozygous for the *F508del* mutation or who have at least one mutation in the *CFTR* gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence.

- If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

**Dosing:**

- Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets) is co-packaged as tezacaftor 100mg/ivacaftor 150mg fixed-dose combination tablets and ivacaftor 150mg tablets.
- The recommended dose for adults and pediatric patients 12 years of age and older is one tablet (containing tezacaftor 100mg/ivacaftor 150mg) in the morning and one tablet (containing ivacaftor 150mg) in the evening, approximately 12 hours apart.
- Symdeko® should be taken with fat-containing food.
- The dose should be reduced in patients with moderate or severe hepatic impairment.
- The dose should be reduced when co-administered with drugs that are moderate or strong CYP3A inhibitors (*see Symdeko® prescribing information for full dosing information*).

**Mechanism of Action:** Tezacaftor facilitates the cellular processing and trafficking of normal and select mutant forms of CFTR (including *F508del*-CFTR) to increase the amount of mature CFTR protein delivered to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface. For ivacaftor to function, CFTR protein must be present at the cell surface. Ivacaftor can potentiate the CFTR protein delivered to the cell surface by tezacaftor, leading to a further enhancement of chloride transport than either agent alone. The combined effect of tezacaftor and ivacaftor is increased quantity and function of CFTR protein at the cell surface, resulting in increases in chloride transport.

**Contraindication(s):** None

**Safety:**

- Elevated Transaminases (ALT or AST): Transaminases should be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter. In patients with a history of transaminase elevations, more frequent monitoring should be considered. Dosing should be interrupted in patients with significant elevations of transaminases [e.g., patients with ALT or AST >5 times the upper limit of normal (ULN), or ALT or AST >3 times the ULN with bilirubin >2 times the ULN]. Following resolution of transaminase elevations, the benefits and risks of resuming treatment should be considered.
- Use with CYP3A Inducers: Concomitant use of Symdeko® with strong CYP3A inducers (e.g., rifampin, St. John's wort) substantially decreases exposure of ivacaftor and may decrease the exposure of tezacaftor, which may reduce therapeutic effectiveness. Co-administration is not recommended.
- Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with Symdeko®. Baseline and follow-up examinations should be recommended in pediatric patients initiating Symdeko® treatment.

**Use in Specific Populations:**

- Pregnancy: There are limited and incomplete human data from clinical trials and post-marketing reports on the use of Symdeko® or its individual components, tezacaftor and ivacaftor, in pregnant women to inform a drug-associated risk.

- **Lactation:** There is no information regarding the presence of tezacaftor or ivacaftor in human milk, the effects on the breastfed infant, or the effects on milk production. Both tezacaftor and ivacaftor are excreted into the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Symdeko<sup>®</sup> and any potential adverse effects on the breastfed child from Symdeko<sup>®</sup> or from the underlying maternal condition.
- **Pediatric Use:** The safety and efficacy of Symdeko<sup>®</sup> in patients with CF younger than 12 years of age have not been studied.
- **Geriatric Use:** Clinical trials of Symdeko<sup>®</sup> did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.
- **Hepatic Impairment:** No dose adjustment is necessary for patients with mild hepatic impairment (Child-Pugh Class A). A reduced dose of Symdeko<sup>®</sup> is recommended in patients with moderate hepatic impairment (Child-Pugh Class B). There is no experience in patients with severe hepatic impairment (Child-Pugh Class C), but tezacaftor/ivacaftor exposure is expected to be higher than in patients with moderate hepatic impairment. Therefore, it is recommended to use with caution at a reduced dose in patients with severe hepatic impairment after weighing the risks and benefits of treatment.
- **Renal Impairment:** Symdeko<sup>®</sup> has not been studied in patients with moderate or severe renal impairment or in patients with end-stage renal disease. No dose adjustment is recommended for mild and moderate renal impairment. Caution should be used in patients with severe renal impairment or end-stage renal disease.
- **Severe Lung Dysfunction:** Trial 1 and Trial 2 included a total of 39 Symdeko<sup>®</sup>-treated patients with ppFEV<sub>1</sub> <40 at baseline (range 30 to 40); there were a total of 39 placebo-treated patients and 13 ivacaftor-treated patients in Trials 1 and 2 with ppFEV<sub>1</sub> <40 at baseline. The safety and efficacy in this subgroup were comparable to the overall results observed in both Trials 1 and 2.

#### **Drug Interactions:**

- **CYP3A Inhibitors:** The Symdeko<sup>®</sup> dose should be reduced when co-administered with strong (e.g., ketoconazole) or moderate (e.g., fluconazole) CYP3A inhibitors. Patients should avoid food containing grapefruit or Seville oranges.

**Adverse Reactions:** The most common adverse drug reactions to Symdeko<sup>®</sup> (occurring in ≥3% of patients) reported in clinical trials were headache, nausea, sinus congestion, and dizziness.

**Efficacy:** The safety and efficacy of Symdeko<sup>®</sup> was studied in three placebo-controlled trials, including one trial in CF patients with two copies of the *F508del* mutation (HoF508), one trial in CF patients with one copy of the *F508del* mutation (HeF508), and a third trial in CF patients who were heterozygous for the *F508del* mutation and a second *CFTR* mutation predicted to be unresponsive to tezacaftor/ivacaftor.

- The primary endpoint in all trials was the absolute change from baseline in ppFEV<sub>1</sub>.
- Patients in all trials continued on their standard-of-care CF therapies (e.g., bronchodilators, inhaled antibiotics, dornase alfa, hypertonic saline) and were eligible to roll over into a 96-week open-label extension study.

- Patients had a ppFEV<sub>1</sub> at screening between 40 and 90%.
- Patients with a history of colonization with organisms associated with a more rapid decline in pulmonary status such as *Burkholderia cenocepacia*, *Burkholderia dolosa*, or *Mycobacterium abscessus*, or who had ≥2 abnormal liver function tests at screening [ALT, AST, alkaline phosphatase, gamma-glutamyl transferase ≥3 times the ULN or total bilirubin ≥2 times the ULN) or AST or ALT ≥5 times the ULN were excluded from the trials.

#### Study 1:

- Study 1, EVOLVE, was a 24-week double-blind, randomized, placebo-controlled, two-arm study in CF patients who were homozygous for the *F508del* mutation in the *CFTR* gene. EVOLVE evaluated 504 patients with CF 12 years of age and older. The mean ppFEV<sub>1</sub> at baseline was 60% (range 27.8% to 96.2%). The treatment difference between Symdeko<sup>®</sup> and placebo for the mean absolute change in ppFEV<sub>1</sub> from baseline through week 24 was 4.0 percentage points [95% confidence interval (CI): 3.1, 4.8; P<0.0001]. Improvements in ppFEV<sub>1</sub> were observed regardless of age, sex, baseline ppFEV<sub>1</sub>, colonization with *Pseudomonas*, concomitant use of standard-of-care medications for CF, and geographic region.

#### Study 2:

- Study 2, EXPAND, was a randomized, double-blind, placebo-controlled, 2-period, 3-treatment, 8-week crossover study in CF patients who were heterozygous for the *F508del* mutation and a second mutation predicted to be responsive to tezacaftor/ivacaftor. EXPAND evaluated 244 patients with CF 12 years of age or older and the mean ppFEV<sub>1</sub> at baseline was 62.3% (range 34.6% to 93.5%).
- Of the 244 patients included in the efficacy analysis, 146 patients had a splice mutation and 98 patients had a missense mutation as the second allele. A total of 161 patients received Symdeko<sup>®</sup>, 156 patients received ivacaftor, and 161 patients received placebo. The primary efficacy endpoint was the mean absolute change from study baseline in ppFEV<sub>1</sub> averaged at weeks 4 and 8 of treatment. The key secondary efficacy endpoint was absolute change in CFQ-R respiratory domain score from study baseline averaged at weeks 4 and 8 of treatment.
- For the overall population, treatment with Symdeko<sup>®</sup> compared to placebo resulted in significant improvement in ppFEV<sub>1</sub> [6.8 percentage points (95% CI: 5.7, 7.8); P<0.0001] and CFQ-R respiratory domain score [11.1 points (95% CI 8.7, 13.6); P<0.0001]. Treatment difference for ppFEV<sub>1</sub> between ivacaftor- and placebo-treated patients was 4.7 percentage points (95% CI: 3.7, 5.8; P<0.0001) and 2.1 percentage points (95% CI: 1.2, 2.9; P<0.0001) between Symdeko<sup>®</sup> and ivacaftor-treated patients, which were statistically significant. Improvements in ppFEV<sub>1</sub> were observed regardless of age, baseline ppFEV<sub>1</sub>, sex, mutation class, colonization with *Pseudomonas*, concomitant use of standard-of-care medications for CF, and geographic region. Statistically significant improvements compared to placebo were also observed in the subgroup of patients with splice mutations and missense mutations.

#### Study 3:

- Study 3 was a 12-week, randomized, double-blind, placebo-controlled, two-arm study in 168 CF patients 12 years of age and older who were heterozygous for the *F508del*

mutation and a second *CFTR* mutation predicted to be unresponsive to tezacaftor/ivacaftor. Mutations predicted to be non-responsive were selected for the study based on biologic plausibility (mutation class), clinical phenotype (pancreatic insufficiency), biomarker data (sweat chloride), and *in vitro* testing to tezacaftor and/or ivacaftor.

- CF patients with the *F508del* mutation and one of the following mutations in the *CFTR* gene were enrolled in the study (listed in decreasing frequency): *W1282X, G542X, N1303K, 621+1G>T, 1717-1G>A, 1898+1G>A, CFTRdele2,3, 2183deIAA>G, 2184insA, R1162X, R553X, 3659delC, 3905insT, G970R, I507del, R1066C, R347P, 1154insTC, 1811+1.6kbA>G, 2184delA, 405+1G>A, E60X, G85E, L1077P, Q39X, S466X, Y1092X, 1078delT, 1248+1G>A, 1677delTA, 1812-1G>A, 2869INSG, 3120+1G>A, 394delTT, 457TAT>G, 711+1G>T, 711+5G>A, 712-1G>T, G673x, L1065P, Q220X, Q493X, R709X, V520F*. The mean ppFEV<sub>1</sub> at baseline was 57.5% (range: 31.0 to 96.7).
- The primary efficacy endpoint was change from baseline in absolute ppFEV<sub>1</sub> through week 12. The overall treatment difference between Symdeko® and placebo for the mean absolute change in ppFEV<sub>1</sub> from baseline through week 12 was 1.2 percentage points (95% CI: -0.3, 2.6). This study was terminated following the planned interim analysis because the pre-specified futility criteria were met.

**Cost:**

Medication	Cost Per Tablet	Cost Per 28 Days	Cost Per Year
<b>Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets) 100/150mg and 150mg</b>	<b>\$400.00</b>	<b>\$22,400.00*</b>	<b>\$291,200.00*</b>
Orkambi® (lumacaftor/ivacaftor) 200/125mg	\$186.78	\$20,919.36 <sup>+</sup>	\$271,951.68 <sup>+</sup>
Kalydeco® (ivacaftor) 150mg	\$426.72	\$23,896.32 <sup>¥</sup>	\$310,652.16 <sup>¥</sup>

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.

\*Symdeko® FDA approved regimen is one tablet (containing tezacaftor 100mg/ivacaftor 150mg) in the morning and one tablet (containing ivacaftor 150mg) in the evening, approximately 12 hours apart.

<sup>+</sup>Orkambi® FDA approved regimen is two tablets every 12 hours.

<sup>¥</sup>Kalydeco® FDA approved regimen is one tablet every 12 hours.

**Recommendations**

The College of Pharmacy recommends the prior authorization of Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets) and recommends updating the current Orkambi® (lumacaftor/ivacaftor) and Kalydeco® (ivacaftor) prior authorization criteria. The following criteria would apply (changes noted in red):

**Symdeko® (Tezacaftor/Ivacaftor) Approval Criteria:**

1. An FDA approved diagnosis of cystic fibrosis (CF) in patients who are homozygous for the *F508del* mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene detected by genetic testing that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence; and



2. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing, when recommended by the mutation test instructions for use; and
3. Member must be 12 years of age or older; and
4. Members using Symdeko® must be supervised by a pulmonary specialist; and
5. If member is currently stabilized on Orkambi® (lumacaftor/ivacaftor) and experiencing adverse effects associated with Orkambi® use, the prescriber must indicate that information on the prior authorization request; and
6. The prescriber must verify that the member has been counseled on proper administration of Symdeko® including taking with a fat-containing food; and
7. The prescriber must verify that ALT, AST, and bilirubin will be assessed prior to initiating Symdeko®, every three months during the first year of treatment, and annually thereafter; and
8. Members must not be taking any of the following medications concomitantly with Symdeko®: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort; and
9. A quantity limit of two tablets per day or 56 tablets per 28 days will apply.
10. 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 FEV<sub>1</sub>, will be required for continued approval. Additionally after six months of utilization, information regarding efficacy as previously mentioned or fewer adverse events must be provided for members who switched from Orkambi® to Symdeko®.

**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 member'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~~ 2 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 **or a quantity limit of two packets per day or 56 packets per 28 days will apply.**
9. **An age restriction of 2 years to 6 years of age will apply to Orkambi® oral granule packets. Members age 7 years or older will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation.**

- 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 FEV<sub>1</sub>, will be required for continued approval.

**Kalydeco® (Ivacaftor) Approval Criteria:**

- An FDA approved indication of cystic fibrosis (CF) with a mutation in the *CFTR* gene detected by genetic testing that is responsive to ivacaftor based on clinical and/or *in vitro* assay data; and
- Documentation must be submitted with results of *CFTR* genetic testing; and
- Member must be **≥ 1** years of age or older; and
- A quantity limit of two tablets or two granule packets per day (56 per 28 days) will apply.
- 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 FEV<sub>1</sub>, will be required for continued approval.

**Utilization Details of CFTR Modulators: Fiscal Year 2018**

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ DAY	COST/ CLAIM	% COST
<b>IVACAFTOR PRODUCTS</b>						
KALYDECO TAB 150MG	95	10	\$2,223,510.31	\$835.91	\$23,405.37	22.06%
KALYDECO PAK 50MG	2	1	\$47,813.36	\$853.81	\$23,906.68	0.47%
<b>SUBTOTAL</b>	<b>97</b>	<b>11</b>	<b>\$2,271,323.67</b>	<b>\$836.28</b>	<b>\$23,415.71</b>	<b>22.53%</b>
<b>TEZACAFTOR/IVACAFTOR AND IVACAFTOR COMBINATION PRODUCTS</b>						
SYMDEKO TAB 100-150MG	44	19	\$986,001.20	\$800.33	\$22,409.12	9.78%
<b>SUBTOTAL</b>	<b>44</b>	<b>19</b>	<b>\$986,001.20</b>	<b>\$800.33</b>	<b>\$22,409.12</b>	<b>9.78%</b>
<b>LUMACAFTOR/IVACAFTOR COMBINATION PRODUCTS</b>						
ORKAMBI TAB 100-125MG	167	20	\$3,414,733.55	\$730.27	\$20,447.51	33.87%
ORKAMBI TAB 200-125MG	164	22	\$3,409,486.34	\$742.48	\$20,789.55	33.82%
<b>SUBTOTAL</b>	<b>331</b>	<b>42</b>	<b>\$6,824,219.89</b>	<b>\$736.32</b>	<b>\$20,616.98</b>	<b>67.69%</b>
<b>TOTAL</b>	<b>472</b>	<b>57*</b>	<b>\$10,081,544.76</b>	<b>\$762.83</b>	<b>\$21,359.21</b>	<b>100%</b>

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

<sup>1</sup> U.S. Food and Drug Administration (FDA) Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Available online at: <https://www.accessdata.fda.gov/scripts/cder/ob/>. Last revised 08/2018. Last accessed 10/11/2018.

<sup>2</sup> Vertex Pharmaceuticals, Inc. FDA Approves Symdeko™ (tezacaftor/ivacaftor and ivacaftor) to treat the Underlying Cause of Cystic Fibrosis in People Ages 12 and Older with Certain Mutations in the CFTR Gene. Available online at <https://investors.vrtx.com/news-releases/news-release-details/fda-approves-symdekotm-tezacaftorivacaftor-and-ivacaftor-treat?ReleaseID=1057241>. Issued 02/12/2018. Last accessed 10/22/2018.

<sup>3</sup> Vertex Pharmaceuticals, Inc. FDA Approves Orkambi® (lumacaftor/ivacaftor) as First Medicine to Treat the Underlying Cause of Cystic Fibrosis for Children Ages 2-5 Years with Most Common Form of the Disease. Available online at: <https://investors.vrtx.com/news-releases/news-release-details/fda-approves-orkambir-lumacaftorivacaftor-first-medicine-treat>. Issued 08/07/2018. Last accessed 10/22/2018.

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- <sup>4</sup> FDA Drug Approvals. Orkambi® (lumacaftor/ivacaftor). Available online at: <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=211358>. Issued 08/07/2018. Last accessed 10/22/2018.
- <sup>5</sup> Vertex Pharmaceuticals, Inc. FDA Approves Orkambi® (lumacaftor/ivacaftor) - the First Medicine to Treat the Underlying Cause of Cystic Fibrosis for People Ages 12 and Older with Two Copies of the F508del Mutation. Available online at: <https://investors.vrtx.com/news-releases/news-release-details/fda-approves-orkambitm-lumacaftorivacaftor-first-medicine-treat>. Issued 07/02/2015. Last accessed 10/22/2018.
- <sup>6</sup> Vertex Pharmaceuticals, Inc. 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 online at: <https://investors.vrtx.com/news-releases/news-release-details/us-food-and-drug-administration-approves-orkambir?ReleaseID=991350>. Issued 09/28/2016. Last accessed 10/22/2018.
- <sup>7</sup> Vertex Pharmaceuticals, Inc. Vertex Announces Positive Results from Open-Label Phase 3 Study of Kalydeco® (ivacaftor) in Children with Cystic Fibrosis Ages 1 to 2 Years. Available online at: <https://investors.vrtx.com/news-releases/news-release-details/vertex-announces-positive-results-open-label-phase-3-study>. Issued 12/07/2017. Last accessed 10/22/2018.
- <sup>8</sup> Kalydeco® (ivacaftor) Prescribing Information. Vertex Pharmaceuticals, Inc. Available online at: [https://pi.vrtx.com/files/uspi\\_ivacaftor.pdf](https://pi.vrtx.com/files/uspi_ivacaftor.pdf). Last revised 08/2018. Last accessed 10/22/2018.
- <sup>9</sup> Vertex Pharmaceuticals, Inc. FDA Approves Kalydeco® (ivacaftor) as First and Only Medicine to Treat Underlying Cause of CF in Children Ages 12 to <24 Months with Certain Mutations in the CFTR Gene. Available online at: <https://investors.vrtx.com/news-releases/news-release-details/fda-approves-kalydeco-ivacaftor-first-and-only-medicine-treat>. Issued 08/15/2018. Last accessed 10/22/2018.
- <sup>10</sup> Institute for Clinical and Economic Review (ICER). A Look At CFTR Modulators For Cystic Fibrosis. Available online at: [http://icer-review.org/wp-content/uploads/2018/06/MWCEPAC\\_RAAG\\_060718.pdf](http://icer-review.org/wp-content/uploads/2018/06/MWCEPAC_RAAG_060718.pdf). Issued 06/2018. Last accessed 10/24/2018.
- <sup>11</sup> FDA News Drug Daily Bulletin. ICER Slams Cost-Effectiveness of Three Vertex Cystic Fibrosis Drugs. Available online at: <https://www.fdanews.com/articles/print/186711-icer-slams-cost-effectiveness-of-three-vertex-cystic-fibrosis-drugs>. Issued 05/09/2018. Last accessed 10/24/2018.
- <sup>12</sup> FDA News Drug Daily Bulletin. Advisory Group Recommends Against Vertex's Orkambi. Available online at: [https://www.fdanews.com/articles/188786-advisory-group-recommends-against-vertexs-orkambi?utm\\_campaign=Drug%20Daily%20Bulletin&utm\\_source=hs\\_email&utm\\_medium=email&utm\\_content=66654012&hsenc=p2ANqtz-AMWohPD16xaFJeaVd8s1lpcODsH2\\_No1E-gUjy86mYo2hg5uWVwwqNb6O02R32i\\_972oHddjLbwYbzslxRpwaDregIVoKL5m9\\_d8XICzhTwzEU&hsmi=66654012](https://www.fdanews.com/articles/188786-advisory-group-recommends-against-vertexs-orkambi?utm_campaign=Drug%20Daily%20Bulletin&utm_source=hs_email&utm_medium=email&utm_content=66654012&hsenc=p2ANqtz-AMWohPD16xaFJeaVd8s1lpcODsH2_No1E-gUjy86mYo2hg5uWVwwqNb6O02R32i_972oHddjLbwYbzslxRpwaDregIVoKL5m9_d8XICzhTwzEU&hsmi=66654012). Issued 10/15/2018. Last accessed 10/24/2018.
- <sup>13</sup> Lenabasum. *Cystic Fibrosis News Today*. Available online at: <https://cysticfibrosisnewstoday.com/resunab-jbt-101-lung-inflammation-cystic-fibrosis/>. Last accessed 10/24/2018.
- <sup>14</sup> Corbus Pharmaceuticals Holdings, Inc. Corbus Pharmaceuticals Announces Agreement with FDA on Phase 2b Cystic Fibrosis Study Design with Pulmonary Exacerbations as Sole Primary Endpoint. Available online at: <https://www.corbuspharma.com/news/press-releases/detail/260/corbus-pharmaceuticals-announces-agreement-with-fda-on>. Issued 01/29/2018. Last accessed 10/24/2018.
- <sup>15</sup> Vertex Pharmaceuticals, Inc. Vertex Initiates Phase 3 Studies of VX-445, Tezacaftor and Ivacaftor as a Triple Combination Regimen for People with Cystic Fibrosis. Available online at: <https://investors.vrtx.com/node/25056/pdf>. Issued 04/26/2018. Last accessed 10/24/2018.
- <sup>16</sup> Galapagos. Topline Results of PELICAN Trial and Update on Triple Combo Development Plans. Available online at: <http://www.glgp.com/press-releases>. Issued 06/28/2018. Last accessed 10/24/2018.
- <sup>17</sup> Vertex Pharmaceuticals, Inc. Vertex Completes Enrollment of Two Phase 3 Studies of VX-659 in Triple Combination with Tezacaftor and Ivacaftor for the Treatment of Cystic Fibrosis. Available online at: <https://investors.vrtx.com/news-releases/news-release-details/vertex-completes-enrollment-two-phase-3-studies-vx-659-triple>. Issued 09/06/2018. Last accessed 10/24/2018.
- <sup>18</sup> Celtasys, Inc. Results from Celtasys' Acebilustat Phase 2 Trial in Cystic Fibrosis Patients Showing Clinically Meaningful Improvement in Pulmonary Exacerbations Presented at the North American Cystic Fibrosis Conference. Available online at: <http://www.celtasys.com/2018/10/22/results-from-celtasys-acebilustat-phase-2-trial-in-cystic-fibrosis-patients-showing-clinically-meaningful-improvement-in-pulmonary-exacerbations-presented-at-the-north-american-cystic-fibrosis/>. Issued 10/22/2018. Last accessed 10/24/2018.
- <sup>19</sup> Symdeko® (tezacaftor/ivacaftor and ivacaftor) Prescribing Information. Vertex Pharmaceuticals, Inc. Available online at: [https://pi.vrtx.com/files/uspi\\_tezacaftor\\_ivacaftor.pdf](https://pi.vrtx.com/files/uspi_tezacaftor_ivacaftor.pdf). Last revised 02/2018. Last accessed 10/22/2018.





# Appendix L



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# 30-Day Notice to Prior Authorize Onpattro™ (Patisiran) and Tegsedi™ (Inotersen)

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Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2</sup>

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Transthyretin (TTR) amyloidosis is a systemic disorder characterized by the extracellular deposition of amyloid fibrils composed of TTR, a plasma transport protein for thyroxine and vitamin A that is produced predominantly by the liver. TTR amyloidosis is the most common form of hereditary amyloidosis (hATTR amyloidosis) and is caused by mutations that destabilize the TTR protein. The mutation causes TTR to become misfolded and accumulate as amyloid fibrils in various organs and tissues, causing progressive dysfunction.

About 120 different mutations or deletions in the *TTR* gene have been reported. Val30Met is the most common mutation and is primarily associated with neuropathy. Other mutations predominantly induce cardiomyopathy. Although certain mutations may be associated with specific symptoms, hATTR amyloidosis remains a multisystemic disorder, and patients may present with a mixed phenotype, showing both neurologic and cardiac symptoms. Additionally, patients may present with gastrointestinal impairment, nephropathy, or ocular deposition. Patients with stage 0 disease are asymptomatic but have both a variant form of the *TTR* gene and evidence of amyloid deposits. Patients with stage I (mild) disease are ambulatory, patients with stage II (moderate) disease are ambulatory but require assistance, and patients with stage III (severe) disease are bedridden or wheelchair-bound. Carriers of the mutation have a circulating variant protein from fetal life but no amyloid deposition or symptomatic disease until adulthood, with development of disease probably controlled by factors associated with the biochemistry of aging. Because gene expression is incomplete, carriers of the gene may live to an advanced age without symptoms of the disease but their children may become clinically affected.

The incidence of hATTR amyloidosis in the United States is estimated to be 1 in 100,000 individuals. The mean duration of disease onset to death is approximately 10 years but may vary depending on endemic region, genotype, symptoms, and other factors. The current guidelines for hATTR amyloidosis with polyneuropathy recommend confirming diagnosis with neurological exam indicating the presence of neuropathy, tissue biopsy showing amyloid deposits, serum variant TTR protein, and genetic confirmation.

Treatment options for hATTR amyloidosis have historically been limited. The current guidelines recommend liver transplant for patients with early-stage disease. This removes roughly 95% of the production of variant TTR and can slow or halt the progression of the disease. Diflunisal, a non-steroidal anti-inflammatory drug (NSAID), has been used off label for management of hATTR amyloidosis. In clinical studies, diflunisal slowed progression of neurologic impairment and was generally well tolerated. Tafamidis, a disease-modifying agent that kinetically stabilizes

TTR, is available in Europe and undergoing clinical trials in the United States. The guidelines further recommend that once patients have developed stage I disease, they should be treated symptomatically regardless of disease presentation, and diflunisal or any other treatments shown to be efficacious should be started at once. The guidelines have not been updated since the U.S. Food and Drug Administration (FDA) approvals of Onpattro™ (patisiran) and Tegsedi™ (inotersen), which are indicated for the treatment of polyneuropathy of hATTR amyloidosis in adults.

## **Onpattro™ (Patisiran) Product Summary<sup>2,3,4,5</sup>**

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**FDA Approval:** August 2018

**Indication(s):** Onpattro™ (patisiran) contains a transthyretin-directed small interfering ribonucleic acid (siRNA) and is indicated for the treatment of the polyneuropathy of hATTR amyloidosis in adults.

### **Dosing:**

- Onpattro™ (patisiran) is supplied as a sterile, preservative-free, 10mg/5mL (2mg/mL) solution for intravenous (IV) infusion in single-dose glass vials.
- Patisiran should be stored at 2°C to 8°C (36°F to 46°F); if refrigeration is not available, patisiran can be stored at room temperature up to 25°C (77°F) for up to 14 days.
- For patients weighing <100kg, the recommended dosage is 0.3mg/kg every 3 weeks via IV infusion.
- For patients weighing ≥100kg, the recommended dosage is 30mg via IV infusion every 3 weeks.
- Patisiran is recommended to be infused over approximately 80 minutes.
- All patients should receive pre-medication prior to patisiran administration to reduce the risk of infusion-related reactions (IRRs). At least 60 minutes prior to the start of infusion all of the following should be administered: IV corticosteroid, oral acetaminophen, IV histamine-1 (H<sub>1</sub>) antagonist, and IV histamine-2 (H<sub>2</sub>) antagonist.

**Mechanism of Action:** Patisiran is a double-stranded siRNA that causes degradation of mutant and wild-type TTR messenger RNA (mRNA) through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

**Contraindication(s):** None

### **Warnings and Precautions:**

- **IRRs:** In clinical studies, all patients received pre-medication with a corticosteroid, acetaminophen, and antihistamines to reduce the risk of IRRs. In a controlled clinical study, 19% of patisiran-treated patients experienced IRRs, compared to 9% of placebo-treated patients. Among patisiran-treated patients who experienced an IRR, 79% experienced the first IRR within the first two infusions. The frequency of IRRs decreased over time. IRRs led to infusion interruption in 5% of patients. IRRs resulted in permanent discontinuation of patisiran in <1% of patients in clinical studies.



- **Reduced Serum Vitamin A Levels and Recommended Supplementation:** Patisiran treatment leads to a decrease in serum vitamin A levels; therefore, supplementation at the recommended daily allowance (RDA) of vitamin A is advised. Higher doses than the RDA of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with patisiran, as serum vitamin A levels do not reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).

#### **Adverse Reactions:**

- Adverse reactions that occurred in  $\geq 5\%$  of patients in the patisiran-treated group and that occurred  $\geq 3\%$  more frequently than in the placebo-treated group in the randomized, controlled clinical trial include the following: upper respiratory tract infections, IRRs, dyspepsia, dyspnea, muscle spasms, arthralgia, erythema, bronchitis, and vertigo.
- Additionally, four serious adverse reactions of atrioventricular (AV) heart block occurred in patisiran-treated patients, including three cases of complete AV block. No serious adverse reactions of AV block were reported in placebo-treated patients.

#### **Use in Specific Populations:**

- **Pregnancy:** There are no available data on patisiran use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Patisiran treatment leads to a decrease in serum vitamin A levels, and vitamin A supplementation is advised for patients taking patisiran. Vitamin A is essential for normal embryofetal development; however, excessive levels of vitamin A are associated with adverse developmental effects. The effects on the fetus of a reduction in maternal serum TTR caused by patisiran and of vitamin A supplementation are unknown.
- **Lactation:** There is no information regarding the presence of patisiran in human milk, the effects on the breastfed infant, or the effects on milk production.
- **Pediatric Use:** The safety and effectiveness of patisiran in pediatric patients have not been established.
- **Geriatric Use:** No dose adjustment is required in patients 65 years of age or older. A total of 62 patients  $\geq 65$  years of age, including 9 patients  $\geq 75$  years of age, received patisiran in the placebo-controlled study. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
- **Hepatic Impairment:** No dose adjustment is necessary in patients with mild hepatic impairment. Patisiran has not been studied in patients with moderate or severe hepatic impairment.
- **Renal Impairment:** No dose adjustment is necessary in patients with mild or moderate renal impairment. Patisiran has not been studied in patients with severe renal impairment or end-stage renal disease (ESRD).

**Efficacy:** The efficacy of patisiran was demonstrated in a randomized, double-blind, placebo-controlled, multicenter clinical trial in adult patients 18 to 85 years of age with a documented pathogenic variant in *TTR* and a diagnosis of polyneuropathy caused by hATTR amyloidosis.

Patients were required to have adequate liver and renal function. Patients with previous liver transplantation or who were planning liver transplantation during the trial period, or who had New York Heart Association (NYHA) class III or IV heart failure were excluded. Additionally, patients with a diagnosis of Type 1 or Type 2 diabetes or with sensorimotor or autonomic neuropathy not related to hATTR amyloidosis were excluded. Patients were randomized in a 2:1 ratio to receive patisiran 0.3mg/kg (N=148) or placebo (N=77), respectively, via IV infusion once every 3 weeks for 18 months. All patients received pre-medication with a corticosteroid, acetaminophen, and H<sub>1</sub> and H<sub>2</sub> antagonists.

- The primary efficacy endpoint was the change from baseline to month 18 in the modified Neuropathy Impairment Score +7 (mNIS+7). The mNIS+7 is an objective assessment of neuropathy and comprises the NIS and Modified +7 composite scores. In the version of the mNIS+7 used in the trial, the NIS objectively measures deficits in cranial nerve function, muscle strength, and reflexes, and the Modified +7 assesses postural blood pressure, quantitative sensory testing, and peripheral nerve electrophysiology. The maximum possible score was 304 points, with higher scores representing a greater severity of disease. The clinical meaningfulness of effects on the mNIS+7 was assessed by the change from baseline to Month 18 in the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score. The Norfolk QoL-DN scale is a patient-reported assessment that evaluates the subjective experience of neuropathy in the following domains: physical functioning/large fiber neuropathy (impaired sensations of vibration and touch), activities of daily living, symptoms, small fiber neuropathy (impaired sensations of pain and temperature), and autonomic neuropathy (impaired involuntary functions such as blood pressure regulation, sweating, and digestion). The version of the Norfolk QoL-DN that was used in the trial had a total score range from -4 to 136, with higher scores representing greater impairment.
- The mean mNIS+7 at baseline was 80.9±41.5 in the patisiran group and 74.6±37.0 in the placebo group; the least-squares mean change from baseline at 18 months was -6.0±1.7 versus 8.0±2.6 in the patisiran and placebo groups, respectively (P<0.001). The mean baseline Norfolk QoL-DN score was 59.6±28.2 in the patisiran group and 55.5±24.3 in the placebo group; the least-squares mean change from baseline was -6.7±1.8 versus 14.4±2.7 in the patisiran and placebo groups, respectively (P<0.001).

**Cost:** The Wholesale Acquisition Cost (WAC) of Onpattro™ (patisiran) is \$1,900 per milliliter. This results in a cost per dose of \$28,500 and a yearly cost of \$484,500 for the maximum dose of 30mg administered every 3 weeks. Dosing is weight-based; therefore, pricing will vary.

## **Tegsedi™ (Inotersen) Product Summary<sup>6,7,8</sup>**

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**FDA Approval:** October 2018

**Indication(s):** Tegsedi™ (inotersen) is a transthyretin-directed antisense oligonucleotide indicated for treatment of the polyneuropathy of hATTR amyloidosis in adults.

**Dosing:**

- Tegsedi™ (inotersen) is supplied in a single-dose, prefilled syringe. Each prefilled syringe of inotersen delivers 1.5mL of solution containing 284mg of inotersen. Inotersen is available in cartons containing one or four prefilled syringes.
- Inotersen should be refrigerated at 2°C to 8°C (36°F to 46°F) in the original container. It can be kept at room temperature [up to 30°C (86°F)] in the original container for up to 6 weeks.
- Inotersen should be allowed to reach room temperature prior to injection.
- The recommended dose of inotersen is 284mg injected subcutaneously (sub-Q) once weekly. For consistency of dosing, the dose should be administered on the same day every week. Injection site rotation is recommended.
- The first injection administered by the patient or caregiver should be performed under the guidance of an appropriately qualified health care professional. Patients and/or caregivers should be trained in the sub-Q administration of inotersen in accordance with the *Instructions for Use* in the product package labeling. qualified health care professional. Patients and/or caregivers should be trained in the sub-Q administration of inotersen in accordance with the *Instructions for Use* in the product package labeling.

**Boxed Warning: Thrombocytopenia and Glomerulonephritis****Thrombocytopenia**

- Inotersen causes reductions in platelet count that may result in sudden and unpredictable thrombocytopenia, which can be life-threatening.
- Inotersen is contraindicated in patients with a platelet count  $<100 \times 10^9/L$ .
- A platelet count should be obtained prior to treatment and monitored weekly during treatment if values are  $\geq 75 \times 10^9/L$  or more frequently if values are  $<75 \times 10^9/L$ .
- If signs or symptoms of thrombocytopenia develop, a platelet count should be obtained as soon as possible, and inotersen should be stopped unless a platelet count is determined to be interpretable and acceptable by a medical professional.
- After discontinuation of treatment for any reason, it is recommended to continue to monitor platelet counts for 8 weeks, or longer if platelet counts are  $<100 \times 10^9/L$  in order to verify that platelet counts remain  $>75 \times 10^9/L$ .

**Glomerulonephritis**

- Inotersen can cause glomerulonephritis that may require immunosuppressive treatment and may result in dialysis-dependent renal failure.
- Inotersen should generally not be initiated in patients with urinary protein to creatinine ratio (UPCR)  $\geq 1,000\text{mg/g}$ .
- Prior to starting inotersen, it is recommended to perform a urinalysis and to measure the serum creatinine, estimated glomerular filtration rate (eGFR), and UPCR.
- During treatment, serum creatinine, eGFR, urinalysis, and UPCR should be monitored every 2 weeks. Inotersen should not be given to patients who develop UPCR  $\geq 1,000\text{mg/g}$ , or eGFR  $<45\text{mL/min}/1.73\text{m}^2$ , pending further evaluation of the cause.
- If a dose is held, once eGFR increases to  $\geq 45\text{mL/min}/1.73\text{m}^2$ , UPCR decreases to  $<1,000\text{mg/g}$ , or the underlying cause of the decline in renal function is corrected, weekly dosing may be reinitiated. In patients with UPCR of  $\geq 2,000\text{mg/g}$ , further

evaluation for acute glomerulonephritis should be performed. If acute glomerulonephritis is confirmed, inotersen should be permanently discontinued.

**Tegsedi™ REMS Program**

- Inotersen is available only through a restricted distribution program called the Tegsedi™ REMS Program.

**Mechanism of Action:** Inotersen is an antisense oligonucleotide that causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

**Contraindication(s):**

- Platelet count  $<100 \times 10^9/L$
- History of acute glomerulonephritis caused by inotersen
- History of hypersensitivity reactions to inotersen

**Warnings and Precautions:**

- **Thrombocytopenia:** Inotersen causes reductions in platelet count that may result in sudden and unpredictable thrombocytopenia that can be life-threatening. In clinical trials, platelet counts  $<100 \times 10^9/L$  occurred in 25% of inotersen-treated patients, compared to 2% of placebo-treated patients. Platelet counts  $<75 \times 10^9/L$  occurred in 14% of inotersen-treated patients, compared to no placebo-treated patients. Three inotersen-treated patients (3%) had sudden severe thrombocytopenia (platelet count  $<25 \times 10^9/L$ ), and one patient in a clinical trial experienced a fatal intracranial hemorrhage. Inotersen should not be initiated in patients with a platelet count  $<100 \times 10^9/L$ .
- **Glomerulonephritis and Renal Toxicity:** Inotersen can cause glomerulonephritis that may result in dialysis-dependent renal failure. In clinical trials, glomerulonephritis occurred in three (3%) inotersen-treated patients and no placebo-treated patients. In these patients, stopping inotersen alone was not sufficient to resolve manifestations of glomerulonephritis, and treatment with an immunosuppressive medication was necessary. One patient did not receive immunosuppressive treatment and remained dialysis-dependent. Inotersen should generally not be initiated in patients with UPCR  $\geq 1,000\text{mg/g}$ .
- **Stroke and Cervicocephalic Arterial Dissection:** Inotersen may cause stroke and cervicocephalic arterial dissection. In clinical studies, 1 of 161 (0.6%) inotersen-treated patients experienced carotid artery dissection and stroke. These events occurred within two days of the first inotersen dose.
- **Inflammatory and Immune Effects:** In clinical studies, serious inflammatory and immune adverse reactions occurred in inotersen-treated patients, including immune thrombocytopenia and glomerulonephritis, as well as a single case of anti-neutrophil cytoplasmic autoantibody (ANCA)-positive systemic vasculitis.
- **Liver Effects:** In clinical studies, 8% of inotersen-treated patients had an increased alanine aminotransferase (ALT) at least 3 times the upper limit of normal (ULN), compared to 3% of patients on placebo; 3% of inotersen-treated patients had an ALT at least 8 times the ULN, compared to no patients on placebo. Monitoring of ALT,

aspartate aminotransferase (AST), and total bilirubin at baseline and every 4 months during treatment with inotersen is recommended.

- Hypersensitivity Reactions/Antibody Formation: In clinical studies, 6 of 161 (4%) inotersen-treated patients stopped treatment because of a hypersensitivity reaction. Antibodies to inotersen were present when the reactions occurred. These reactions generally occurred within 2 hours of administration.
- Uninterpretable Platelet Counts: Reaction Between Antiplatelet Antibodies and Ethylenediaminetetra-Acetic Acid (EDTA): In one study, 23% of inotersen-treated patients had at least one uninterpretable platelet count caused by platelet clumping, compared to 13% of patients on placebo. In two cases of severe thrombocytopenia with platelet count  $<25 \times 10^9/L$ , one of which resulted in death, clumped platelet samples caused a delay in diagnosis and treatment. Platelet clumping can be caused by a reaction between antiplatelet antibodies and EDTA. If there is suspicion of EDTA-mediated platelet clumping, it is recommended to perform a repeat platelet count using a different anticoagulant and to hold inotersen dosing until an acceptable platelet count is confirmed with an interpretable blood sample.
- Reduced Serum Vitamin A Levels and Recommended Supplementation: Inotersen treatment leads to a decrease in serum vitamin A levels; therefore, supplementation at the RDA of vitamin A is advised. Higher doses than the RDA of vitamin A should not be given to try to achieve normal serum vitamin A levels during treatment with inotersen, as serum vitamin A levels do not reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).

**Adverse Reactions:** The most common adverse reactions that occurred in at least 20% of inotersen-treated patients and more frequently than in placebo-treated patients were injection site reactions, nausea, headache, fatigue, thrombocytopenia, and fever.

#### **Use in Specific Populations:**

- Pregnancy: There are no data on the developmental risks associated with the use of inotersen in pregnant women. Inotersen treatment leads to a decrease in serum vitamin A levels. Vitamin A is essential for normal embryofetal development; however, excessive levels of Vitamin A are associated with adverse developmental effects. The effects on the fetus of a reduction in maternal serum TTR caused by inotersen and of vitamin A supplementation are unknown.
- Lactation: There is no information regarding the presence of inotersen in human milk, the effects on the breast-fed infant, or the effects on milk production. A study in lactating mice has shown excretion of inotersen in milk.
- Pediatric Use: The safety and effectiveness of inotersen in pediatric patients have not been established.
- Geriatric Use: Clinical studies of inotersen included 69 patients (45%) 65 years of age or older. No differences in pharmacokinetics or effectiveness were observed between these patients and younger patients.

- **Renal Impairment:** No dose adjustment is necessary in patients with mild-to-moderate renal impairment (eGFR  $\geq 30$  to  $< 90$  mL/min/1.73m<sup>2</sup>). Inotersen has not been studied in patients with severe renal impairment or ESRD.
- **Hepatic Impairment:** No dose adjustment is necessary in patients with mild hepatic impairment. Inotersen has not been studied in patients with other degrees of hepatic impairment.

**Efficacy:** The efficacy of inotersen was demonstrated in a randomized, double-blind, placebo-controlled, multicenter clinical trial in adult patients 18 to 82 years of age diagnosed with stage 1 (patient is ambulatory) or stage 2 (patient is ambulatory with assistance) polyneuropathy caused by hATTR amyloidosis. Patients included in the trial also had a NIS of 10 to 130, a TTR mutation determined by genotyping, and documented amyloid deposits determined on biopsy. The NIS scale ranges from 0 to 244 points, with a higher score indicating poorer function and a minimal clinically meaningful difference of 2 points. Patients with polyneuropathy from causes other than hATTR amyloidosis, previous liver transplantation, and NYHA class III heart failure or higher were excluded. Patients were randomized in a 2:1 ratio to receive either inotersen 284mg (N=113) or placebo (N=60), respectively, as a sub-Q injection administered once weekly for 65 weeks (3 doses were administered during the first week of treatment). The co-primary efficacy endpoints were the change from baseline to week 66 in the mNIS+7 composite score and the Norfolk QoL-DN total score. A decrease in scores indicated improvement.

- Both primary endpoints, the mNIS+7 and the Norfolk QoL-DN score, achieved significant differences between the inotersen group and the placebo group at week 66. For the mNIS+7, the difference in the least-squares mean change from baseline to week 66 between the two groups was -19.7 points [95% confidence interval (CI),  $P < 0.001$ ] in favor of inotersen. For the Norfolk QoL-DN score, the difference in the least-squares mean change from baseline to week 66 between the two groups was -11.7 points (95% CI,  $P < 0.001$ ) in favor of inotersen.

**Cost:** The cost of inotersen is currently unavailable; however, the annual price of inotersen is expected to be \$450,000 for 284mg dosed once weekly.

## Market News and Updates<sup>9,10</sup>

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### News:

- **October 2018:** The Institute for Clinical and Economic Review (ICER) released a Final Evidence Report and Report-at-a-Glance on inotersen and patisiran for the treatment of hATTR amyloidosis. The report was reviewed at a September 2018 public meeting of the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC), one of ICER's three independent evidence appraisal committees. The CEPAC found that both inotersen and patisiran provide a substantial net health benefit when compared to best supportive care alone, but evidence is insufficient to distinguish between the two treatments. However, current pricing far exceeds commonly cited thresholds for cost effectiveness. The CEPAC unanimously recognized that the novel mechanism of action was an important benefit for treating individuals with such a high lifetime burden of illness. A majority also recognized that the new treatments may reduce family and

caregiver burden and may improve a patient's ability to return to work. These CEPAC members emphasized that the burden that a hereditary disease places on families cannot be understated, and that these new treatments may also have a positive psychological effect on multiple generations of a family. Ultimately, the CEPAC voted unanimously that, despite the net health benefit, both inotersen and patisiran represent a low long-term value for money. The votes were influenced heavily by the \$450,000 annual list price of patisiran, and the assumption that inotersen would be priced similarly. Key recommendations included the following:

- Given that newly approved treatments for hATTR have new mechanisms of action, lack long-term safety and efficacy data, and are very expensive, it is reasonable for insurers and other payers to develop prior authorization criteria to ensure prudent use of these treatments.
- Manufacturers should bring the price for innovative treatments for hATTR down to a level that aligns fairly with the added benefits for patients.

#### **Pipeline:**

- **Tafamidis:** In August 2018, Pfizer Inc. announced primary results from the tafamidis Phase 3 TTR cardiomyopathy (ATTR-ACT) study, which showed tafamidis significantly reduced the hierarchical combination of both all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo over a 30-month period (P=0.0006) in patients with wild-type or variant (hereditary) TTR amyloid cardiomyopathy (ATTR-CM). ATTR-CM is a rare, fatal, and underdiagnosed condition associated with progressive heart failure for which there are no approved pharmacologic treatments. Tafamidis was granted Orphan Drug designation for the treatment of ATTR-CM in the United States and Europe in 2012. In June 2017 and May 2018, respectively, the FDA granted tafamidis Fast Track and Breakthrough Therapy designations for the treatment of ATTR-CM.

#### **Recommendations**

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The College of Pharmacy recommends the prior authorization of Onpattro™ (patisiran) and Tegsedi™ (inotersen) with the following criteria:

##### **Onpattro™ (Patisiran) Approval Criteria:**

1. An FDA approved indication for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
  - a. Tissue biopsy confirming amyloid deposits; and
  - b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Onpattro™ must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist; and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and

5. Prescriber must confirm that member will be pre-medicated with intravenous (IV) corticosteroid, oral acetaminophen, IV histamine-1 (H<sub>1</sub>) antagonist, and IV histamine-2 (H<sub>2</sub>) antagonist 60 minutes prior to Onpattro™ administration to reduce the risk of infusion-related reactions; and
6. Onpattro™ will not be approved for concomitant use with Tegsedi™; and
7. 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; and
8. Onpattro™ approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

**Tegsedi™ (Inotersen) Approval Criteria:**

1. An FDA approved indication for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis; and
2. Diagnosis confirmed by the following:
  - a. Tissue biopsy confirming amyloid deposits; and
  - b. Genetic confirmation of transthyretin (*TTR*) gene mutation (e.g., Val30Met); and
3. Tegsedi™ must be prescribed by or in consultation with a cardiologist, geneticist, or neurologist or an advanced care practitioner with a supervising physician who is a cardiologist, geneticist, or neurologist; and
4. Prescriber must confirm the member will take the recommended daily allowance of vitamin A; and
5. Prescriber must agree to monitor ALT, AST, and total bilirubin prior to initiation of Tegsedi™ and every 4 months during treatment; and
6. Prescriber must confirm the first injection of Tegsedi™ administered by the patient or caregiver will be performed under the guidance of a health care professional; and
7. Prescriber must confirm the patient or caregiver has been trained by a health care professional on the subcutaneous (sub-Q) administration and proper storage of Tegsedi™; and
8. Tegsedi™ will not be approved for concomitant use with Onpattro™; and
9. Prescriber, pharmacy, and member must be enrolled in the Tegsedi™ Risk Evaluation and Mitigation Strategy (REMS) program and maintain enrollment throughout therapy; and
10. Tegsedi™ approvals will be for the duration of six months. Reauthorization may be granted if the prescriber documents the member is responding well to treatment; and
11. A quantity limit of four syringes per 28 days will apply.



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- <sup>1</sup> Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis* 2013; 8(1):31-48.
- <sup>2</sup> Adams D, Suhr OB, Dyck PJ, et al. Trial design and rationale for APOLLO, a Phase 3, placebo-controlled study of patisiran in patients with hereditary ATTR amyloidosis with polyneuropathy. *BMC Neurology* 2017; 17(1):181-192.
- <sup>3</sup> Onpattro™ Prescribing Information. Alnylam Pharmaceuticals, Inc. Available online at: <http://www.alnylam.com/wp-content/uploads/2018/08/ONPATTRO-Prescribing-Information.pdf>. Last revised 08/2018. Last accessed 10/24/2018.
- <sup>4</sup> Adams D, Gonzalez-Duarte A, O’Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. *N Engl J Med* 2018; 379(1):11-21.
- <sup>5</sup> National Institute of Neurological Disorders and Stroke. Peripheral Neuropathy Fact Sheet. U.S. National Institutes of Health. Available online at: <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Peripheral-Neuropathy-Fact-Sheet>. Last revised 08/16/2018. Last accessed 10/24/2018.
- <sup>6</sup> Tegsedi™ Prescribing Information. Akcea Therapeutics, Inc. Available online at: <https://tegsedi.com/prescribing-information.pdf>. Last revised 10/2018. Last accessed 10/24/2018.
- <sup>7</sup> Benson MD, Waddington-Cruz M, Berk JL et al. Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. *N Engl J Med* 2018; 379(1):22-31.
- <sup>8</sup> Liu A. Ionis’ Tegsedi launches into head-to-head with Alnylam, but Pfizer’s waiting in the wings. *FiercePharma*. Available online at: <https://www.fiercepharma.com/pharma/ionis-new-tegsedi-launches-into-head-to-head-alnylam-but-pfizer-s-waiting-wings>. Issued 10/08/2018. Last accessed 10/24/2018.
- <sup>9</sup> Institute for Clinical and Economic Review (ICER). Institute for Clinical and Economic Review Final Report Highlights Uncertainty in Long-Term Safety and Effectiveness of New Treatments for Hereditary Transthyretin Amyloidosis, Discusses Options for Insurance Coverage Criteria. Available online at: <https://icer-review.org/announcements/institute-for-clinical-and-economic-review-final-report-highlights-uncertainty-in-long-term-safety-and-effectiveness-of-new-treatments-for-hereditary-transthyretin-amyloidosis-discusses-options-for-i/>. Issued 10/04/2018. Last accessed 10/24/2018.
- <sup>10</sup> Pfizer, Inc. Tafamidis Phase 3 Transthyretin Amyloid Cardiomyopathy (ATTR-ACT) Study Results Presented as Late-Breaking Data at the ESC Congress 2018. *Business Wire*. Available online at: [https://www.pfizer.com/news/press-release/press-release-detail/tafamidis\\_phase\\_3\\_transthyretin\\_amyloid\\_cardiomyopathy\\_attr\\_act\\_study\\_results\\_presented\\_as\\_late\\_breaking\\_data\\_at\\_the\\_esc\\_congress\\_2018](https://www.pfizer.com/news/press-release/press-release-detail/tafamidis_phase_3_transthyretin_amyloid_cardiomyopathy_attr_act_study_results_presented_as_late_breaking_data_at_the_esc_congress_2018). Issued 08/27/2018. Last accessed 10/24/2018.





# Appendix M





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# Fiscal Year 2018 Annual Review of Various Systemic Antibiotics and 30-Day Notice to Prior Authorize Zemdri™ (Plazomicin), Xerava™ (Eravacycline), Nuzyra™ (Omadacycline), Seysara™ (Sarecycline), and Ximino™ (Minocycline Extended-Release)

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Oklahoma Health Care Authority  
November 2018

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## Current Prior Authorization Criteria

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### 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 alternative(s) cannot be used.
2. The following oral antibiotics currently require prior authorization and the special formulation approval criteria will apply:
  - Amoxicillin 500mg tablets
  - Amoxicillin/clavulanate potassium extended-release (ER) tablets (Augmentin XR®)
  - Amoxicillin 775mg ER tablets (Moxatag®)
  - Cephalexin 250mg and 500mg tablets
  - Cephalexin 750mg capsules
  - Doxycycline hyclate 75mg and 150mg tablets (Acticlate®)
  - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
  - Doxycycline monohydrate 75mg and 150mg capsules and tablets
  - Doxycycline monohydrate 40mg DR capsules (Oracea®)
  - Minocycline ER tablets (Minolira™)
  - Minocycline ER tablets (Solodyn®)

### 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 carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s).
5. A quantity limit of 42 vials per 14 days will apply.

**Baxdela™ (Delafloxacin) Tablet and Vial Approval Criteria:**

1. An FDA approved diagnosis of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria; and
2. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, doxycycline, trimethoprim/sulfamethoxazole, or other cost-effective therapeutic equivalent alternative(s).
3. Approval quantity will be based on Baxdela™ prescribing information and FDA approved dosing regimen(s).
  - a. For Baxdela™ vials, an initial quantity limit of 6 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

**Ciprofloxacin 100mg Tablet Approval Criteria:**

1. Approval requires a patient-specific, clinically significant reason why the member cannot use alternative strengths of ciprofloxacin tablets, levofloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

**Ciprofloxacin 500mg and 1000mg Extended-Release (ER) Tablets Approval Criteria:**

1. Approval requires a patient-specific, clinically significant reason why the member cannot use the immediate-release formulation of ciprofloxacin tablets, levofloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

**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 alternative(s).
3. A quantity limit of three vials per seven days will apply.

**Levofloxacin 25mg/mL Oral Solution, Ciprofloxacin 250mg/5mL Oral Suspension, and Ciprofloxacin 500mg/5mL Oral Suspension Approval Criteria:**

1. Members older than six years of age require a patient-specific, clinically significant reason why the oral tablet formulations cannot be used.

**Minocycline Immediate-Release Tablets Approval Criteria:**

1. Approval requires a patient-specific, clinically significant reason why the member requires the immediate-release tablet formulation and cannot use the immediate-release capsule formulation or other cost-effective therapeutic equivalent alternative(s).

**Ofloxacin 300mg and 400mg Tablet and Moxifloxacin 400mg Tablet Approval Criteria:**

1. Approval requires a patient-specific, clinically significant reason why the member cannot use ciprofloxacin tablets, levofloxacin tablets, or other cost-effective therapeutic equivalent alternative(s).

**Sivextro® (Tedizolid) Tablet and Vial 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 alternative(s).
3. A quantity limit of six tablets or vials per six days will apply.

**Solosec™ (Secnidazole) Oral Granules Approval Criteria:**

1. An FDA approved diagnosis of bacterial vaginosis; and
2. A patient-specific, clinically significant reason why the member cannot use metronidazole, tinidazole, or other cost-effective therapeutic equivalent alternative(s).
3. A quantity limit of 1 packet per 30 days will apply.

**Suprax® (Cefixime) and Cedax® (Ceftibuten) Approval Criteria:**

1. An indicated diagnosis or infection known to be susceptible to requested agent; and
2. A patient-specific, clinically significant reason why the member cannot use cephalexin, cefdinir, or other cost-effective therapeutic equivalent alternative(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, or other cost-effective therapeutic equivalent alternative(s).

**Vabomere™ (Meropenem/Vaborbactam) Approval Criteria:**

1. An FDA approved diagnosis of complicated urinary tract infection (cUTI) or pyelonephritis; and
2. A patient-specific, clinically significant reason why the member cannot use piperacillin/tazobactam or other cost-effective therapeutic equivalent alternative(s).
3. Approval quantity will be based on Vabomere™ prescribing information and FDA approved dosing regimen(s).

**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 carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a

cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s).

- A quantity limit of 42 vials per 14 days will apply.

### Utilization of Various Systemic Antibiotics: Fiscal Year 2018

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

#### Comparison of Fiscal Years: Pharmacy Claims

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2017	258	366	\$108,840.02	\$297.38	\$23.22	35,388	4,688
2018	255	350	\$80,181.08	\$229.09	\$18.78	37,900	4,269
% Change	-1.20%	-4.40%	-26.30%	-23.00%	-19.10%	7.10%	-8.90%
Change	-3	-16	-\$28,658.94	-\$68.29	-\$4.44	2,512	-419

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

#### Fiscal Year 2018 Utilization of Various Systemic Antibiotics: Medical Claims

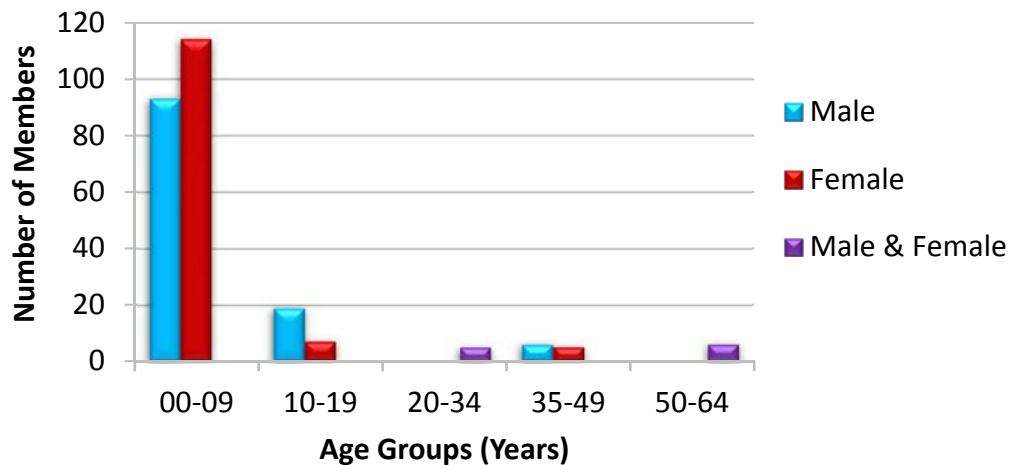
Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Claims/Member
2018	2	2	\$8,739.00	\$4,369.50	1

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

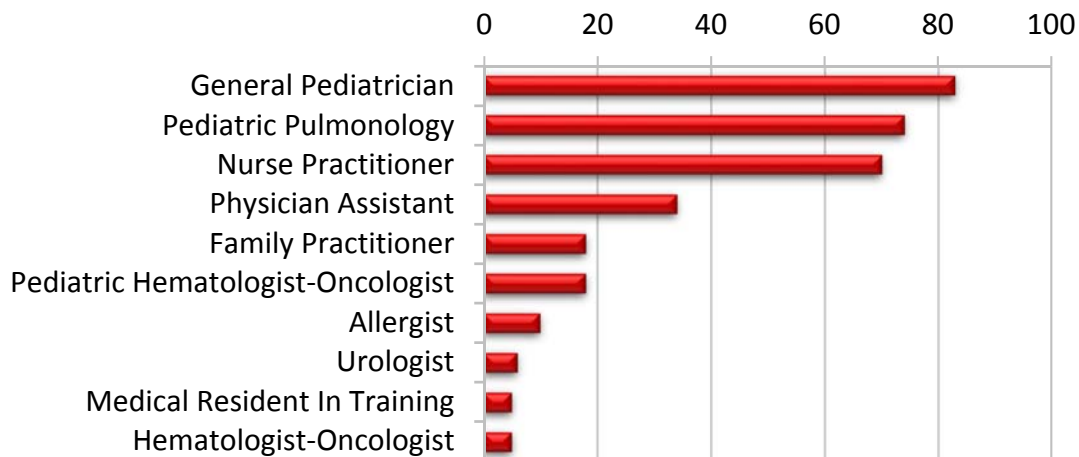
Please note, there were no medical claims for the various systemic antibiotics during fiscal year 2017.

#### Demographics of Members Utilizing Various Systemic Antibiotics



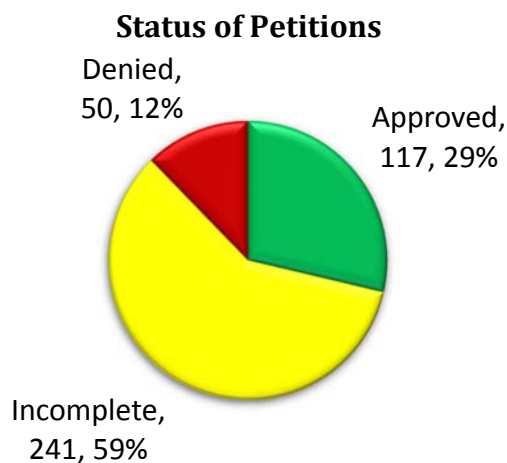


## Top Prescriber Specialties of Various Systemic Antibiotics by Number of Claims



## Prior Authorization of Various Systemic Antibiotics

There were 408 prior authorization requests submitted for various systemic antibiotics during fiscal year 2018. The following chart shows the status of the submitted petitions for fiscal year 2018.



## Market News and Updates<sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16</sup>

### Anticipated Patent Expiration(s):

- Augmentin XR<sup>®</sup> [amoxicillin/clavulanate potassium extended-release (ER) tablet]: April 2020
- Dalvance<sup>®</sup> [dalbavancin vial for intravenous (IV) infusion]: December 2023
- Solodyn<sup>®</sup> (minocycline ER tablet): March 2027
- Moxatag<sup>®</sup> (amoxicillin ER tablet): May 2027
- Doryx<sup>®</sup> [doxycycline hyclate delayed-release (DR) tablet]: February 2028
- Suprax<sup>®</sup> (cefixime 500mg/5mL oral suspension): December 2028
- Baxdela<sup>™</sup> (delafloxacin tablet): December 2029
- Sivextro<sup>®</sup> (tedizolid tablet and vial for IV infusion): December 2030

- Vabomere® (meropenem/vaborbactam vial for IV infusion): August 2031
- Avycaz® (ceftazidime/avibactam vial for IV infusion): June 2032
- Baxdela™ (delafloxacin vial for IV infusion): February 2033
- Zerbaxa® (ceftolozane/tazobactam vial for IV infusion): May 2034
- Orbactiv® (oritavancin vial for IV infusion): July 2035

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

- **January 2018:** The FDA approved Firvanq™ (vancomycin for oral solution) for the treatment of *Clostridium difficile*-associated diarrhea (CDAD) and enterocolitis caused by *Staphylococcus aureus*, including methicillin-resistant strains. Firvanq™ is the only FDA approved vancomycin oral liquid treatment option for CDAD. Firvanq™ is available in two strengths (25mg/mL and 50mg/mL) and two bottle sizes (150mL and 300mL) and is supplied as a kit containing 1 bottle of vancomycin powder and 1 bottle of pre-measured grape-flavored diluent for reconstitution. The recommended dose of Firvanq™ for CDAD in adults is 125mg orally four times daily for 10 days. The National Average Drug Acquisition Cost (NADAC) for a 150mL bottle of Firvanq™ 50mg/mL is \$120.45, which would be an adequate quantity for the recommended adult dosing for CDAD.
- **February 2018:** The FDA approved Avycaz® (ceftazidime/avibactam) for the treatment of adult patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by designated susceptible Gram-negative microorganisms. Ceftazidime/avibactam was first FDA approved in 2015 for the treatment of adult patients with complicated intra-abdominal infections (cIAI), used in combination with metronidazole, or complicated urinary tract infections (cUTI), including pyelonephritis, caused by designated susceptible Gram-negative microorganisms. The recommended dosage of ceftazidime/avibactam for all FDA-approved indications is 2.5 grams (2 grams ceftazidime and 0.5 grams avibactam) administered every 8 hours by IV infusion over 2 hours in patients 18 years of age and older with creatinine clearance (CrCl) >50mL/min (*refer to Avycaz® prescribing information for recommended dosing in patients with renal impairment*). The recommended duration of treatment for cIAI is 5 to 14 days, and the recommended duration of treatment for cUTI, including pyelonephritis, or HABP/VABP is 7 to 14 days. For treatment of cIAI, metronidazole should be given concurrently. To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftazidime/avibactam and other antibacterial drugs, ceftazidime/avibactam should be used to treat only indicated infections that are proven or strongly suspected to be caused by susceptible bacteria (*refer to Avycaz® prescribing information for specific microbiology information*).
- **June 2018:** The FDA approved Zemdri™ (plazomicin), an aminoglycoside antibacterial, for the treatment of adult patients with cUTI, including pyelonephritis, caused by designated susceptible microorganisms.
- **August 2018:** The FDA approved Xerava™ (eravacycline), a tetracycline-class antibacterial, for the treatment of adult patients with cIAI caused by designated susceptible microorganisms.

- **October 2018:** The FDA approved Nuzyra™ (omadacycline), a tetracycline-class antibacterial, for the treatment of adult patients with community-acquired bacterial pneumonia (CABP) or acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible microorganisms.
- **October 2018:** The FDA approved Seysara™ (sarecycline), a tetracycline-class antibacterial, for the treatment of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris in patients 9 years of age and older.

#### News:

- **February 2018:** The results of a study comparing the effect of meropenem/vaborbactam versus piperacillin/tazobactam on clinical cure or improvement and microbial eradication in cUTI were published in *The Journal of the American Medical Association (JAMA)*. The non-inferiority randomized trial included 550 patients with cUTI, including acute pyelonephritis, and the difference in the composite outcome of complete resolution or improvement of symptoms along with microbial eradication met the non-inferiority margin of 15% when comparing meropenem/vaborbactam versus piperacillin/tazobactam (98.4% vs. 94.0%), thus demonstrating the non-inferiority of meropenem/vaborbactam for the treatment of cUTI. The study concludes that further research is needed to understand the spectrum of patients in whom meropenem/vaborbactam offers a clinical advantage.
- **July 2018:** The FDA required safety labeling changes for fluoroquinolones to strengthen the warnings about the risks of mental health side effects and serious blood sugar disturbances and to make these warnings more consistent across labeling for all fluoroquinolones taken by mouth or given by injection. The safety labeling changes were based on a comprehensive review of the FDA's adverse event reports and case reports published in medical literature. The new class-wide labeling changes will require that the mental health side effects be listed separately from other central nervous system (CNS) side effects and be consistent across the labeling of the fluoroquinolone class. The mental health side effects to be included in the labeling are disturbances in attention, disorientation, agitation, nervousness, memory impairment, and delirium. Additionally, the recent FDA review found instances of hypoglycemic coma where users of fluoroquinolones experienced hypoglycemia. As a result, the *Blood Glucose Disturbances* subsection of the labeling for all systemic fluoroquinolones will now be required to explicitly reflect the potential risk of coma with hypoglycemia. The FDA also published a drug safety communication about these updates.
- **August 2018:** Antibiotic resistance poses a great threat to global public health, with the overuse of antibiotics generally considered as the major contributing factor. However, little is known about whether non-antibiotic drugs could play potential roles in the emergence of antibiotic resistance. Findings of a study published online in the journal *Environment International* demonstrated that the exposure to the antidepressant fluoxetine induces multiple antibiotic resistance in *Escherichia coli* via the reactive oxygen species (ROS)-mediated mutagenesis (e.g., deletion, insertion, substitution). In the study, *Escherichia coli* K12 was exposed to different concentrations of fluoxetine and the resistant strains were isolated by plating on antibiotic containing plates. Exposure

of *Escherichia coli* to fluoxetine at 5 to 100mg/L after repeated subculture in lysogeny broth for 30 days promoted its mutation frequency resulting in increased resistance against the antibiotics chloramphenicol, amoxicillin, and tetracycline. Isolated mutants with resistance to one of these antibiotics also exhibited multiple resistances against fluoroquinolones, aminoglycosides, beta-lactams, tetracycline, and chloramphenicol. The study concludes that further work is required to investigate the effects of fluoxetine on the dissemination of antibiotic resistance in mixed culture with long-term evolution periods under environmentally relevant fluoxetine concentrations.

- **September 2018:** The founder and president of Nostrum Pharmaceuticals commented that his company had a “moral requirement to sell the product at the highest price”, regarding the decision to raise the price of Furadantin® (nitrofurantoin oral suspension) from about \$500 per bottle to more than \$2,300. FDA Commissioner Dr. Scott Gottlieb responded with “there’s no moral imperative to price gouge and take advantage of patients”. Currently, there are multiple generic products available at a lower cost; however, the College of Pharmacy will monitor these products for cost increases and market availability and will consider prior authorization if necessary.

#### **Pipeline:**

- **Doxycycline Products:** Dr. Reddy’s and Promius Pharma have submitted a New Drug Application (NDA) for Zenavod™ (doxycycline 40mg capsules) and Sun Pharmaceutical Industries has submitted an NDA for Xyrosa™ (doxycycline 40mg tablets), both for the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients. Both products show tentative FDA approval, meeting required quality, safety, and efficacy standards for approval, but are subject to an automatic stay of final approval for up to 30 months pending a patent infringement process.
- **Contezolid/Contezolid Acefosalil (MRX-1/MRX-4):** MicuRx Pharmaceuticals is currently developing MRX-1, a potent oxazolidinone antibiotic against Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin-resistant *Streptococcus pneumoniae* (PRSP), penicillin-intermediate *Streptococcus pneumoniae* (PISP), and vancomycin-resistant enterococci (VRE). Orally administered MRX-1 showed the same or better efficacy compared to linezolid in systemic and local infection mouse models. MRX-1 is currently in a Phase 3 clinical trial in China. MRX-4, a prodrug of MRX-1, is currently in a Phase 1 clinical trial in the United States, with a Phase 2 clinical trial scheduled to begin in the second half of 2018. In September 2018, MicuRx announced the receipt of the Qualified Infectious Disease Product (QIDP) classification and Fast Track designation from the FDA for contezolid (MRX-1) and its prodrug contezolid acefosalil (MRX-4) for the treatment of ABSSSI.
- **Lefamulin:** In May 2018, Nabriva Therapeutics announced positive, topline results from a pivotal Phase 3 clinical trial of oral lefamulin for the treatment of CABP. Lefamulin is a novel, semi-synthetic, pleuromutilin antibiotic. Nabriva plans to file an NDA with the FDA in the fourth quarter of 2018. Nabriva is evaluating the continued development of lefamulin for additional indications and is developing a formulation of lefamulin appropriate for pediatric use.

## Zemdri™ (Plazomicin) Product Summary<sup>17</sup>

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**Indication(s):** Zemdri™ (plazomicin) is indicated in patients 18 years of age or older for the treatment of cUTI, including pyelonephritis, caused by designated susceptible microorganism(s).

- As only limited clinical safety and efficacy data for plazomicin are currently available, plazomicin should be reserved for use in patients with cUTI who have limited or no alternative treatment options.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of plazomicin and other antibacterial drugs, plazomicin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

### **Boxed Warning: Nephrotoxicity, Ototoxicity, Neuromuscular Blockage, and Fetal Harm**

- Nephrotoxicity has been reported with plazomicin. The risk of nephrotoxicity is greater in patients with impaired renal function, the elderly, and in those receiving concomitant nephrotoxic medications. CrCl should be assessed in all patients prior to initiating therapy and daily during therapy. Therapeutic Drug Monitoring (TDM) is recommended for cUTI patients with CrCl <90mL/min to avoid potentially toxic levels.
- Ototoxicity, manifested as hearing loss, tinnitus, and/or vertigo, has been reported with plazomicin. Symptoms of aminoglycoside-associated ototoxicity may be irreversible and may not become evident until after completion of therapy. Aminoglycoside-associated ototoxicity has been observed primarily in patients with a family history of hearing loss, patients with renal impairment, and in patients receiving higher doses and/or longer durations of therapy than recommended.
- Aminoglycosides have been associated with neuromuscular blockade. During therapy with plazomicin, patients should be monitored for adverse reactions associated with neuromuscular blockade, particularly high-risk patients, such as patients with underlying neuromuscular disorders (including myasthenia gravis) or in patients concomitantly receiving neuromuscular blocking agents.
- Aminoglycosides, including plazomicin, can cause fetal harm when administered to a pregnant woman.

**Microbiology:** Plazomicin is indicated for the treatment of cUTI, including pyelonephritis, caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae*.

### **Dosing:**

- Zemdri™ is supplied as a 500mg/10mL single-dose vial (SDV) for injection.
- The recommended dosage of plazomicin for patients with CrCl >90mL/min is 15mg/kg administered every 24 hours by IV infusion over 30 minutes. The dosage of plazomicin should be calculated based on total body weight (TBW). For patients with TBW > ideal body weight (IBW) by 25% or more, adjusted body weight based on the following equation should be used:  $IBW + 0.4 \times (TBW - IBW)$ .

- The duration of therapy should be guided by the severity of the infection and the patient’s clinical status. An appropriate oral therapy may be considered after 4 to 7 days of plazomicin therapy to complete a total duration of 7 to 10 days (IV plus oral). The maximum duration of plazomicin therapy for cUTI is 7 days.
- Plazomicin dosage should be adjusted in patients with renal impairment. Patients with CrCl  $\geq 15$  mL/min and  $< 90$  mL/min receiving plazomicin may require subsequent dosage adjustments based on change in renal function and/or TDM as appropriate (*refer to Zemdri™ prescribing information for recommended dosing and TDM in patients with renal impairment*). There is insufficient information to recommend a dosage regimen in patients with CrCl  $< 15$  mL/min or on renal replacement therapy, including hemodialysis or continuous renal replacement therapy.

**Mechanism of Action:** Plazomicin is a semi-synthetic aminoglycoside antibacterial that acts by binding to bacterial 30S ribosomal subunit, thereby inhibiting protein synthesis. Plazomicin has concentration-dependent bactericidal activity.

**Efficacy:** A total of 609 adults hospitalized with cUTI (including pyelonephritis) were randomized in a multinational, double-blind, non-inferiority trial comparing plazomicin (15mg/kg IV once daily) to meropenem (1g IV every 8 hours). Switch to an oral antibacterial drug, such as levofloxacin, was allowed after a minimum of 4 and maximum of 7 days of IV therapy, for a total of 7 to 10 days of treatment. Efficacy was assessed in the microbiological modified intent-to-treat (mMITT) population, which included all patients who received study medication and had at least 1 baseline uropathogen. The mMITT population consisted of 388 patients with cUTI, including 162 (41.8%) with pyelonephritis. The median treatment duration of IV study drug was 6 days in both groups. Plazomicin demonstrated efficacy for composite cure at day 5 and at the test-of-cure (TOC) visit. Composite cure at day 5 was defined as resolution or improvement of clinical cUTI symptoms and a microbiological outcome of eradication. Composite cure at the TOC visit (day 17  $\pm$  2 from the first dose of study drug) was defined as resolution of cUTI symptoms and a microbiological outcome of eradication. The following table (Table 1) summarizes the composite cure rates in the mMITT population.

**Table 1. Composite Cure Rates in cUTI Patients (mMITT Population)**

Analysis Visit	Plazomicin N=191 n (%)	Meropenem N=197 n (%)	Treatment Difference* (95% CI)
<b>Day 5</b>	<b>168 (88.0)</b>	<b>180 (91.4)</b>	<b>-3.4 (-10.0, 3.1)</b>
Clinical cure or improvement	171 (89.5)	182 (92.4)	
Microbiological eradication	188 (98.4)	193 (98.0)	
<b>TOC</b>	<b>156 (81.7)</b>	<b>138 (70.1)</b>	<b>11.6 (2.7, 20.3)</b>
Clinical cure	170 (89.0)	178 (90.4)	
Microbiological eradication	171 (89.5)	147 (74.6)	

cUTI = complicated urinary tract infection; mMITT = microbiological modified intent-to-treat; N = number of patients in the mMITT population; n = number of patients within a specific category with a clinical cure and/or microbiological eradication; % = percentage CI = confidence interval; TOC = test-of-cure

\*Treatment difference = plazomicin – meropenem.

**Cost:** The Wholesale Acquisition Cost (WAC) of Zemdri™ is \$315 per 500mg/10mL SDV. The estimated cost of 7 days of Zemdri™ therapy for a patient weighing 60kg is \$4,410.

## **Xerava™ (Eravacycline) Product Summary<sup>18</sup>**

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**Indication(s):** Xerava™ (eravacycline) is indicated in patients 18 years of age or older for the treatment of cIAI caused by designated susceptible microorganism(s).

- **Limitation of use:** Eravacycline is not indicated for the treatment of cUTI.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of eravacycline and other antibacterial drugs, eravacycline should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

**Microbiology:** Eravacycline is indicated for the treatment of cIAI caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii*, *Enterobacter cloacae*, *Klebsiella oxytoca*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Streptococcus anginosus* group, *Clostridium perfringens*, *Bacteroides* species, and *Parabacteroides distasonis*.

### **Dosing:**

- Xerava™ is supplied as a 50mg SDV that contains sterile dry powder for reconstitution and dilution prior to IV infusion.
- The recommended dosage of eravacycline is 1mg/kg administered every 12 hours by IV infusion over approximately 60 minutes. The dosage of eravacycline should be calculated based on actual body weight.
- The recommended duration of treatment with eravacycline for cIAI is 4 to 14 days. The duration of therapy should be guided by the severity and location of the infection and the patient's clinical response.
- Eravacycline dosage should be adjusted in patients with severe hepatic impairment. In patients with severe hepatic impairment (Child Pugh C), eravacycline should be administered as 1mg/kg every 12 hours on day 1, followed by 1mg/kg every 24 hours starting on day 2 for a total duration of 4 to 14 days.
- Eravacycline dosage should be adjusted in patients with concomitant use of a strong CYP3A inducer(s). In those patients, eravacycline should be administered as 1.5mg/kg every 12 hours for a total duration of 4 to 14 days. No dosage adjustment is warranted in patients with concomitant use of weak or moderate CYP3A inducer(s).

**Mechanism of Action:** Eravacycline is a synthetic fluorocycline antibacterial within the tetracycline class of antibacterial drugs that acts by binding to the bacterial 30S ribosomal subunit, thereby disrupting bacterial protein synthesis. In general, eravacycline is bacteriostatic against Gram-positive bacteria (e.g., *Staphylococcus aureus*, *Enterococcus faecalis*); however, *in vitro* bactericidal activity has been demonstrated against certain strains of *Escherichia coli* and *Klebsiella pneumoniae*.

**Efficacy:** A total of 1,041 adults hospitalized with cIAI were enrolled in two Phase 3, randomized, double-blind, active-controlled, multinational, multicenter trials, comparing

eravacycline (1mg/kg IV every 12 hours) with either ertapenem (1g IV every 24 hours) or meropenem (1g IV every 8 hours) as the active comparator for 4 to 14 days of therapy. Patients with appendicitis, cholecystitis, diverticulitis, gastric/duodenal perforation, intra-abdominal abscess, perforation of the intestine, or peritonitis were included in the cIAI trial. The microbiologic intent-to-treat (micro-ITT) population, which included all patients who had at least one baseline intra-abdominal pathogen, consisted of 846 patients in the two trials. The most common primary cIAI diagnosis was intra-abdominal abscess(es), occurring in 60% in patients. Clinical cure was defined as complete resolution or significant improvement of signs or symptoms of the index infection at the TOC visit, which occurred 25 to 31 days after randomization. The following table (Table 2) summarizes the clinical cure rates in the micro-ITT population in both Phase 3 trials.

**Table 2. Clinical Cure Rates at TOC in the Phase 3 cIAI Trials (micro-ITT Population)**

	Trial 1		Trial 2	
	Eravacycline N=220 n (%)	Ertapenem N=226 n (%)	Eravacycline N=195 n (%)	Meropenem N=226 n (%)
<b>Clinical cure</b>	191 (86.8)	198 (87.6)	177 (90.8)	187 (91.2)
<b>Treatment difference (95% CI)*</b>	-0.80 (-7.1, 5.5)		-0.5 (-6.3, 5.3)	

TOC = test-of-cure; cIAI = complicated intra-abdominal infection; microITT = microbiologic intent-to-treat; N = number of patients in the micro-ITT population; n = number of patients within a specific category with a clinical cure; % = percent; CI = confidence interval

\*Treatment difference = eravacycline – ertapenem or meropenem.

**Cost:** The WAC of Xerava™ is \$43.75 per 50mg SDV. The estimated cost of 14 days of Xerava™ therapy for a patient weighing 60kg is \$2,450.00.

### **Nuzyra™ (Omadacycline) Product Summary<sup>19</sup>**

**Indication(s):** Nuzyra™ (omadacycline) is indicated in adult patients 18 years of age or older for the treatment of CABP or ABSSSI caused by designated susceptible microorganism(s).

- To reduce the development of drug-resistant bacteria and maintain the effectiveness of omadacycline and other antibacterial drugs, omadacycline should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

**Microbiology:** Omadacycline is indicated for the treatment of the following infections caused by the listed susceptible microorganisms:

- **CABP:** *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*.
- **ABSSSI:** *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Staphylococcus lugdunensis*, *Streptococcus pyogenes*, *Streptococcus anginosus* group (includes *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), *Enterococcus faecalis*, *Enterococcus cloacae*, and *Klebsiella pneumoniae*.



**Dosing:**

- Nuzyra™ is supplied as 150mg oral tablets and as 100mg SDV that contain lyophilized powder that must be reconstituted and further diluted prior to IV infusion.
- For oral dosing, patients should fast for at least 4 hours prior to taking omadacycline tablets. Tablets should be taken with water and after oral dosing, no food or drink (except water) should be consumed for 2 hours and no dairy products, antacids, or multivitamins for 4 hours.
- The recommended dosage of omadacycline is included in the following table (Table 3).

**Table 3. Recommended Dosage of Omadacycline in Adult Patients with CABP or ABSSSI**

Diagnosis	Loading Doses	Maintenance Doses	Treatment Duration
CABP	200mg* IV on day 1; or 100mg <sup>†</sup> IV twice on day 1	100mg <sup>†</sup> IV once daily; or 300mg PO once daily	7 to 14 days
ABSSSI	200mg* IV on day 1; or 100mg <sup>†</sup> IV twice on day 1	100mg <sup>†</sup> IV once daily; or 300mg PO once daily	7 to 14 days
	450mg PO once daily on day 1 and day 2	300mg PO once daily	

CABP = community-acquired bacterial pneumonia; ABSSSI = acute bacterial skin and skin structure infection; IV = intravenous; PO = orally

\*200mg IV infusion administered over 60 minutes

<sup>†</sup>100mg IV infusion administered over 30 minutes

**Mechanism of Action:** Omadacycline is an aminomethylcycline, which is a semisynthetic derivative of the tetracycline class of antibacterial drugs that acts by binding to the bacterial 30S ribosomal subunit, thereby blocking bacterial protein synthesis. In general, omadacycline is considered bacteriostatic; however, omadacycline has demonstrated bactericidal activity against some isolates of *Streptococcus pneumoniae* and *Haemophilus influenzae*.

**Efficacy:**

- **CABP:** A total of 774 adults with CABP were randomized in a multinational, double-blind, double-dummy trial (Trial 1) comparing omadacycline (100mg IV every 12 hours for two doses on day 1, followed by 100mg IV daily or 300mg orally daily) with moxifloxacin (400mg IV or orally daily) for 7 to 14 days of therapy. All enrolled patients were expected to require a minimum of at least 3 days of IV treatment. Efficacy and safety of an oral loading dose was not evaluated in CABP. A total of 386 patients were randomized to omadacycline and 388 patients were randomized to moxifloxacin. Clinical success at the early clinical response (ECR) timepoint, 72 to 120 hours after the first dose, was defined as survival with improvement in at least two of four symptoms (cough, sputum production, chest pain, and dyspnea) without deterioration in any of these four symptoms in the ITT population, which consisted of all randomized patients. Clinical response was also assessed by the investigator at the post-therapy evaluation (PTE) visit, 5 to 10 days after the last dose of study drug and was defined as survival and improvement in signs and symptoms of CABP, based on the clinician's judgement, to the extent that further antibacterial therapy is not necessary. The following table (Table 4) summarizes the clinical success rates in the ITT population for Trial 1.

**Table 4. Clinical Success Rates in Trial 1 for CABP (ITT Population)**

Endpoint	Omadacycline (%)	Moxifloxacin (%)	Treatment Difference (95% CI)
Clinical Success at ECR Timepoint	81.1	82.7	-1.6 (-7.1, 3.8)
Clinical Success at PTE Visit	87.6	85.1	2.5 (-2.4, 7.4)

CABP = community-acquired bacterial pneumonia; ITT = intent-to-treat; CI = confidence interval; ECR = early clinical response; PTE = post-therapy evaluation

- **ABSSSI:** A total of 1,390 adults with ABSSSI were randomized in two multicenter, multinational, double-blind, double-dummy trials (Trial 2 and Trial 3) comparing 7 to 14 days of omadacycline with linezolid. Patients with cellulitis, major abscess, or wound infection were enrolled in the trials.
  - In Trial 2, 329 patients were randomized to omadacycline (100mg IV every 12 hours for two doses followed by 100mg IV every 24 hours, with the option to switch to 300mg orally every 24 hours) and 326 patients were randomized to linezolid (600mg IV every 12 hours, with the option to switch to 600mg orally every 12 hours). The most common ABSSSI diagnosis in Trial 2 was cellulitis (38%).
  - In Trial 3, 368 patients were randomized to omadacycline (450mg orally once daily on days 1 and 2, followed by 300mg orally once daily) and 367 were randomized to linezolid (600mg orally every 12 hours). The most common ABSSSI diagnosis in Trial 3 was wound infection (58%).

In both ABSSSI trials, efficacy was determined by the successful ECR at 48 to 72 hours after the first dose in the modified ITT (mITT) population and was defined as a  $\geq 20\%$  decrease in lesion size. The mITT population was defined as all randomized subjects without a sole Gram-negative causative pathogen at screening. Clinical response was also assessed at the PTE visit, 7 to 14 days after the last dose, and was defined as survival after completion of study treatment without receiving any alternative antibacterial therapy other than omadacycline, without unplanned major surgical intervention, and sufficient resolution of infection such that further antibacterial therapy is not needed. The following table (Table 5) summarizes the clinical success rates in the mITT population for Trial 2 and Trial 3.

**Table 5. Clinical Success Rates in Trial 2 and Trial 3 for ABSSSI (mITT Population)**

Endpoint	Study	Omadacycline (%)	Linezolid (%)	Treatment Difference (95% CI)
Clinical Success at ECR Timepoint	Trial 2	84.8	85.5	-0.7 (-6.3, 4.9)
	Trial 3	87.3	82.2	5.1 (-0.2, 10.5)
Clinical Success at PTE Visit	Trial 2	86.1	83.6	2.5 (-3.2, 8.2)
	Trial 3	83.9	80.5	3.4 (-2.3, 9.1)

ABSSSI = acute bacterial skin and skin structure infection; mITT = modified intent-to-treat; CI = confidence interval; ECR = early clinical response; PTE = post therapy evaluation

**Cost:** Cost information for Nuzyra™ is not available.

## Seysara™ (Sarecycline) Product Summary<sup>20</sup>

**Indication(s):** Seysara™ (sarecycline) is indicated for the treatment of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris in patients 9 years of age and older.

- **Limitations of Use:** Efficacy of sarecycline beyond 12 weeks and safety beyond 12 months have not been established. Sarecycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, sarecycline should be used only as indicated.

### Dosing:

- Seysara™ is supplied as 60mg, 100mg, and 150mg oral tablets.
- The recommended dosage of sarecycline is once daily with or without food, based on body weight:
  - 60mg for patients who weigh 33 to 54kg;
  - 100mg for patients who weigh 55 to 84kg;
  - 150mg for patients who weigh 85 to 136kg.
- If there is no improvement after 12 weeks, treatment with sarecycline should be reassessed.
- To reduce the risk of esophageal irritation and ulceration, sarecycline should be taken with adequate amounts of fluid.

**Mechanism of Action:** Sarecycline is tetracycline-class antibacterial drug. The mechanism of action of sarecycline in treating acne vulgaris is not known.

**Efficacy:** The safety and efficacy of once daily sarecycline was assessed in two 12-week multicenter, randomized, double-blind, placebo-controlled studies (Study 1 and Study 2). Efficacy was assessed in a total of 2,002 patients 9 years of age and older, and patients were randomized to receive either sarecycline or placebo once daily. The two co-primary efficacy endpoints were the percentage of patients with Investigator's Global Assessment (IGA) success [a score of clear (0) or almost clear (1) and 2-point decrease from baseline IGA score at week 12] and absolute reduction from baseline in inflammatory lesion counts at week 12. The following table (Table 6) summarizes the efficacy results at week 12 for Study 1 and Study 2.

**Table 6. Clinical Success Rates in Study 1 and Study 2 for Acne Vulgaris**

	Study 1		Study 2	
	Sarecycline N=483	Placebo N=485	Sarecycline N=519	Placebo N=515
<b>Investigator's Global Assessment (IGA)</b>				
IGA Success	21.9%	10.5%	22.6%	15.3%
<b>Inflammatory Lesions</b>				
Mean absolute reduction	15.3	10.2	15.5	11.1
Mean percent reduction	52.2%	35.2%	50.8%	36.4%

**Cost:** Cost information for Seysara™ is not available.

## Cost Comparison

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There are several cost-effective generic options available for SoonerCare members who require antibiotic therapy. The following table shows a cost comparison of minocycline ER and immediate-release (IR) products. Currently, Solodyn®, Minolira™, and minocycline IR tablets require prior authorization. Minocycline IR capsules are available without prior authorization.

### Minocycline Products:

Product	Cost Per Unit	Cost Per 30-Day Course of Therapy <sup>†</sup>
<b>Ximino™ (minocycline) 90mg extended-release (ER) capsule</b>	<b>\$23.30</b>	<b>\$699.00</b>
Solodyn® (minocycline) 105mg ER tablet	\$38.80	\$1,164.00
Minolira™ (minocycline) 105mg ER tablet	\$21.67	\$650.10
minocycline 100mg tablet	\$2.51	\$150.60
minocycline 100mg capsule	\$0.37	\$22.20

<sup>†</sup>Based on recommended dosing regimen for acne vulgaris.

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

## Recommendations

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The College of Pharmacy recommends the prior authorization of Zemdri™ (plazomicin vial for IV infusion), Xerava™ (eravacycline vial for IV infusion), Nuzyra™ (omadacycline tablet and vial for IV infusion), and Seysara™ (sarecycline tablet) with the following criteria:

### Zemdri™ (Plazomicin) Approval Criteria:

1. An FDA approved diagnosis of complicated urinary tract infection (cUTI), including pyelonephritis, caused by designated susceptible microorganisms; and
2. A patient-specific, clinically significant reason why the member cannot use an appropriate alternative aminoglycoside (e.g., gentamicin, tobramycin) or other cost-effective therapeutic equivalent alternative(s); 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.

### Xerava™ (Eravacycline) Approval Criteria:

1. An FDA approved diagnosis of complicated intra-abdominal infections (cIAI) caused by designated susceptible microorganisms; and
2. Member must be 18 years of age or older; and
3. 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 alternative(s); 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.

**Nuzyra™ (Omadacycline) Approval Criteria [Community-Acquired Bacterial Pneumonia (CABP) Diagnosis]:**

1. An FDA approved diagnosis of CABP caused by designated susceptible microorganisms; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use an appropriate beta-lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin/sulbactam) in combination with a macrolide (e.g., azithromycin, clarithromycin) or doxycycline, monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, gemifloxacin), or other cost-effective therapeutic equivalent alternative(s).
4. Approval quantity will be based on Nuzyra™ prescribing information and FDA approved dosing regimen(s).
  - a. For Nuzyra™ vials, an initial quantity limit of 4 vials for a 3-day supply will apply. Continued authorization will require a patient-specific, clinically significant reason why the member cannot switch to the oral tablets for the remainder of therapy.

**Nuzyra™ (Omadacycline) Approval Criteria [Acute Bacterial Skin and Skin Structure Infections (ABSSSI) Diagnosis]:**

1. An FDA approved diagnosis of ABSSSI caused by designated susceptible microorganisms; and
2. Member must be 18 years of age or older; and
3. A patient-specific, clinically significant reason why the member cannot use vancomycin, linezolid, doxycycline, trimethoprim/sulfamethoxazole, or other cost-effective therapeutic equivalent alternative(s); and
4. Use of Nuzyra™ vials will require a patient-specific, clinically significant reason why the member cannot use the oral tablet formulation; and
5. Approval quantity will be based on Nuzyra™ prescribing information and FDA approved dosing regimen(s).

**Seysara™ (Sarecycline) Approval Criteria:**

1. An FDA approved diagnosis of inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris; and
2. Member must be 9 years of age or older; and
3. Seysara™ is not covered for members older than 20 years of age; and
4. A patient-specific, clinically significant reason why the member cannot use minocycline, doxycycline, tetracycline, or other cost-effective therapeutic equivalent alternative(s); and
5. The member's recent weight must be provided on the prior authorization request in order to authorize the appropriate strength according to package labeling; and
6. A quantity limit of 30 tablets per 30 days will apply.

The College of Pharmacy also recommends the following changes to the Various Systemic Antibiotics Prior Authorization category:

1. Add Ximino™ (minocycline ER capsules) to the Antibiotic Special Formulation category. Current special formulation criteria will apply.
2. Update the current approval criteria for Avycaz® (ceftazidime/avibactam) based on the new FDA approved indication for the treatment of HABP/VABP.

The proposed changes can be seen in red in 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 alternative(s) cannot be used.
2. The following oral antibiotics currently require prior authorization and the special formulation approval criteria will apply:
  - Amoxicillin 500mg tablets
  - Amoxicillin/clavulanate potassium extended-release (ER) tablets (Augmentin XR®)
  - Amoxicillin 775mg ER tablets (Moxatag®)
  - Cephalexin 250mg and 500mg tablets
  - Cephalexin 750mg capsules
  - Doxycycline hyclate 75mg and 100mg tablets (Acticlate®)
  - Doxycycline hyclate delayed-release (DR) tablets (Doryx®)
  - Doxycycline monohydrate 75mg and 150mg capsules and tablets
  - Doxycycline monohydrate 40mg DR capsules (Oracea®)
  - **Minocycline ER capsules (Ximino™)**
  - Minocycline ER tablets (Minolira™)
  - Minocycline ER tablets (Solodyn®)

**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; or
  - c. **Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP); 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 carbapenem (e.g., ertapenem, meropenem, imipenem/cilastatin), a cephalosporin (e.g., ceftriaxone, ceftazidime) in combination with metronidazole, or other cost-effective therapeutic equivalent alternative(s).
5. A quantity limit of 42 vials per 14 days will apply.

## Utilization Details of Various Systemic Antibiotics: Fiscal Year 2018

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

### Pharmacy Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
<b>CIPROFLOXACIN PRODUCTS</b>						
CIPRO (5%) SUS 250MG/5ML	102	79	\$14,920.81	\$146.28	1.3	18.61%
CIPRO (10%) SUS 500MG/5ML	50	43	\$8,306.99	\$166.14	1.2	10.36%
CIPROFLOXACN SUS 250MG/5ML	2	2	\$216.14	\$108.07	1.0	0.27%
<b>SUBTOTAL</b>	<b>154</b>	<b>124</b>	<b>\$23,443.94</b>	<b>\$152.23</b>	<b>1.2</b>	<b>29.24%</b>
<b>LEVOFLOXACIN PRODUCTS</b>						
LEVOFLOXACIN SOL 25MG/ML	1	95	\$16,413.07	\$129.24	1.3	20.47%
<b>SUBTOTAL</b>	<b>127</b>	<b>95</b>	<b>\$16,413.07</b>	<b>\$129.24</b>	<b>1.3</b>	<b>20.47%</b>
<b>CEFIXIME PRODUCTS</b>						
CEFIXIME SUS 100/5ML	14	7	\$3,288.43	\$234.89	2.0	4.10%
CEFIXIME SUS 200/5ML	14	14	\$5,496.50	\$392.61	1.0	6.86%
SUPRAX CAP 400MG	5	5	\$1,044.49	\$208.90	1.0	1.30%
SUPRAX CHW 200MG	1	1	\$401.14	\$401.14	1.0	0.50%
SUPRAX CHW 100MG	1	1	\$205.84	\$205.84	1.0	0.26%
<b>SUBTOTAL</b>	<b>35</b>	<b>28</b>	<b>\$10,436.40</b>	<b>\$298.18</b>	<b>1.3</b>	<b>13.02%</b>
<b>TETRACYCLINE PRODUCTS</b>						
TETRACYCLINE CAP 250MG	9	3	\$2,875.98	\$319.55	3.0	3.59%
TETRACYCLINE CAP 500MG	6	6	\$1,794.53	\$299.09	1.0	2.24%
<b>SUBTOTAL</b>	<b>15</b>	<b>9</b>	<b>\$4,670.51</b>	<b>\$311.37</b>	<b>1.7</b>	<b>5.82%</b>
<b>MINOCYCLINE PRODUCTS</b>						
SOLODYN TAB 65MG	5	1	\$5,596.78	\$1,119.36	5.0	6.98%
MINOCYCLINE TAB 65MG ER	2	1	\$2,111.32	\$1,055.66	2.0	2.63%
<b>SUBTOTAL</b>	<b>7</b>	<b>2</b>	<b>\$7,708.10</b>	<b>\$1,101.16</b>	<b>3.5</b>	<b>9.61%</b>
<b>CEFTOLOZANE/TAZOBACTAM PRODUCTS</b>						
ZERBAXA INJ 1.5GM	5	1	\$14,034.12	\$2,806.82	5.0	17.50%
<b>SUBTOTAL</b>	<b>5</b>	<b>1</b>	<b>\$14,034.12</b>	<b>\$2,806.82</b>	<b>5.0</b>	<b>17.50%</b>
<b>MOXIFLOXACIN PRODUCTS</b>						
MOXIFLOXACIN TAB 400MG	4	4	\$218.90	\$54.73	1.0	0.27%
<b>SUBTOTAL</b>	<b>4</b>	<b>4</b>	<b>\$218.90</b>	<b>\$54.73</b>	<b>1.0</b>	<b>0.27%</b>
<b>TEDIZOLID PRODUCTS</b>						
SIVEXTRO TAB 200MG	1	1	\$2,088.30	\$2,088.30	1.0	2.60%
<b>SUBTOTAL</b>	<b>1</b>	<b>1</b>	<b>\$2,088.30</b>	<b>\$2,088.30</b>	<b>1.0</b>	<b>2.60%</b>
<b>DOXYCYCLINE HYCLATE PRODUCTS</b>						
DOXYCYCL HYC TAB 200MG	1	1	\$1,052.62	\$1,052.62	1.0	1.31%
<b>SUBTOTAL</b>	<b>1</b>	<b>1</b>	<b>\$1,052.62</b>	<b>\$1,052.62</b>	<b>1.0</b>	<b>1.31%</b>
<b>AMOXICILLIN/CLAVULANATE POTASSIUM PRODUCTS</b>						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER	% COST
AMOX/K CLA TAB ER 1000/62.5MG	1	1	\$115.12	\$115.12	1.0	0.14%
<b>SUBTOTAL</b>	<b>1</b>	<b>1</b>	<b>\$115.12</b>	<b>\$115.12</b>	<b>1.0</b>	<b>0.14%</b>
<b>TOTAL</b>	<b>350</b>	<b>255*</b>	<b>\$80,181.08</b>	<b>\$229.09</b>	<b>1.4</b>	<b>100.00%</b>

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

## Medical Claims

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	COST/ CLAIM	CLAIMS/ MEMBER
<b>DALBAVANCIN PRODUCTS</b>					
DALVANCE J0875	2	2	\$8,739.00	\$4,369.50	1
<b>TOTAL</b>	<b>2</b>	<b>2*</b>	<b>\$8,739.00</b>	<b>\$4,369.50</b>	<b>1</b>

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

<sup>1</sup> 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 09/2018. Last accessed 10/23/2018.

<sup>2</sup> CutisPharma News Release: CutisPharma Announces FDA Approval of Firvanq™. Available online at: <https://cutispharma.com/cutispharma-announces-fda-approval-firvanq/>. Issued 01/28/2018. Last accessed 10/26/2018.

<sup>3</sup> Allergan News Release. FDA Approves Avycaz® (Ceftazidime and Avibactam) for the Treatment of Patients with Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia. Available online at: <https://www.allergan.com/news/news/thomson-reuters/fda-approves-avycaz-ceftazidime-and-avibactam-for>. Issued 02/01/2018. Last accessed 10/24/2018.

<sup>4</sup> Avycaz® (Ceftazidime/Avibactam) Prescribing Information. Allergan. Available online at: [http://www.allergan.com/assets/pdf/avycaz\\_pi](http://www.allergan.com/assets/pdf/avycaz_pi). Last revised 02/2018. Last accessed 10/24/2018.

<sup>5</sup> Achaogen News Release. Update -- Zemdri™ Approved by FDA for the Treatment of Adults with Complicated Urinary Tract Infections (cUTI). Available online at: <http://investors.achaogen.com/news-releases/news-release-details/update-zemdrim-plazomicin-approved-fda-treatment-adults>. Issued 06/26/2018. Last accessed 10/24/2018.

<sup>6</sup> Tetrphase Pharmaceuticals News Release. Tetrphase Pharmaceuticals Announces FDA Approval of Xerava™ (Eravacycline) for Complicated Intra-Abdominal Infections (cIAI). Available online at: <https://ir.tphase.com/news-releases/news-release-details/tetrphase-pharmaceuticals-announces-fda-approval-xeravatm>. Issued 08/27/2018. Last accessed 10/24/2018.

<sup>7</sup> Paratek News Release. Paratek Announces FDA Approval of Nuzyra™ (Omadacycline). *GlobeNewswire*. Available online at: <https://globenewswire.com/news-release/2018/10/02/1600459/0/en/Paratek-Announces-FDA-Approval-of-NUZYRA-Omadacycline.html>. Issued 10/02/2018. Last accessed 10/24/2018.

<sup>8</sup> Paratek News Release. FDA Approves Seysara™ (Sarecycline) for the Treatment of Moderate to Severe Acne. *GlobeNewswire*. Available online at: <https://globenewswire.com/news-release/2018/10/02/1588602/0/en/FDA-Approves-SEYSARA-Sarecycline-for-the-Treatment-of-Moderate-to-Severe-Acne.html>. Issued 10/02/2018. Last accessed 10/24/2018.

<sup>9</sup> Kaye KS, Bhowmick T, Metallidis S, et al. Effect of Meropenem-Vaborbactam vs Piperacillin-Tazobactam on Clinical Cure or Improvement and Microbial Eradication in Complicated Urinary Tract Infection: The TANGO I Randomized Clinical Trial. *JAMA* 2018; 319(8):788-799.

<sup>10</sup> FDA News Release. FDA Updates Warnings for Fluoroquinolone Antibiotics on Risks of Mental Health and Low Blood Sugar Adverse Reactions. Available online at: <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm612995.htm>. Issued 07/10/2018. Last accessed 10/26/2018.

<sup>11</sup> Jin M, Lu J, Chen Z, et al. Antidepressant Fluoxetine Induces Multiple Antibiotics Resistance in *Escherichia Coli* via ROS-Mediated Mutagenesis. *Environment International* 2018; 120:421-430.

<sup>12</sup> Drash W. Report: Pharma Exec Says He Had 'Moral Requirement' to Raise Drug Price 400%. *CNN*. Available online at: <https://www.cnn.com/2018/09/11/health/drug-price-hike-moral-requirement-bn/index.html>. Issued 09/12/2018. Last accessed 10/26/2018.

<sup>13</sup> Dr. Reddy's Laboratories News Release. Dr. Reddy's Laboratories Receives USFDA Tentative Approval for Zenavod™ (Doxycycline) Capsules. *BusinessWire*. Available online at: <https://www.businesswire.com/news/home/20160131005058/en/Dr.-Reddy%E2%80%99s-Laboratories-Receives-USFDA-Tentative-Approval>. Issued 02/01/2016. Last accessed 10/30/2018.



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- <sup>14</sup> Drugs@FDA: FDA Approved Drug Products. Xyrosa™ (Doxycycline) Tentative Approval. Available online at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/applletter/2017/209259Orig1s000TA1tr.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2017/209259Orig1s000TA1tr.pdf). Issued 04/26/2017. Last accessed 10/30/2018.
- <sup>15</sup> MicuRx Pharmaceuticals News Release. MicuRx Announces Receipt of FDA's QIDP and Fast Track Designations for Contezolid and Contezolid Acefosamil. *BusinessWire*. Available online at: <https://www.businesswire.com/news/home/20180921005016/en/MicuRx-Announces-Receipt-FDA%E2%80%99s-QIDP-Fast-Track>. Issued 09/21/2018. Last accessed 10/26/2018.
- <sup>16</sup> Nabriva Therapeutics News Release. Nabriva Therapeutics Announces Positive Topline Results from Pivotal Phase 3 Clinical Trial of Oral Lefamulin for the Treatment of Community-Acquired Bacterial Pneumonia. *GlobeNewswire*. Available online at: <https://globenewswire.com/news-release/2018/05/21/1509267/0/en/Nabriva-Therapeutics-Announces-Positive-Topline-Results-from-Pivotal-Phase-3-Clinical-Trial-of-Oral-Lefamulin-for-the-Treatment-of-Community-Acquired-Bacterial-Pneumonia.html>. Issued 05/21/2018. Last accessed 10/26/2018.
- <sup>17</sup> Zemdri™ (Plazomicin) Prescribing Information. Achaogen, Inc. Available online at: <https://www.zemdri.com/assets/pdf/Prescribing-Information.pdf>. Last revised 06/2018. Last accessed 10/25/2018.
- <sup>18</sup> Xerava™ (Eravacycline) Prescribing Information. Tetrphase Pharmaceuticals, Inc. Available online at: <https://www.xerava.com/assets/pdf/prescribinginformation.pdf>. Last revised 08/2018. Last accessed 10/25/2018.
- <sup>19</sup> Nuzyra™ (Omadacycline) Prescribing Information. Paratek Pharmaceuticals, Inc. Available online at: <http://nuzyra.com/PI.pdf>. Last revised 10/2018. Last accessed 10/26/2018.
- <sup>20</sup> Seysara™ (Sarecycline) Prescribing Information. Allergan. Available online at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/209521s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/209521s000lbl.pdf). Last revised 10/2018. Last accessed 10/26/2018.





# Appendix N





# Fiscal Year 2018 Annual Review of Hepatitis C Medications

Oklahoma Health Care Authority  
November 2018

## Introduction<sup>1,2</sup>

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 2014 allowing for prior authorization implementation of the hepatitis C virus (HCV) 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 Drug Utilization Review (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, Zepatier® (elbasvir/grazoprevir) was reviewed in April 2016, Epclusa® (sofosbuvir/velpatasvir) and Viekira XR™ [dasabuvir/ombitasvir/paritaprevir/ritonavir extended-release (ER)] were reviewed in December 2016, and Mavyret™ (glecaprevir/pibrentasvir) and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) were reviewed in December 2017.

In February 2017, the DUR Board voted to remove the minimum fibrosis score requirement with a full implementation date of January 1, 2018. The minimum fibrosis score was lowered from F2 to F1 effective July 1, 2017 and from F1 to F0 effective January 1, 2018. In April 2018, the DUR Board voted to update the viral load requirements to ensure treated members have chronic HCV; the viral load requirements were implemented in May 2018 and are reflected in the current prior authorization criteria section of this report.

	Fiscal Year 2014	Fiscal Year 2015	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
<b>Total HCV Drug Spending</b>	\$17,993,807.47	\$21,863,385.60	\$32,105,818.63	\$26,475,372.50	\$36,248,488.07

Costs do not reflect rebated prices or net costs.

State fiscal year = July 1<sup>st</sup> to June 30<sup>th</sup>.

Minimum fibrosis score lowered to F1 on 07/01/2017 and to F0 on 01/01/2018.

## Current Prior Authorization Criteria

Harvoni® (sofosbuvir/ledipasvir), Zepatier® (elbasvir/grazoprevir), Epclusa® (sofosbuvir/velpatasvir), Mavyret™ (glecaprevir/pibrentasvir), and Vosevi® (sofosbuvir/velpatasvir/voxilaprevir) are the preferred DAAs for the treatment of chronic HCV genotype 1. Use of an alternative regimen including Viekira Pak® (ombitasvir/paritaprevir/ritonavir/dasabuvir), Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir ER), Sovaldi® (sofosbuvir) alone, or Sovaldi® (sofosbuvir) and Daklinza™ (daclatasvir) in combination for the treatment of HCV genotype 1 requires patient-specific, clinically significant reasoning why the preferred DAAs are not

appropriate for the member. The following is a template for standard prior authorization criteria for the preferred hepatitis C medications. The criteria for each medication is based on FDA approved regimens and American Association for the Study of Liver Diseases (AASLD) and Infectious Disease Society of America (IDSA) guidance-recommended regimens. Specific hepatitis C medication criteria will vary based on product labeling, FDA approved indications, guidance recommendations, drug interaction potential, and use in specific populations.

**Hepatitis C Medication Approval Criteria:**

1. Member must be 18 years of age or older; and
2. An FDA approved diagnosis of chronic hepatitis C (CHC) and an FDA-indicated genotype appropriate to the requested medication; and
3. Requested hepatitis C medication 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
4. Hepatitis C virus (HCV) genotype testing must be confirmed and indicated on the prior authorization request; and
5. Member has chronic HCV infection defined by:
  - a. If the member has a liver fibrosis score  $\geq$ F1 (METAVIR equivalent) then only one detectable and quantifiable HCV RNA ( $>15$  IU/mL) test within the last 12 months is required; or
  - b. If the member has a liver fibrosis score  $<$ F1 (METAVIR equivalent) then the following must be met:
    - i. Positive (i.e., reactive) HCV antibody test that is at least six months old and has a detectable and quantifiable HCV RNA ( $>15$  IU/mL) test six months after date of positive HCV antibody test; or
    - ii. Two detectable and quantifiable HCV RNA ( $>15$  IU/mL) tests at least six months apart; and
6. FDA approved regimens and requirements based on cirrhosis status, viral genotype, treatment history, and viral load thresholds will apply; and
7. Member must sign and submit the Hepatitis C Intent to Treat Contract; and
8. Member's pharmacy must submit the Hepatitis C Therapy Pharmacy Agreement for each member on therapy; and
9. 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
10. Prescriber must agree to counsel members on the potential harms of illicit intravenous (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
11. Must have documentation of initiation of immunization with the hepatitis A and B vaccines; and
12. Member must not have decompensated cirrhosis or moderate or severe hepatic impairment (Child-Pugh B or C); and
13. Member must not have a limited life expectancy (less than 12 months) that cannot be remediated by treating HCV, liver transplantation, or another directed therapy; 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
15. Member must not be taking any medications not recommended for use with the requested hepatitis C medication; and
16. All other clinically significant issues must be addressed prior to starting therapy including but not limited to the following: neutropenia, anemia, thrombocytopenia, surgery, depression, psychosis, epilepsy, obesity, weight-management, severe concurrent medical diseases, such as but not limited to, retinal disease, or autoimmune thyroid disease; and
17. Prescribing physician must verify that they will work with the member to ensure the member remains adherent to hepatitis C therapies; and
18. Members must be adherent for continued approval. Treatment gaps of therapy longer than 3 days/month will result in denial of subsequent requests for continued therapy; and
19. Approvals for treatment regimen initiation for 8 or 12 weeks of therapy will not be granted prior to the 10th of a month, and for 16 weeks of therapy prior to the 15th of a month in order to prevent prescription limit issues from affecting the member's compliance.

### Hepatitis C Summary Statistics for Treated Members

Parameter	Details
<b>Number of Unduplicated Treated Members*</b>	1,592 Members
<b>Genotype</b>	<b>Genotype 1:</b> 67.5% <b>Genotype 2:</b> 17.0% <b>Genotype 3:</b> 14.5% <b>Genotype 4:</b> 0.5% <b>Multiple Genotypes:</b> 0.4%
<b>Fibrosis Score</b>	<b>Average:</b> 2.53 <b>F0:</b> 8.1% <b>F1:</b> 12.7% <b>F2:</b> 29.2% <b>F3:</b> 17.9% <b>F4:</b> 31.8% <b>Decompensated:</b> 0.2%
<b>Pre-Treatment Viral Load (HCV RNA)</b>	<b>Average:</b> 3,569,625 IU/mL
<b>Prior Treatment Experience</b>	<b>Treatment-Experienced Members:</b> 11.3% <b>Treatment-Naïve Members:</b> 88.7%
<b>Treatment Length</b>	<b>Average:</b> 11.45 weeks <b>8 weeks:</b> 33.5% <b>12 weeks:</b> 59.1% <b>16 weeks:</b> 1.7% <b>24 weeks:</b> 59.1%
<b>Compliance<sup>‡</sup></b>	<b>Before PA:</b> 18.8% of members noncompliant <b>After PA:</b> 3.2% of members noncompliant

Parameter	Details
SVR Cure Rate/Cost Per Cure	94.2% Cure Rate <sup>+</sup> Based on cure rate and drug spending during allotted time frame (01/01/2014 to 02/15/2018), the estimated cost per cure in the SoonerCare population is \$90,354.23 to \$190,385.19. Range due to partial SVR response rate.

\*Table includes data collected from 07/01/2014 to 10/15/2018

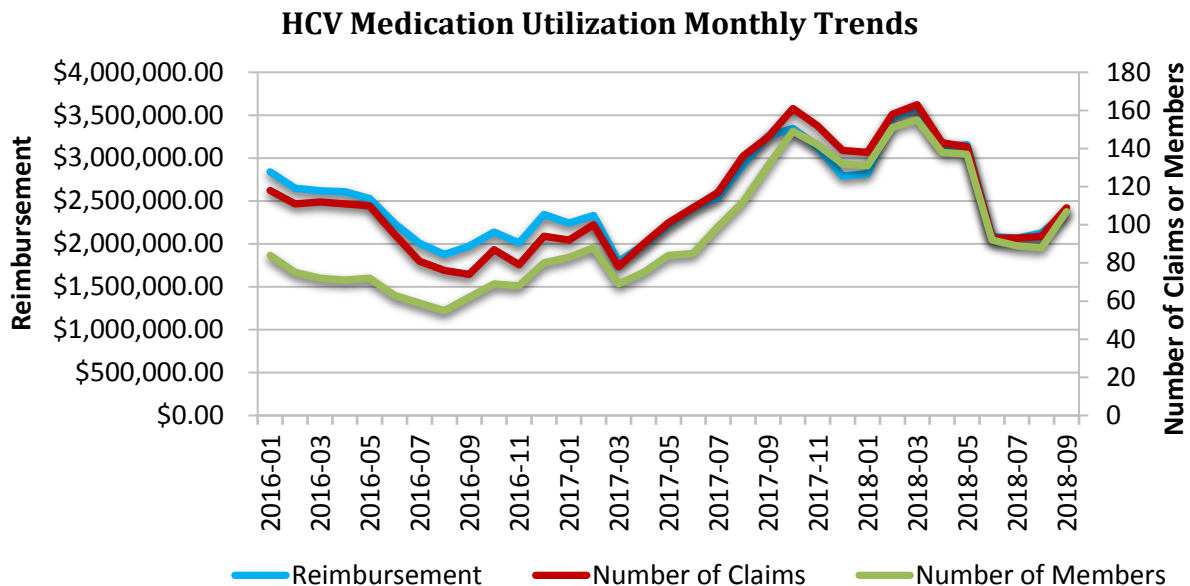
HCV RNA = hepatitis C virus ribonucleic acid; PA = prior authorization; SVR = sustained virologic response at least 12 weeks after therapy completion

<sup>‡</sup>Compliance before prior authorization was defined as an appropriate regimen length of 12 or 24 weeks.

<sup>+</sup>SVR cure rate includes data from members who started therapy from 12/01/2013 to 02/15/2018. The cure rate is based only on members for whom SoonerCare was able to obtain SVR responses (SVR response rate: 66.1%). Costs do not reflect rebated prices or net costs.

## Trends of Hepatitis C Medication Utilization: Trends 2016-2018

The following is a line graph representing the monthly trend in reimbursement, number of claims, and number of members utilizing HCV medications since January 2016. A steep increase can be seen following the minimum METAVIR fibrosis score change of F2 to F1 (July 1, 2017), and again following the change to F0 (January 1, 2018). The combined monthly totals for January and February 2017 in comparison to January and February 2018 resulted in a 38.28% increase in reimbursement and a 55.21% and 66.08% increase in the number of claims and members, respectively. Recently in the 2<sup>nd</sup> and 3<sup>rd</sup> quarters of 2018, reimbursement, the number of claims, and the number of members have since declined to similar totals experienced in June 2017, the month just prior to the F2 to F1 change.

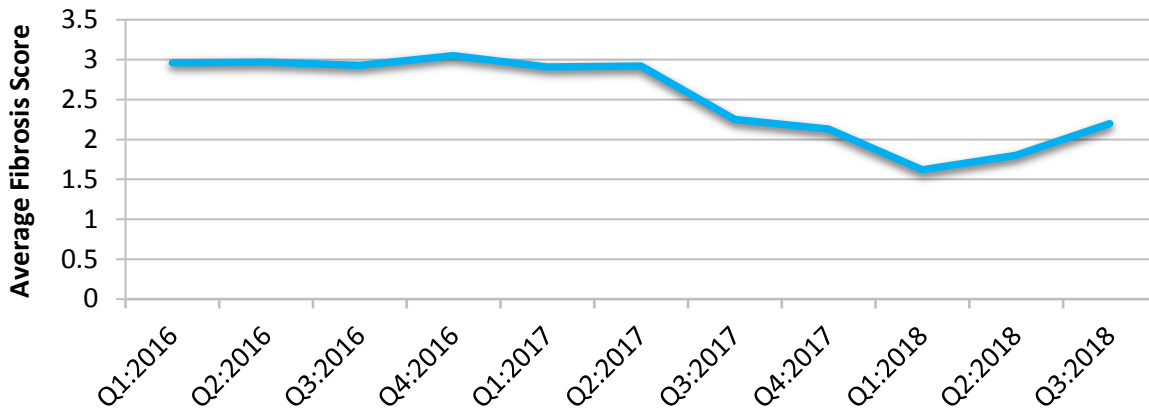


The following graph outlines the trends in average METAVIR equivalent fibrosis score by quarter. An immediate decline in average fibrosis score can be seen following the change to F1 in July 2017, and again following the change to F0 in January 2018. The average fibrosis score dropped by 45.3% from quarter one 2016 (Q1:2016) to quarter one 2018 (Q1:2018). Recently in



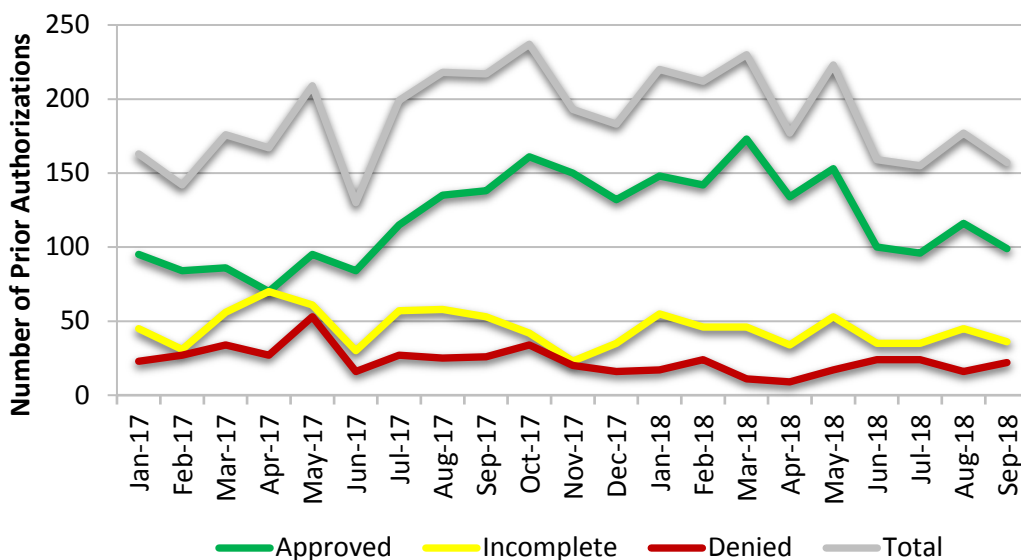
quarter three 2018 (Q3:2018), the average fibrosis score trended to levels similar to quarter three 2017 (Q3:2017).

### HCV Fibrosis Score Quarterly Trends



Prior authorization requests as well as approvals increased following the F1 and F0 transitions. For comparison, total requests increased by 35.0% when comparing January 2017 to January 2018. Additionally, the percentage of approved prior authorizations per month increased from 58.3% to 67.2% for January 2017 and January 2018, respectively. Recent trends in the 3<sup>rd</sup> quarter of 2018 show a trend towards total requests similar to June 2017; however, the percentage of approved prior authorizations remains consistently greater than prior to the F2 to F1 transition (July 2017). Incomplete prior authorizations are typically a result of incomplete prior authorization submissions or failure to complete the prior authorization form. Denials are rare and most commonly a result of the member being dual eligible in which their primary prescription drug plan would reimburse for the medication. Approvals are granted for 28 days of therapy each time to monitor adherence, so members will have a prior authorization request for each refill of therapy.

### HCV Medication Prior Authorization Monthly Trends



## Utilization of Hepatitis C Medications: Fiscal Year 2018

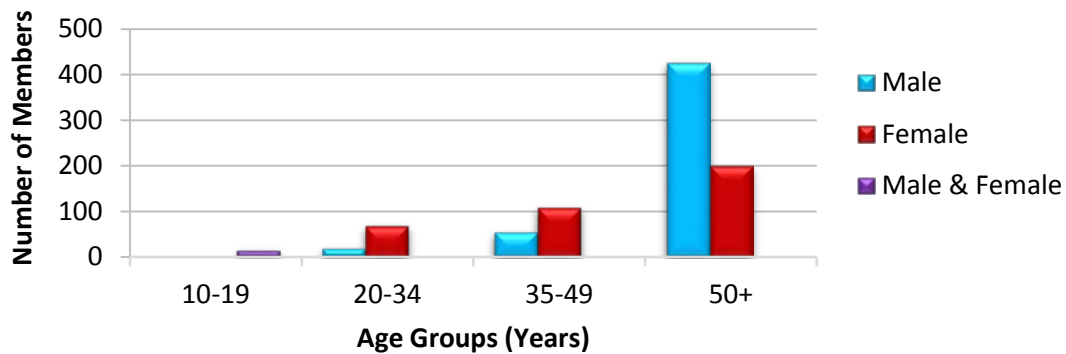
### Comparison of Fiscal Years

Fiscal Year	*Total Members	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2017	369	1,061	\$25,351,810.41	\$23,894.26	\$852.56	48,621	29,736
2018	683	1,687	\$36,248,488.07	\$21,486.95	\$767.65	77,199	47,220
% Change	85.10%	59.00%	43.00%	-10.10%	-10.00%	58.80%	58.80%
Change	314	626	\$10,896,677.66	-\$2,407.31	-\$84.91	28,578	17,484

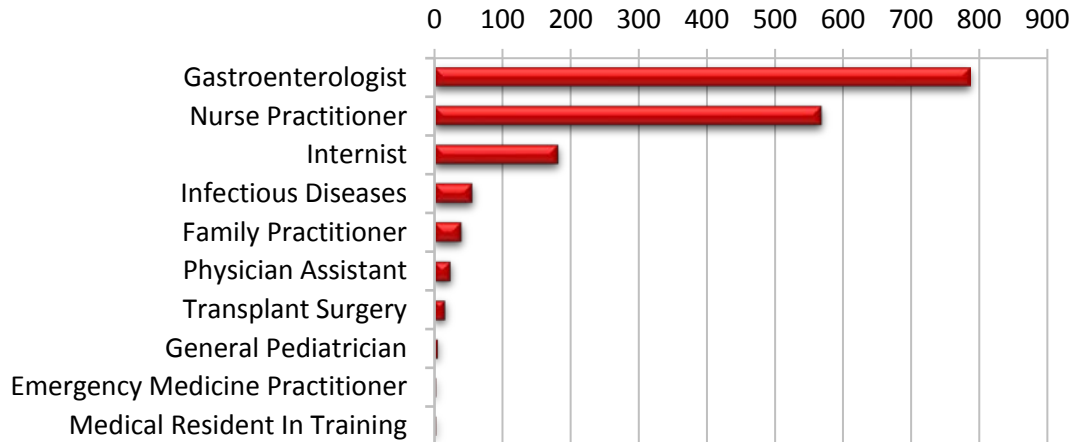
\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

### Demographics of Members Utilizing Hepatitis C Medications

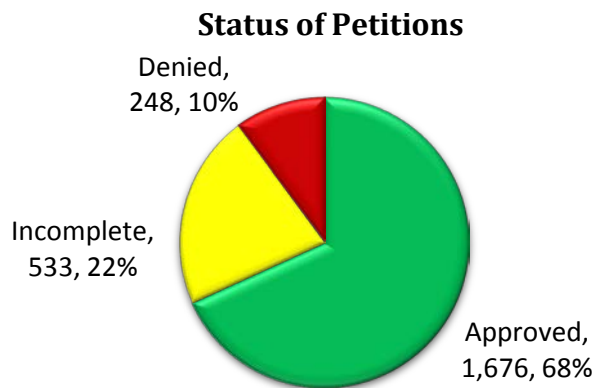


### Top Prescriber Specialties of Hepatitis C Medications by Number of Claims



### Prior Authorization of Hepatitis C Medications

There were 2,457 prior authorization requests submitted for 798 unique members for hepatitis C medications during fiscal year 2018. 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 for fiscal year 2018.



## Market News and Updates<sup>3,4,5,6,7,8,9,10,11,12,13,14,15</sup>

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### Anticipated Patent Expiration(s):

- Sovaldi® (sofosbuvir): December 2030
- Zepatier® (elbasvir/grazoprevir): May 2031
- Daklinza™ (daclatasvir): June 2031
- Epclusa® (sofosbuvir/velpatasvir): January 2034
- Harvoni® (ledipasvir/sofosbuvir): January 2034
- Vosevi® (sofosbuvir/velpatasvir/voxilaprevir): July 2034
- Mavyret™ (glecaprevir/pibrentasvir): June 2035

### Discontinuation(s):

- **Olysio® (simeprevir):** In December 2017, Janssen announced the discontinuation of Olysio®. The discontinuation is voluntary and is not related to product quality, safety, or efficacy. Olysio® was no longer available effective May 25, 2018.
- **Technivie™ (ombitasvir/paritaprevir/ritonavir) and Viekira XR™ (ombitasvir/paritaprevir/ritonavir/dasabuvir ER):** In May 2018, AbbVie, Inc. announced the discontinuation of Technivie™ and Viekira XR™. The discontinuation is voluntary and is not related to product quality, safety, or efficacy. Both products are estimated to be available until January 1, 2019.

### News:

- **October 2017:** A study published in the Center for Disease Control and Prevention's (CDC) *Morbidity and Mortality Weekly Report (MMWR)* in October 2017 analyzed Wisconsin Medicaid recipients between 2011 and 2015. Authors found a 93% increase in the proportion of HCV-infected pregnant women (1 in 368 pregnancies to 1 in 192 pregnancies). Of tested infants born to women infected with HCV during pregnancy, mother-to-infant transmission was reported in 4% of the infants. AASLD/IDSA HCV treatment guidance recommend screening pregnant women for HCV but do not recommend antiviral treatment during pregnancy due to the lack of safety and efficacy data. Current recommendations from the Society for Maternal-Fetal Medicine (SMFM) for pregnant women at risk of HCV infection or who are infected include the following:
  - Providers should screen women who are at increased risk for HCV infection at the first prenatal visit; if the initial results are negative, HCV screening should be repeated later in pregnancy in women with persistent or new risk factors.

- DAA regimens should be used only in the setting of a clinical trial, and antiviral treatment should be deferred to the postpartum period, as these regimens are not currently approved for use in pregnancy.
  - Providers should not perform cesarean delivery solely for the indication of HCV.
  - Providers should not discourage breastfeeding based on a positive HCV infection status.
- **December 2017:** A meta-analysis of nine cohort studies evaluating the efficacy and safety of DAAs in HCV-infected patients taking proton pump inhibitors (PPIs) was published in the *Journal of Clinical and Translational Hepatology*. Concomitant use of PPIs with DAAs was associated with lower odds of achieving sustained virologic response (SVR) compared with non-PPI users [pooled odds ratio (OR): 0.74, 95% confidence interval (CI): 0.63 to 0.88].
  - **April 2018:** A study supported by AbbVie, Inc. of HCV infected patients in the United Kingdom found that treatment initiation at mild fibrosis stages (F0 to F1) lowered the lifetime risk of cirrhosis than if treatment is initiated in moderate fibrosis stages (F2 to F3; 12.4% vs. 23.0%). Additionally, estimated lifetime direct medical costs would be lower when treatment is initiated during the mild fibrosis stage than when initiated during moderate or advanced fibrosis stage (F4; \$47,161 vs. \$50,208 vs. \$87,133).
  - **June 2018:** A study of national specialty pharmacy data published in *Open Forum Infectious Diseases* found that over a 16-month period, a total of 35.5% of HCV patients were denied access to DAA treatment by their insurance. The authors noted that denial of treatment was more common among patients with commercial insurance (52.4%) compared with those with Medicaid (34.5%) or Medicare (14.7%, P<0.001 for both).
  - **June 2018:** A study of National Health and Nutrition Examination Survey (NHANES) data from 2000 to 2010 evaluated 311 HCV-infected patients for factors associated with HCV infection and HCV-related death. Researchers found that HCV-infected patients were more likely to have Medicaid or be uninsured. The presence of HCV significantly increased mortality [hazard ratio (HR) 2.04, 95% CI: 1.17 to 3.35], particularly among patients on Medicaid (HR 9.64, 95% CI: 1.66 to 55.97). HCV-positive Medicaid patients also demonstrated higher rates of comorbidities such as diabetes, congestive heart failure (CHF), and stroke (P<0.05).
  - **July 2018:** The AASLD/IDSA HCV treatment guidance was updated in May adding recommendations for pregnant women and populations with a high burden of HCV infection including people who inject drugs, men who have sex with men, and people in correctional settings.
  - **July 2018:** Merck & Co., Inc. announced it will lower the price of Zepatier® (elbasvir/grazoprevir) by 60%. In July 2018, the Wholesale Acquisition Cost (WAC) of Zepatier® was \$54,600 for 12 weeks of therapy. The WAC of Zepatier® effective October 2018 is \$21,840 for 12 weeks of therapy.
  - **August 2018:** Louisiana has proposed a prescription-based model to increase access to hepatitis C medications in the Medicaid and prison populations. The state has proposed taking the money they would normally spend towards HCV treatment and working with manufacturers to negotiate an amount for unlimited access to the medication over a 3 to 5 year period. Louisiana is currently seeking public input on the idea and then will later select a manufacturer for the proposal.

- September 2018:** Gilead Sciences, Inc. announced plans to launch authorized generic versions of Epclusa® (sofosbuvir/velpatasvir) and Harvoni® (ledipasvir/sofosbuvir) through a subsidiary, Asegua Therapeutics, LLC. The authorized generics will launch at a list price of \$24,000 for the most common course of therapy and will be available in January 2019. Gilead also announced they are pursuing other innovative financing models including a potential subscription model.

### Regimen Comparison<sup>8,16,17,18,19</sup>

The following table shows the current AASLD/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 excludes regimens considered “alternative” in the guidance as opposed to “recommended”; regimens are ordered as they are recommended in the guidance. Specific regimens are used in particular patient populations depending on comorbidities, pre-treatment viral load, prior HCV treatment experience, fibrosis stage, cirrhosis status, and baseline viral polymorphisms. 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	Treatment-naïve, Non-cirrhotic	EBR/GZR 12 wks	\$21,840.00	92% <sup>+</sup>
		GLEC/PIB 8 wks	\$25,761.12	99% (1a & 1b) <sup>Ω</sup>
		LED/SOF 8 or 12 wks	\$61,540.64-\$92,310.96	93% or 96%
		VEL/SOF 12 wks	\$73,034.64	98% <sup>¥</sup>
	Treatment-naïve, Cirrhotic	EBR/GZR 12 wks	\$21,840.00	92% <sup>+</sup>
		GLEC/PIB 12 wks	\$38,641.68	99% (1a & 1b) <sup>Ω</sup>
		LED/SOF 12 wks	\$92,310.96	94% (1a & 1b)
		VEL/SOF 12 wks	\$73,034.64	98% <sup>¥</sup>
Genotype 1b	Treatment-naïve, Non-cirrhotic	EBR/GZR 12 wks	\$21,840.00	98% <sup>¥</sup>
		GLEC/PIB 8 wks	\$25,761.12	99% (1a & 1b) <sup>Ω</sup>
		LED/SOF 8 or 12 wks	\$61,540.64-\$92,310.96	98%
		VEL/SOF 12 wks	\$73,034.64	99% <sup>¥</sup>
	Treatment-naïve, Cirrhotic	EBR/GZR 12 wks	\$21,840.00	98%
		GLEC/PIB 12 wks	\$38,641.68	99% (1a & 1b) <sup>Ω</sup>
		LED/SOF 12 wks	\$92,310.96	94% (1a & 1b)
		VEL/SOF 12 wks	\$73,034.64	99% <sup>¥</sup>
Genotype 2	Treatment-naïve, Non-cirrhotic	GLEC/PIB 8 wks	\$25,761.12	98% <sup>Ω</sup>
		VEL/SOF 12 wks	\$73,034.64	99%-100% <sup>¥</sup>
	Treatment-naïve, Cirrhotic	VEL/SOF 12 wks	\$73,034.64	99%-100% <sup>¥</sup>
		GLEC/PIB 12 wks	\$38,641.68	100% <sup>Ω</sup>
Genotype 3	Treatment-naïve, Non-cirrhotic	GLEC/PIB 8 wks	\$25,761.12	94.9%
		VEL/SOF 12 wks	\$73,034.64	98%

Genotype	Host Factors	Treatment Regimen	Total Cost	SVR**
	Treatment-naïve, Cirrhotic	GLEC/PIB 12 wks	\$38,641.68	98%
		VEL/SOF 12 wks	\$73,034.64	93%
Genotype 4	Treatment-naïve, Non-cirrhotic	GLEC/PIB 8 wks	\$25,761.12	93% <sup>□</sup>
		VEL/SOF 12 wks	\$73,034.64	100% <sup>¥</sup>
		EBR/GZR 12 wks	\$21,840.00	97%
		LED/SOF 12 wks	\$92,310.96	93%-100%
	Treatment-naïve, Cirrhotic	VEL/SOF 12 wks	\$73,034.64	100% <sup>¥</sup>
		GLEC/PIB 12 wks	\$38,641.68	100% <sup>□</sup>
		EBR/GZR 12 wks	\$21,840.00	97%
		LED/SOF 12 wks	\$92,310.96	93%-100%
Genotype 5 or 6	Treatment-naïve, Cirrhotic & Non	GLEC/PIB 8 wks (non) 12 wks (cirrhotic)	\$25,761.12-\$38,641.68	GT5: 100%, GT6: 100% <sup>□</sup> GT5: 100%, GT6: 100% <sup>□</sup>
		VEL/SOF 12 wks	\$73,034.64	GT5: 97%, GT6: 100%
		LED/SOF 12 wks	\$92,310.96	GT5: 93%, GT6: 96%

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

\*\*SVR = Sustained virologic response 12 weeks after therapy completion in clinical studies

+Lower % accounts for those with baseline resistance associated variants (RAVs); lower % shown is for 12 weeks without ribavirin.

<sup>□</sup>May include some treatment-experienced patients.

<sup>¥</sup>Percentage includes cirrhotic & non-cirrhotic patients.

SOF = sofosbuvir; LED = ledipasvir; GT = genotype; EBR = elbasvir; GZR = grazoprevir; VEL = velpatasvir; GLEC = glecaprevir; PIB = pibrentasvir

## Recommendations

The College of Pharmacy does not recommend any changes to the current hepatitis C medication prior authorization criteria at this time.

## Utilization Details of Hepatitis C Medications: Fiscal Year 2018

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	% COST	COST/CLAIM
<b>SOFOSBUVIR/LEDIPASVIR PRODUCTS</b>						
HARVONI TAB 90-400MG	519	248	\$15,933,872.05	2.09	43.96%	\$30,701.10
<b>SUBTOTAL</b>	<b>519</b>	<b>248</b>	<b>\$15,933,872.05</b>	<b>2.09</b>	<b>43.96%</b>	<b>\$30,701.10</b>
<b>SOFOSBUVIR/VELPATASVIR PRODUCTS</b>						
EPCLUSA TAB 400-100MG	394	150	\$9,545,422.66	2.63	26.33%	\$24,226.96
<b>SUBTOTAL</b>	<b>394</b>	<b>150</b>	<b>\$9,545,422.66</b>	<b>2.63</b>	<b>26.33%</b>	<b>\$24,226.96</b>
<b>GLECAPREVIR/PIBRENTASVIR PRODUCTS</b>						
MAVYRET TAB 100-40MG	316	154	\$4,173,662.90	2.05	11.51%	\$13,207.79
<b>SUBTOTAL</b>	<b>316</b>	<b>154</b>	<b>\$4,173,662.90</b>	<b>2.05</b>	<b>11.51%</b>	<b>\$13,207.79</b>
<b>ELBASVIR/GRAZOPREVIR PRODUCTS</b>						
ZEPATIER TAB 50-100MG	295	109	\$5,244,710.30	2.71	14.47%	\$17,778.68
<b>SUBTOTAL</b>	<b>295</b>	<b>109</b>	<b>\$5,244,710.30</b>	<b>2.71</b>	<b>14.47%</b>	<b>\$17,778.68</b>
<b>SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR PRODUCTS</b>						
VOSEVI TAB 400-100-100MG	32	11	\$797,665.60	2.91	2.20%	\$24,927.05
<b>SUBTOTAL</b>	<b>32</b>	<b>11</b>	<b>\$797,665.60</b>	<b>2.91</b>	<b>2.20%</b>	<b>\$24,927.05</b>
<b>SOFOSBUVIR PRODUCTS</b>						

PRODUCT UTILIZED	TOTAL CLAIMS	TOTAL MEMBERS	TOTAL COST	CLAIMS/MEMBER	% COST	COST/CLAIM
SOVALDI TAB 400MG	15	7	\$418,759.05	2.14	1.16%	\$27,917.27
<b>SUBTOTAL</b>	<b>15</b>	<b>7</b>	<b>\$418,759.05</b>	<b>2.14</b>	<b>1.16%</b>	<b>\$27,917.27</b>
<b>DACLATASVIR PRODUCTS</b>						
DAKLINZA TAB 60MG	3	1	\$61,292.85	3	0.17%	\$20,430.95
<b>SUBTOTAL</b>	<b>3</b>	<b>1</b>	<b>\$61,292.85</b>	<b>3</b>	<b>0.17%</b>	<b>\$20,430.95</b>
<b>OMBITASVIR/PARITAPREVIR/RITONAVIR/DASABUVIR PRODUCTS</b>						
VIEKIRA XR TAB 200-8.33-50-33.33MG	2	1	\$55,567.10	2	0.15%	\$27,783.55
<b>SUBTOTAL</b>	<b>2</b>	<b>1</b>	<b>\$55,567.10</b>	<b>2</b>	<b>0.15%</b>	<b>\$27,783.55</b>
<b>RIBAVIRIN PRODUCTS</b>						
RIBAVIRIN TAB 200MG	92	36	\$9,007.30	2.56	0.02%	\$97.91
RIBASPHERE TAB 200MG	12	6	\$1,367.21	2	0.00%	\$113.93
RIBAVIRIN CAP 200MG	4	1	\$435.26	4	0.00%	\$108.82
<b>SUBTOTAL</b>	<b>108</b>	<b>42</b>	<b>\$10,809.77</b>	<b>2.57</b>	<b>0.02%</b>	<b>\$100.09</b>
<b>INTERFERON PRODUCTS</b>						
INTRON A INJ 25MU	2	1	\$5,419.60	2	0.01%	\$2,709.80
INTRON A INJ 18MU	1	1	\$1,306.19	1	0.00%	\$1,306.19
<b>SUBTOTAL</b>	<b>3</b>	<b>2</b>	<b>\$6,725.79</b>	<b>1.5</b>	<b>0.01%</b>	<b>\$2,241.93</b>
<b>TOTAL</b>	<b>1,687</b>	<b>683*</b>	<b>\$36,248,488.07</b>	<b>2.47</b>	<b>100%</b>	<b>\$21,486.95</b>

\*Total number of unduplicated members.

Costs do not reflect rebated prices or net costs.

<sup>1</sup> Gilead Sciences, Inc. U.S. Food and Drug Administration Approves Gilead's Sovaldi™ (Sofosbuvir) for the Treatment of Chronic Hepatitis C. *Business Wire*. Available online at: <http://www.gilead.com/news/press-releases/2013/12/us-food-and-drug-administration-approves-gileads-sovaldi-sofosbuvir-for-the-treatment-of-chronic-hepatitis-c>. Issued 12/06/2013. Last accessed 10/15/2018.

<sup>2</sup> Janssen Therapeutics. Olysio™ (simeprevir) Receives FDA Approval for Combination Treatment of Chronic Hepatitis C. Available online at: <https://www.inj.com/media-center/press-releases/olysio-simeprevir-receives-fda-approval-for-combination-treatment-of-chronic-hepatitis-c>. Issued 11/22/2013. Last accessed 10/15/2018.

<sup>3</sup> 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 09/2018. Last accessed 10/16/2018.

<sup>4</sup> OptumRx. Olysio® (simeprevir) – Drug discontinuation. Available online at: [https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-recalls-shortages/drugwithdrawal\\_olysio\\_2018-0420.pdf](https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-recalls-shortages/drugwithdrawal_olysio_2018-0420.pdf). Issued 12/2017. Last accessed 10/17/2018.

<sup>5</sup> Han DH. Two Hepatitis C Virus Infection Treatments to Be Discontinued. *Monthly Prescribing Reference (MPR)*. Available online at: <https://www.empr.com/news/technivie-viekira-xr-discontinued-hepatitis-c-virus-treatments/article/768368/>. Issued 05/24/2018. Last accessed 10/16/2018.

<sup>6</sup> Wysong P. HCV in Pregnant Women on Rise. *Medpage Today*. Available online at: <https://www.medpagetoday.com/reading-room/aga/lower-gi/71627>. Issued 03/08/2018. Last accessed 10/17/2018.

<sup>7</sup> Highleyman L. Updated HCV Guidelines Focus on Key Populations. *Medpage Today*. Available online at: <https://www.medpagetoday.com/reading-room/aga/lower-gi/74239>. Issued 07/26/2018. Last accessed 10/17/2018.

<sup>8</sup> 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 05/24/2018. Last accessed 10/17/2018.

<sup>9</sup> Wijarnpreecha K, Chesdachai S, Thongprayoon C, et al. Efficacy and Safety of Direct-acting Antivirals in Hepatitis C Virus-infected Patients Taking Proton Pump Inhibitors. *J Clin Transl Hepatol* 2017; 5(4):327-334.

<sup>10</sup> Osterweil N. Hep C Treatments Save Care Costs if Administered Early. *Medscape*. Available online at: [https://www.medscape.com/viewarticle/895236#vp\\_2](https://www.medscape.com/viewarticle/895236#vp_2). Issued 04/16/2018. Last accessed 10/17/2018.

<sup>11</sup> Walker M. Over One-Third of HCV Patients Denied DAA Tx by Payers. *Medpage Today*. Available online at: <https://www.medpagetoday.com/infectiousdisease/hepatitis/73368>. Issued 06/07/2018. Last accessed 10/17/2018.

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- <sup>12</sup> Basen R. Medicaid or No Insurance Tied to Higher Death Risk in HCV. *Medpage Today*. Available online at: <https://www.medpagetoday.com/meetingcoverage/ddw/73307>. Issued 06/05/2018. Last accessed 10/17/2018.
- <sup>13</sup> Merck To Steeply Cut Price of Hepatitis C Drug Zepatier. *Managed Care Magazine*. Available online at: <https://www.managedcaremag.com/dailynews/20180720/merck-steeply-cut-price-hepatitis-c-drug-zepatier>. Issued 07/20/2018. Last accessed 10/17/2018.
- <sup>14</sup> Crisp E. Louisiana considering new method for increasing access to Hep C drugs. *The Advocate*. Available on line at: [https://www.theadvocate.com/baton\\_rouge/news/politics/article\\_a38024fe-a006-11e8-8380-6fde3459ab35.html](https://www.theadvocate.com/baton_rouge/news/politics/article_a38024fe-a006-11e8-8380-6fde3459ab35.html). Issued 08/14/2018. Last accessed 10/17/2018.
- <sup>15</sup> Gilead Sciences, Inc. Gilead Subsidiary to Launch Authorized Generics of Eplclusa® (Sofosbuvir/Velpatasvir) and Harvoni® (Ledipasvir/Sofosbuvir) for the Treatment of Chronic Hepatitis C. *Business Wire*. Available online at: <http://www.gilead.com/news/press-releases/2018/9/gilead-subsidiary-to-launch-authorized-generics-of-eplclusa-sofosbuvirvelpatasvir-and-harvoni-ledipasvirsofosbuvir-for-the-treatment-of-chronic-hepatitis-c>. Issued 09/24/2018. Last accessed 10/16/2018.
- <sup>16</sup> Mavyret™ Product Information. AbbVie, Inc. Available online at: [http://www.rxabbvie.com/pdf/mavyret\\_pi.pdf](http://www.rxabbvie.com/pdf/mavyret_pi.pdf). Last revised 08/2018. Last accessed 10/17/2018.
- <sup>17</sup> Harvoni® Product Information. Gilead Sciences, Inc. Available online at: [http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/harvoni/harvoni\\_pi.pdf](http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf). Last revised 11/2017. Last accessed 10/17/2018.
- <sup>18</sup> Eplclusa® Product Information. Gilead Sciences, Inc. Available online at: [http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/eplclusa/eplclusa\\_pi.pdf](http://www.gilead.com/~media/Files/pdfs/medicines/liver-disease/eplclusa/eplclusa_pi.pdf). Last revised 11/2017. Last accessed 10/17/2018.
- <sup>19</sup> Zepatier™ Product Information. Merck and Co., Inc. Available online at: [http://www.merck.com/product/usa/pi\\_circulars/z/zepatier/zepatier\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf). Last revised 06/2018. Last accessed 10/17/2018.





# Appendix O





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## **30-Day Notice to Prior Authorize Signifor® LAR (Pasireotide)**

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**Oklahoma Health Care Authority  
November 2018**

### **Acromegaly Summary<sup>1,2,3</sup>**

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Acromegaly is the result of persistent hypersecretion of growth hormone (GH). Excess GH causes the liver to secrete insulin-like growth factor-1 (IGF-1), which is the cause of many of the clinical manifestations of acromegaly. Acromegaly is most commonly seen in adults with a mean age of 40 to 45 years. Excess GH in children prior to the closure of the epiphyseal growth plates results in pituitary gigantism and not acromegaly. Some clinical manifestations of acromegaly include overgrowth of the skin, connective tissues, cartilage, bone, and viscera, excessive sweating, jaw overgrowth, joint pain, and cardiomyopathy.

The estimated prevalence of acromegaly is 40 to 125 per one million people. The most common cause of acromegaly is a somatotroph (GH-secreting) adenoma of the anterior pituitary, which accounts for nearly one-third of patients with acromegaly. Other causes include a specific gene mutation and various neuroendocrine tumors. The goals of acromegaly treatment are to normalize IGF-1 and GH levels, reverse the effects of the tumor, and to minimize risk of long-term mortality.

Acromegaly treatment guidelines recommend pituitary surgery as the primary treatment option in patients with adenomas. Medication therapy is recommended in patients who have persistent disease after surgery or for patients in which surgical intervention is not an option. There are three medication classes that are used as adjuvant treatment in patients with acromegaly: dopamine agonists (DAs), somatostatin analogs (SSAs), and GH receptor antagonists. Cabergoline and bromocriptine are two DAs, which are considered first-line because they are orally administered and relatively inexpensive compared to the other treatment options. SSAs are often used second-line because they are effective in normalizing IGF-1 and GH in more than half of patients, but can be more expensive than DAs. There are three SSAs that are used to treat acromegaly, all of which are available in long-acting formulations: octreotide, lanreotide, and pasireotide. Currently the guidelines do not recommend one SSA over the others. Pegvisomant is a GH receptor antagonist that is given as a daily subcutaneous (sub-Q) injection, but because of side effects and risk of increasing tumor size, pegvisomant is reserved for patients that have an inadequate response or intolerance to SSAs.

### **Cushing's Disease Summary<sup>4,5</sup>**

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Cushing's disease is caused by a pituitary gland tumor that over secretes adrenocorticotrophic hormone (ACTH) causing hypercortisolemia that results in the manifestation of Cushing's syndrome. Nearly 80% of cases of Cushing's syndrome are caused by Cushing's disease, or an ACTH-secreting pituitary adenoma. The estimated prevalence of Cushing's syndrome is 40 cases per one million people. Cushing's disease is most commonly seen in adults in the 3<sup>rd</sup> and 4<sup>th</sup> decade of life, and it is more prevalent in women than men.

Diagnosing Cushing's disease can be difficult because the symptoms can be non-specific. Clinical characteristics of Cushing's syndrome include obesity, buffalo-hump, rounded face, osteoporosis, protein wasting, hirsutism, menstrual irregularities, and mild-to-severe psychiatric disturbances. A diagnostic cortisol level in conjunction with clinical characteristics can confirm Cushing's syndrome. There are several lab tests that can then be used in conjunction with the presence of a pituitary tumor to confirm that the patient has Cushing's disease.

Guidelines suggest transsphenoidal surgery as first-line therapy for Cushing's disease. For patients who are not cured by surgery or who are not candidates for surgery, medical treatments can decrease the synthesis and secretion of cortisol. Steroidogenesis inhibitors, mitotane, ketoconazole, metyrapone, and etomidate, work through different mechanisms to reduce cortisol. Mifepristone, a glucocorticoid receptor antagonist, can be used to control the clinical symptoms of Cushing's disease. ACTH-lowering agents, including DAs and pasireotide, can also decrease the levels of cortisol in patients. Radiation therapy is another option for patients with Cushing's disease. The goal of therapy is to keep patients from being in a chronic hypercortisol state, which can increase morbidity and mortality due to cardiovascular factors leading to heart defects.

## **Market News and Updates**<sup>6,7,8,9</sup>

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### **Recent U.S. Food and Drug Administration (FDA) Approvals:**

- **June 2018:** The FDA approved a supplemental New Drug Application (sNDA) for Signifor® LAR (pasireotide) for the treatment of Cushing's disease. Previously, Signifor® LAR (long-acting release) was FDA approved for the treatment of acromegaly. Signifor® LAR was approved in two additional strengths, 10mg and 30mg, for the new indication. Pasireotide is also available as Signifor® injection, a short-acting formulation that is indicated for Cushing's disease, but is not indicated for acromegaly.

### **Pipeline:**

- **Seliciclib:** In September 2018, the FDA announced that they awarded twelve new clinical trial research grants totaling over \$18 million, one of which went to Cedars-Sinai Medical Center for \$2 million dollars over four years for the Phase 2 trial of seliciclib to treat Cushing's disease. These grants were issued to enhance the development of medical products for patients with rare diseases.
- **Mycapssa® (octreotide) capsule:** Mycapssa® is an octreotide capsule that is currently in a Phase 3 trial under a special protocol assessment (SPA) agreement with the FDA to support the resubmission of a New Drug Application (NDA). Mycapssa® was originally submitted by Chiasma, Inc. for approval in 2016. The FDA issued a Complete Response Letter (CRL) to the company indicating the application was not approvable in its current form. The SPA changed a few of the secondary endpoints and allowed for an additional Phase 3 trial to evaluate the proportion of acromegaly patients that maintain their biochemical response when switched to Mycapssa®. Data from the Phase 3 trial is expected to be available in late 2019.

## Signifor® LAR (Pasireotide) Product Summary<sup>6</sup>

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**Indication(s):** Signifor® LAR (pasireotide) is an SSA indicated for the treatment of the following:

- Patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option.
- Patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

**Dosing:**

- Signifor® LAR (pasireotide) is available as 10mg, 20mg, 30mg, 40mg, and 60mg vials intended for intramuscular (IM) injection.
- Pasireotide LAR should be reconstituted and administered immediately IM by a health care professional. IM injections should be administered in the left or right gluteus.
- Recommended initial dosing:
  - Acromegaly: 40mg IM once every 4 weeks
  - Cushing's Disease: 10mg IM once every 4 weeks
- Dose adjustments may be required based on response and tolerability (*refer to the Signifor® LAR prescribing information for detailed information regarding dose adjustment and monitoring*).
- The pasireotide LAR dose should be adjusted in patients with moderate hepatic impairment (Child-Pugh B) and pasireotide LAR use should be avoided in severe hepatic impairment (Child-Pugh C).

**Mechanism of Action:** Pasireotide exerts its pharmacological activity by binding to somatostatin receptors (SSTR). There are 5 known human SSTR subtypes. Pasireotide binds with high affinity to 4 of the 5 subtypes (SSTR 1, 2, 3, and 5).

**Contraindication(s):** None

**Warnings and Precautions:**

- Hyperglycemia and Diabetes: Pasireotide LAR can cause increased blood glucose levels. Patients that develop significant hyperglycemia may require anti-diabetic treatment.
- Bradycardia and QT Prolongation: QTc >480ms and bradycardia have been reported in patients treated with pasireotide LAR. Caution should be used in patients who are at risk of developing prolongation of the QT interval.
- Liver Test Elevations: Elevated liver function tests (LFTs) were noted in patients treated with pasireotide LAR for both indications. It is recommended that LFTs be assessed periodically when starting treatment and throughout treatment.
- Cholelithiasis: Cholelithiasis was reported during clinical trials. It is recommended to monitor patients periodically.
- Pituitary Hormone Deficiencies: Pasireotide LAR can cause suppression of the anterior pituitary hormones including thyroid, adrenal, and gonadal hormones. Patients should be monitored routinely for hormone insufficiencies.

**Use in Specific Populations:**

- Pregnancy and Lactation: There is limited data on the effects of pasireotide on pregnancy and lactation.

- **Females and Males of Reproductive Potential:** Improved fertility may be seen in patients that have a reduction of GH, normalized IGF-1, and normalized serum cortisol levels.
- **Pediatric Patients:** The safety and efficacy of pasireotide LAR has not been established in pediatric patients.
- **Geriatric Patients:** Pasireotide LAR clinical trials did not contain enough patients 65 of age or older to determine if they respond differently compared to younger patients. In general, dose selection for geriatric patients should be cautious, usually starting at the low end of the dosing range.
- **Hepatic Impairment:** Dose adjustments are not required for patients with mild hepatic impairment (Child-Pugh A), but are required for patients with moderately impaired hepatic function (Child-Pugh B). The safety and efficacy have not been established in patients with severe hepatic impairment (Child-Pugh C), and there are no current dosing recommendations.
- **Renal Impairment:** Clinical studies of pasireotide LAR in patients with renal impairment have not been conducted. Based on studies of pasireotide subcutaneous (sub-Q) injections, dosage adjustments may not be needed in patients with renal impairment.

**Adverse Reactions:** Common adverse reactions associated with pasireotide LAR ( $\geq 10\%$ ) during clinical studies included the following: hyperglycemia, diabetes mellitus, diarrhea, abdominal pain, nausea, cholelithiasis, and fatigue.

**Efficacy:** The efficacy of pasireotide LAR was established in three randomized, double-blind studies.

- **Acromegaly:** A multicenter, randomized, double-blind study was conducted to assess the safety and efficacy of pasireotide LAR in patients with acromegaly. A total of 358 patients that were treatment-naïve were randomized 1:1 to pasireotide LAR or octreotide LAR. The patients were stratified based on whether they previously had pituitary surgery or not. The primary efficacy endpoint was the proportion of patients with a mean GH level  $< 2.5\text{mcg/L}$  and a normal age and sex adjusted IGF-1 level at 12 months. The proportion of patients meeting the primary endpoint was 31.3% and 19.2% for the pasireotide LAR and octreotide LAR comparator, respectively.
- An additional study for patients with acromegaly that were inadequately controlled on the other SSAs was also conducted. This study was a double-blind, multicenter, randomized, three-arm study. Patients were randomized to pasireotide LAR 40mg or pasireotide LAR 60mg or continued open-label pre-trial SSA therapies at maximal dose(s). Patients had to be treated with another SSA for at least six months prior to randomization. A total of 181 patients completed the trial. Inadequate control was defined by those that had a GH  $> 2.5\text{mcg/L}$  and a sex and age adjusted IGF-1  $> 1.3$  times the upper limit of normal (ULN). The primary efficacy endpoint was the proportion of patients that were controlled with a GH level  $< 2.5\text{mcg/L}$  and a normal IGF-1 level. The proportion of patients meeting the primary endpoint at six months was 15.4% and 20.2% for pasireotide LAR 40mg and 60mg, respectively.
- **Cushing's Disease:** The safety and efficacy of pasireotide LAR was evaluated in a Phase 3, randomized, double-blind, multicenter study. The study enrolled 150 patients for a 12-month treatment period. Patients with a mean urinary free cortisol level (mUFC)  $\geq 1.5$

and  $\geq 5$  times ULN were randomized to receive a starting dose of pasireotide LAR 10mg or 30mg IM once every 28 days. Patients were stratified based on their mUFC (1.5 to  $< 2$  x ULN vs. 2 to 5 x ULN) at screening. After 4 months, patients that still had a mUFC  $> 1.5$  x ULN had their dose increased, provided there were no tolerability concerns. After 12 months, patients were given the option to enter an extension phase if they benefited from treatment. The primary efficacy endpoint was the proportion of patients in each arm who achieved a mUFC  $< ULN$  after 7 months of treatment. The proportion of patients that responded at 7 months was 39.2% (95% CI: 28.0, 51.2) and 40.8% (95% CI: 29.7, 52.7) in the 10mg and 30mg starting dose groups, respectively.

**Cost Comparison:**

Medication	Cost Per Unit	Cost Per 28 Days
<b>Signifor® LAR (pasireotide) 40mg vial</b>	<b>\$12,308.80/vial</b>	<b>\$12,308.80</b>
Sandostatin® LAR Depot (octreotide) 20mg vial	\$3,535.49/vial	\$3,535.49
Somatuline® Depot (lanreotide) 90mg/0.3mL	\$5,295.87/0.3mL	\$5,295.87

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.

Unit = vial or 0.3mL

**Recommendations**

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The College of Pharmacy recommends the prior authorization of Signifor® LAR (pasireotide) with the following criteria:

**Signifor® LAR (Pasireotide) Approval Criteria:**

1. An FDA approved diagnosis of one of the following:
  - a. Members with acromegaly who have had an inadequate response to surgery or for whom surgery is not an option; or
  - b. Members with Cushing’s disease for whom pituitary surgery is not an option or has not been curative; and
2. For a diagnosis of acromegaly, the member must have a documented trial with octreotide long-acting or lanreotide depot with an inadequate response or have a patient-specific, clinically significant reason why the other long-acting somatostatin analog (SSAs) are not appropriate for the member; and
3. Pasireotide LAR must be prescribed by or in consultation with an endocrinologist; and
4. Pasireotide LAR must be administered by a health care professional in a health care setting; and
5. Prescriber must document that the member has had an inadequate response to surgery or is not a candidate for surgery; and
6. Prescriber must verify liver function tests (LFTs) (e.g., ALT, AST, bilirubin) will be monitored when starting treatment and periodically thereafter; and
7. Authorizations will be for the duration of 12 months; and
8. Reauthorization may be granted if the prescriber documents the member is responding well to treatment.

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- <sup>1</sup> Melmed S, Katznelson L. Diagnosis of Acromegaly. *UpToDate*. Available online at: [https://www.uptodate.com/contents/diagnosis-of-acromegaly?search=acromegaly&source=search\\_result&selectedTitle=1~87&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/diagnosis-of-acromegaly?search=acromegaly&source=search_result&selectedTitle=1~87&usage_type=default&display_rank=1). Last revised 04/30/2018. Last accessed 09/26/2018.
- <sup>2</sup> Katznelson L, Atkinson J, Cook D, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Acromegaly. *Endocrine Practice* 2011; 17(4).
- <sup>3</sup> Melmed S, Katznelson L. Causes and Clinical Manifestations of Acromegaly. *UpToDate*. Available online at: [https://www.uptodate.com/contents/diagnosis-of-acromegaly?search=acromegaly&source=search\\_result&selectedTitle=1~87&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/diagnosis-of-acromegaly?search=acromegaly&source=search_result&selectedTitle=1~87&usage_type=default&display_rank=1). Last revised 04/30/2018. Last accessed 09/26/2018.
- <sup>4</sup> Castinetti T, Morange I, et al. Cushing's Disease. *Orphanet Journal of Rare Diseases* 2012; 7:41.
- <sup>5</sup> Nieman L. Overview of the Treatment of Cushing's Syndrome. *UpToDate*. Available online at: [https://www.uptodate.com/contents/overview-of-the-treatment-of-cushings-syndrome?topicRef=119&source=related\\_link#H1158422206](https://www.uptodate.com/contents/overview-of-the-treatment-of-cushings-syndrome?topicRef=119&source=related_link#H1158422206). Last revised 11/28/2017. Last accessed 09/26/2018.
- <sup>6</sup> Signifor® LAR Prescribing Information. Novartis Pharmaceuticals, Corp. Available online at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/203255s004lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/203255s004lbl.pdf). Last revised 06/2018. Last accessed 10/16/2018.
- <sup>7</sup> U.S. Food and Drug Administration (FDA). FDA News Release: FDA awards 12 grants to fund new clinical trials to advance the development of medical products for the treatment of rare diseases. Available online at: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm621490.htm>. Issued 09/24/2018. Last accessed 10/16/2018.
- <sup>8</sup> Chiasma, Inc. FDA Issues Complete Response Letter for Mycapssa New Drug Application. *Globe Newswire*. Available online at: <https://globenewswire.com/news-release/2016/04/15/829428/0/en/FDA-Issues-Complete-Response-Letter-for-Mycapssa-New-Drug-Application.html>. Issued 04/15/2016. Last Accessed 10/16/2018.
- <sup>9</sup> Chiasma, Inc. Octreotide Capsules. Available online at: <http://www.chiasmapharma.com/octreotide-capsules>. Last accessed 09/26/2018.





# Appendix P





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# Industry News and Updates

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Oklahoma Health Care Authority

November 2018

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## Introduction

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

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## News and Updates<sup>1,2,3,4,5,6</sup>

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### News:

- **Medication Disposal:** According to Karen Bastianelli, associate professor of pharmacy at the University of Minnesota College of Pharmacy, the most effective way to dispose of unwanted or outdated prescription drugs is through medication take-back events. The Drug Enforcement Agency (DEA) has held these events for 15 years and collected approximately 1 million pounds of drugs during its annual National Prescription Drug Take Back Day. Another option is medication disposal boxes; these can be found at police departments or pharmacies. Patients can also pick up envelopes at a pharmacy, place the medications inside, and send them for incineration. Bastianelli recommends that if medications are disposed of in the trash that they are made unpalatable first by adding coffee grounds or kitty litter, pouring liquid in, and sealing it up with strong tape in an opaque container. A final option is flushing drugs down the toilet. “The only things we want people to flush are those very potent meds that could kill a person who has never used a narcotic before with one dose,” Bastianelli says. The U.S. Food and Drug Administration (FDA) has a “Flush List” which includes 15 medications, primarily opioids and other controlled substances. “We don’t want these getting into the hands of kids, especially, so just flush them immediately,” she adds.
- **Vaccinations:** The Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC) recommend that all women who are or might be pregnant during influenza season receive the influenza vaccine, which can be administered any time during pregnancy. The ACIP also recommends that women receive tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines during each pregnancy, preferably between 27 and 36 weeks’ gestation. Vaccinating pregnant women with influenza and Tdap vaccines can reduce the risk of influenza and pertussis for themselves and their infants. According to a study conducted by the CDC, the influenza vaccine reduced a pregnant woman’s risk of being hospitalized from influenza by an average of 40% over the course of the six influenza seasons analyzed. However, results of a recent survey of pregnant women found that many are unvaccinated. The survey was conducted during March 28 to April 10, 2018 and included 1,771 survey respondents who were pregnant during the peak influenza vaccination period (October 2017 to January 2018). Among the survey respondents,

49.1% reported receiving the influenza vaccine before or during their pregnancy. Among 700 survey respondents who had a live birth, 54.4% reported they received the Tdap vaccine during their pregnancy. Reported reasons for non-vaccination included lack of knowledge regarding the need for Tdap vaccination during every pregnancy and concern about the effectiveness of the influenza vaccine. Providers are encouraged to strongly recommend vaccines that their patients need and administer the needed vaccine, or refer their patients to a vaccination provider. Vaccination coverage was highest among pregnant women when a provider offered vaccination.

- **Alzheimer’s Disease:** Some companies, researchers, and advocacy groups are trying to prevent Alzheimer’s disease in the first place rather than trying to find a cure for it after-the-fact. United Neuroscience is one of those companies and has completed a Phase 2 trial of an Alzheimer’s vaccine. United Neuroscience is working to develop a vaccine that could be prophylactic against Alzheimer’s disease. The disease presents itself with misfolded brain proteins, which can form plaques. The hope is that the company’s therapy can “teach your body to create antibodies against those plaques.”
- **Brand Name Drug Prices:** According to AARP’s latest drug pricing report, brand name prescription drug prices increased four times faster than inflation last year. The report covers the period of 2006 to 2017 and shows that drug prices rise or fall without any correlation to inflation. In Medicaid, if a drug’s price increases more quickly than inflation, an additional rebate penalty is included based on the change in price compared with the consumer price index (CPI). The CPI penalty of the federal rebate is designed to keep Medicaid net cost relatively flat despite increases in drug prices.

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<sup>1</sup> Mitchell H. What’s the best way to get rid of drugs you don’t use? *Wall Street Journal*. Available online at: <https://www.pharmacist.com/article/whats-best-way-get-rid-drugs-you-dont-use>. Issued 09/26/2018. Last accessed 10/03/2018.

<sup>2</sup> Kahn KE, Black CL, Ding H, et al. Influenza and Tdap Vaccination Coverage Among Pregnant Women – United States, April 2018. *MMWR Morb Mortal Wkly Rep* 2018; 67:1055–1059. DOI: <http://dx.doi.org/10.15585/mmwr.mm6738a3>.

<sup>3</sup> Centers for Disease Control and Prevention (CDC). Flu vaccine reduces risk of flu hospitalization among pregnant women. Available online at: <https://www.cdc.gov/media/releases/2018/p1011-flu-vaccine-reduces-risk-pregnant-women.html>. Issued 10/11/2018. Last accessed 10/15/2018.

<sup>4</sup> Mukherjee S. Is an Alzheimer’s Vaccine Possible? *Fortune*. Available online at: <http://fortune.com/2018/10/03/alzheimers-vaccine-fortune-mpw/>. Issued 10/03/2018. Last accessed 10/04/2018.

<sup>5</sup> Report: Brand Name Drug Prices Increased Faster Than Inflation. *FDANews*. Available online at: [https://www.fdanews.com/articles/188722-report-brand-name-drug-prices-increased-faster-than-inflation?utm\\_campaign=Drug%20Daily%20Bulletin&utm\\_source=hs\\_email&utm\\_medium=email&utm\\_content=66553797&hsenc=p2ANqtz-8gWAUOI-2lpOoD-WvWZIHvMIeUhlTgwBESHU9HL8YyvJFHVCFV4Ymxjqcrm42z7-vZdulp7hfP3OKa4EiXsL1dC1KmXz\\_YLeRcwk8IY0hnwGOzDUY&hsmi=66553797](https://www.fdanews.com/articles/188722-report-brand-name-drug-prices-increased-faster-than-inflation?utm_campaign=Drug%20Daily%20Bulletin&utm_source=hs_email&utm_medium=email&utm_content=66553797&hsenc=p2ANqtz-8gWAUOI-2lpOoD-WvWZIHvMIeUhlTgwBESHU9HL8YyvJFHVCFV4Ymxjqcrm42z7-vZdulp7hfP3OKa4EiXsL1dC1KmXz_YLeRcwk8IY0hnwGOzDUY&hsmi=66553797). Issued 10/10/2018. Last accessed 10/11/2018.

<sup>6</sup> Peters CP. The Basics: The Medicaid Drug Rebate Program. National Health Policy Forum. Available Online at: [https://www.nhpf.org/library/the-basics/Basics\\_MedicaidDrugRebate\\_04-13-09.pdf](https://www.nhpf.org/library/the-basics/Basics_MedicaidDrugRebate_04-13-09.pdf). Issued 04/13/2009. Last accessed 10/22/2018.



# Appendix Q





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

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## **Safety Announcements**

### **FDA updates on angiotensin II receptor blocker (ARB) recalls**

*FDA alerts patients and health care professionals to ScieGen's irbesartan recall due to N-Nitrosodiethylamine (NDEA)*

*Investigation ongoing – statement to be updated as more information is available*

**[10/30/2018]** The FDA is alerting patients and health care professionals to ScieGen's voluntary recall of certain lots of irbesartan, an ARB, because they contain NDEA, a known animal and suspected human carcinogen. FDA laboratory testing confirmed NDEA in some lots of ScieGen's irbesartan. ScieGen's irbesartan products are labeled as Westminster Pharmaceuticals and Golden State Medical Supply, Inc. (GSMS). This is the first non-valsartan drug product the agency has found to contain the NDEA impurity. ScieGen's recall affects approximately 1% of the irbesartan drug products in the U.S. market. Additionally, Aurobindo, which manufactures the active pharmaceutical ingredient (API) for ScieGen's irbesartan products, is recalling all unexpired lots of its irbesartan API supplied to the U.S. market with NDEA. FDA and Aurobindo laboratory testing confirmed NDEA in certain lots of their irbesartan API. The FDA reminds patients taking any recalled ARB to continue taking their current medicine until their pharmacist provides a replacement or their doctor provides an alternative treatment option. Not all ARBs contain NDEA or N-Nitrosodimethylamine (NDMA), a probable human carcinogen previously found in certain recalled valsartan products, so pharmacists may be able to provide a refill of medication not affected by the recall, or prescribers may prescribe a different medication that treats the same condition. To date, ScieGen is the only manufacturer of irbesartan drug products found to contain NDEA. The FDA continues to test all ARBs for the presence of impurities and has publicly posted two methods for manufacturers and regulatory agencies around the world to test their ARBs for the unexpected NDMA and NDEA impurities. The combined headspace method and the combined direct injection method can detect and quantify NDMA and NDEA simultaneously in ARB API and finished drug products. The FDA continues to work with API and drug manufacturers to ensure their products are not at risk for NDMA or NDEA formation. The agency reminds manufacturers they are responsible for developing and using suitable methods to detect impurities, including when they make changes to their manufacturing processes. If a manufacturer detects new or higher levels of impurities, they should fully evaluate the impurities and take action to ensure the product is safe for patients.

## **Safety Announcements**

### **Extended Use Dates Provided by Impax Generics to Assist with Epinephrine Auto-Injector Intermittent Supply Interruptions**

**[10/25/2018]** Due to the intermittent supply interruptions of epinephrine auto-injectors, the FDA is alerting health care professionals and patients of updated dates through which some epinephrine injection, USP, 0.15mg and 0.30mg auto-injectors, distributed by Impax Generics, may be used beyond the manufacturer's labeled expiration date. To help ensure patient safety, these products should have been, and should continue to be stored as labeled.

Based on stability data provided by Impax Generics and reviewed by the FDA, the following extended-use dates are supported for specific batches. Patients that have the specific batch numbers will be able to use them through new use dates to help with supply. As data become available, the batches may continue to expand.

The FDA is not requiring or recommending that the identified batches be relabeled with their new use dates. However, if a replacement product becomes available during the extension period, then the agency expects the lots will be replaced and properly disposed of as soon as possible.

## **Current Drug Shortages Index (as of November 6<sup>th</sup>, 2018):**

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

<a href="#">Abciximab (ReoPro) Injection</a>	<i>Currently in Shortage</i>
<a href="#">Amino Acids</a>	<i>Currently in Shortage</i>
<a href="#">Aminophylline Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Asparaginase Erwinia Chrysanthemi (Erwinaze)</a>	<i>Currently in Shortage</i>
<a href="#">Atenolol Tablets</a>	<i>Currently in Shortage</i>
<a href="#">Atropine Sulfate Injection</a>	<i>Currently in Shortage</i>
<a href="#">Azithromycin (Azasite) Ophthalmic Solution 1%</a>	<i>Currently in Shortage</i>
<a href="#">Belatacept (Nulojix) Lyophilized Powder for Injection</a>	<i>Currently in Shortage</i>
<a href="#">Belladonna and Opium Suppository</a>	<i>Currently in Shortage</i>
<a href="#">Bumetanide Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Bupivacaine Hydrochloride and Epinephrine Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Bupivacaine Hydrochloride Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Calcium Chloride Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Calcium Gluconate Injection</a>	<i>Currently in Shortage</i>
<a href="#">Carbidopa and Levodopa Extended Release Tablets</a>	<i>Currently in Shortage</i>
<a href="#">Cefepime Injection</a>	<i>Currently in Shortage</i>
<a href="#">Cefotaxime Sodium (Claforan) Injection</a>	<i>Currently in Shortage</i>
<a href="#">Cefotetan Disodium Injection</a>	<i>Currently in Shortage</i>
<a href="#">Deferoxamine Mesylate for Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Dexrazoxane Injection</a>	<i>Currently in Shortage</i>
<a href="#">Dextrose 5% Injection Bags</a>	<i>Currently in Shortage</i>
<a href="#">Dextrose 50% Injection</a>	<i>Currently in Shortage</i>
<a href="#">Diazepam Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Diltiazem Hydrochloride</a>	<i>Currently in Shortage</i>
<a href="#">Diltiazem Hydrochloride ER (Twice-a-Day) Capsules</a>	<i>Currently in Shortage</i>
<a href="#">Diphenhydramine Injection</a>	<i>Currently in Shortage</i>
<a href="#">Disopyramide Phosphate (Norpace) Capsules</a>	<i>Currently in Shortage</i>
<a href="#">Dobutamine Hydrochloride Injection</a>	<i>Currently in Shortage</i>
<a href="#">Dopamine Hydrochloride Injection</a>	<i>Currently in Shortage</i>
<a href="#">Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution</a>	<i>Currently in Shortage</i>
<a href="#">Dorzolamide Hydrochloride Ophthalmic Solution</a>	<i>Currently in Shortage</i>
<a href="#">Eflornithine Hydrochloride (Vaniga) Cream</a>	<i>Currently in Shortage</i>
<a href="#">Epinephrine Injection, 0.1 mg/mL</a>	<i>Currently in Shortage</i>
<a href="#">Epinephrine Injection, Auto-Injector</a>	<i>Currently in Shortage</i>
<a href="#">Erythromycin Lactobionate for Injection, USP</a>	<i>Currently in Shortage</i>
<a href="#">Ethiodized Oil (Lipiodol) Injection</a>	<i>Currently in Shortage</i>
<a href="#">Etoposide Injection</a>	<i>Currently in Shortage</i>
<a href="#">Etoposide Phosphate (Etopophos) Injection</a>	<i>Currently in Shortage</i>
<a href="#">Fentanyl Citrate (Sublimaze) Injection</a>	<i>Currently in Shortage</i>
<a href="#">Fluorescein Injection</a>	<i>Currently in Shortage</i>
<a href="#">Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution</a>	<i>Currently in Shortage</i>
<a href="#">Fluorescein Strips</a>	<i>Currently in Shortage</i>
<a href="#">Gemifloxacin Mesylate (Factive) Tablets</a>	<i>Currently in Shortage</i>
<a href="#">Guanfacine Hydrochloride Tablets</a>	<i>Currently in Shortage</i>



<a href="#">Haloperidol Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Heparin Sodium and Sodium Chloride 0.9% Injection</a>	<b>Currently in Shortage</b>
<a href="#">Hydromorphone Hydrochloride Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Imipenem and Cilastatin for Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Isocarboxazid Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Ketamine Injection</a>	<b>Currently in Shortage</b>
<a href="#">Ketoprofen Capsules</a>	<b>Currently in Shortage</b>
<a href="#">Ketorolac Tromethamine Injection</a>	<b>Currently in Shortage</b>
<a href="#">L-Cysteine Hydrochloride Injection</a>	<b>Currently in Shortage</b>
<a href="#">Labetalol Hydrochloride Injection</a>	<b>Currently in Shortage</b>
<a href="#">Letermovir (Prevymis) Injection</a>	<b>Currently in Shortage</b>
<a href="#">Leucovorin Calcium Lyophilized Powder for Injection</a>	<b>Currently in Shortage</b>
<a href="#">Leuprolide Acetate Injection</a>	<b>Currently in Shortage</b>
<a href="#">Lidocaine Hydrochloride (Xylocaine) and Dextrose Injection Solution-Premix Bags</a>	<b>Currently in Shortage</b>
<a href="#">Lidocaine Hydrochloride (Xylocaine) Injection</a>	<b>Currently in Shortage</b>
<a href="#">Lidocaine Hydrochloride (Xylocaine) Injection with Epinephrine</a>	<b>Currently in Shortage</b>
<a href="#">Liotrix (Thyrolar) Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Lorazepam Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Magnesium Sulfate Injection</a>	<b>Currently in Shortage</b>
<a href="#">Methadone Hydrochloride Injection</a>	<b>Currently in Shortage</b>
<a href="#">Methocarbamol Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Methotrexate Sodium Injection</a>	<b>Currently in Shortage</b>
<a href="#">Methyldopa Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Methylphenidate Hydrochloride (QUILLICHEW ER) Extended-Release Chewable Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Methylphenidate Hydrochloride (QUILLIVANT XR) for Extended-Release Oral Suspension</a>	<b>Currently in Shortage</b>
<a href="#">Metoclopramide Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Metronidazole Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Molindone Hydrochloride Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Morphine Sulfate Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Multi-Vitamin Infusion (Adult and Pediatric)</a>	<b>Currently in Shortage</b>
<a href="#">Mupirocin Calcium Nasal Ointment</a>	<b>Currently in Shortage</b>
<a href="#">Nelarabine (Arranon) Injection</a>	<b>Currently in Shortage</b>
<a href="#">Ondansetron Hydrochloride Injection</a>	<b>Currently in Shortage</b>
<a href="#">Penicillamine (Depen) Titratable Tablets</a>	<b>Currently in Shortage</b>
<a href="#">Penicillin G Procaine Injection</a>	<b>Currently in Shortage</b>
<a href="#">Peritoneal Dialysis Solutions</a>	<b>Currently in Shortage</b>
<a href="#">Phenytoin Sodium Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Phosphate Injection Products</a>	<b>Currently in Shortage</b>
<a href="#">Piperacillin and Tazobactam (Zosyn) Injection</a>	<b>Currently in Shortage</b>
<a href="#">Potassium Chloride Injection</a>	<b>Currently in Shortage</b>
<a href="#">Potassium Phosphate Injection</a>	<b>Currently in Shortage</b>
<a href="#">Procainamide Hydrochloride Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Progesterone Injection, USP</a>	<b>Currently in Shortage</b>
<a href="#">Promethazine (Phenergan) Injection</a>	<b>Currently in Shortage</b>
<a href="#">Ranitidine Injection, USP</a>	<b>Currently in Shortage</b>

